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Editorial

Getting Your Work Published: Personal Reflections

Time Restricted Feeding: Implications to Healthy Well-Being

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Abstract:

Circadian rhythmicity optimizes the health and physiology by coordinating temporally the cellular functions, tissue functions, and behavior. These endogenously generated rhythms gets dampen with age and therefore compromise the temporal coordination. The pattern of fasting and feeding sets an external cue that profoundly influences the robustness of daily circadian rhythms. Irregular eating patterns can change the temporal coordination of physiology and metabolism leading to chronic diseases. Robust sustaining of fasting and feeding cycle, without altering nutrition quality, can reverse or prevent the chronic diseases as already depicted in an animal model. However, in humans, studies have shown that erratic pattern of eating can elevate the risk of diseases, whereas sustained fasting and feeding cycle, or prolonged overnight fasting, is correlated with protection from different cancers. Therefore, by just optimizing the external cues timing well defined eating patterns, can thus sustain a robust circadian clock, which may result in preventing many diseases and can improve the prognosis. Time-restricted feeding (TRF) is a form of intermittent fasting, comprising a longer daily fasting period. Preliminary studies report that TRF improves cardiometabolic diseases, diabetes and cancer in rodents and humans.

KEYWORDS: circadian rhythm, lifespan, time-restricted feeding, diseases

"For everything there is a season, and time for every matter under heaven:
a time to be born, and a time to die;
a time to plant, and a time to pluck up what is planted;
a time to weep, and a time to laugh, God has made everything beautiful in its time"
Ecclesiastes 3:1

Nearly all living organisms present on Earth, ranging from archaea to mammals displays the circadian rhythms. Circadian (circa – approximately; dian – day) rhythms are approximately 24 hour oscillations that can be found at the molecular, physiological, and behavioral level in all living beings. (1) The circadian rhythms regulates the sleep and activity cycle and the associated rhythms in metabolic states emerging from a complex interplay of endogenous autonomous circadian oscillators, including daily exposure to light and darkness, and daily patterns of feeding and fasting. These daily behavioral rhythms easily oscillates or cues the functions of almost all organ systems: including metabolic organs, digestive system, immune system, reproductive system, endocrine systems, cardiovascular system, and several brain systems. The cells circadian oscillator in mammals is based on interlocked transcription-translation feedback loops. The circadian molecular clock regulates the cell's internal environment including redox state, NAD+ levels, Ca2+ levels and energy state (ATP/AMP ratio) (2). The invention of electric light, override the natural cycle of mechanism of diurnal rhythm by self-selecting a sleep-wake pattern that is according to the working schedule, which resulted to associated alterations in the fasting and feeding cycle, the biggest culprit in human health. Such a chronic disruption of circadian rhythms can therefore compromise the health and wellbeing through multiple discrete mechanisms. Reduced sleep thus disrupted the metabolic homeostasis by mechanisms that are yet to be fully understood with (3,4). Lights during the night time suppress sleep and promote extended wakefulness time, thus allowing the disturbed and injested behavior to continue late into the night. This extended eating period may contribute to elevated caloric intake that often correlates with modern human lifestyle. Therefore, eating at sub-optimal time of the 24 hours day can promote excessive energy storage, leading to obesity and metabolic syndrome. Quality of nutrition can also impact hunger, satiety, and hedonic drive for intake of food and thereby affecting the daily pattern of eating, leading to impact the robustness of circadian oscillators in various organs. Chronic disruption in circadian rhythm due to erratic lifestyle or shift work compromises health and wellbeing and results in the increase of several chronic diseases that are associated with aging (5,6). Conversely, recent research has shown that maintaining a defined daily feeding-fasting rhythm, as in time-restricted feeding (TRF), can prevent or attenuate several chronic diseases.

TRF is well defined as eating within a ≤10 hour period and fasting for at least 14 hours per day. TRF has a broad class of interventions that have alternate eating periods and extended fasting time. In animal models, TRF, has reported to improve cardiometabolic health, slow tumor growth, reduce cancer incidence, regenerate organs by increasing stem cell production, and increase lifespan (7,8). In humans, TRF related data is little but it suggest that it lowers the body weight, insulin levels, blood pressure, inflammation, and appetite, and by improving the insulin sensitivity and lipid profiles (9,10). These clinical features are driven by a reduction in insulin levels; improved insulin signaling; a reduction in oxidative stress; an increase in antioxidant defenses and autophagy; a reprogramming of aging-related pathways and hormones such as sirtuin 1 (SIRT1), brain-derived neurotrophic factor (BDNF), mechanistic target of rapamycin (mTOR), and insulin-like growth factor (IGF-1) and other mechanisms (11). Although TRF can also be included in the venture of Ramadan fasting, Several studies in rodents model reported that TRF has reduced the body weight, improved glycemic index, lowered the insulin levels, reduced the blood pressure, prevented hyperlipidemia, decreased hepatic fat, improved the inflammatory markers, slowed down the tumor growth, and increased the lifespan, even when food intake is matched to the control group. (12,13,14) Several studies on TRF have already been conducted in Humans, Interestingly, they resulted in weight loss and improvements in cardiometabolic events like insulin levels, insulin sensitivity, and blood pressure when participants ate early or in the middle of the day (15,16,17) but worsened cardio-metabolic health when they ate late in the day (18,19).

These endogenously generated circadian rhythm system may greatly explain these effects on health. The circadian system orchestrates, approximately 24-hour circadian period in a day, it therefore changes the normal rhythm in metabolism, physiology, and behavior of an individual. It produces these rhythms through coordinated transcriptional–translational feedback loops involving circadian genes such as *BMAL1, CLOCK, PER1/2,* and *CRY1/2,* which causes oscillations in downstream targets. For example, sensitivity in insulin and the thermic food effect exhibits a 24-hour rhythm that peaks in the morning (20). A large number of plasma lipids and age-related hormones such as cortisol, insulin, and growth hormone also vary across the 24-hour day. Metabolic and hormonal rhythms peak in the morning and are downregulated in the evening time, thus implicating morning time as optimal for food intake time (20). Therefore, eating in

sync with these rhythms may improve cardiometabolic health and overall health of an individual. In contrast, when eating in the circadian misalignment for example eating late in the day, worsens several cardiometabolic endpoints, particularly glucose tolerance and disturbs the stomach enzymes rhythmic pattern of digestion (21,22) Therefore, TRF interventions where food intake is limited to early in the day time may be particularly effective in improving cardiometabolic health and overall wellbeing.

TRF also improves several facets of health through both circadian and mechanisms related to fasting. It improves glycemic index by lowering 24-hour glucose levels, reducing glycemic excursions, and potentially by improving signaling of insulin. Importantly, these improvements in glycemic index may be driven not only by eating earlier in the day time but also by having a short meal time interval, suggesting that TRF interventions with longer inter-meal intervals may be less effective at improving glucose levels. TRF also alters the diurnal patterns in fasting cholesterol, ketones, cortisol, and diurnal clock genes; particularly, it modestly elevates ketone levels in the morning time and improves the amplitude of the cortisol rhythmicity. Furthermore, TRF also affects hormones and genes related to longevity and autophagy. These important findings demonstrate that TRF improves cardiometabolic health, alters diurnal rhythms, and may also have anti-aging effects.

Conflict of Interest: None declared

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Sleep Quality And Body Composition Indices Of Obese Female Adolescents Improved Using Indigenous *Ampe* Exercise Programme

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Abstract

Background: Participation in the *ampe* exercise programme has been shown to improve the anthropometric and physiological characteristics of children, but its effectiveness on sleep quality and body composition indices of obese female adolescents is yet to be determined. This study confirms that *ampe* exercise programme improves sleep quality and body composition indices in obese female adolescents.

Methods: The study adopted a pretest-posttest experimental design, with fifteen obese female adolescents recruited to participate in a 6-week *ampe* exercise programme. Before and after intervention, sleep quality, visceral fat, body mass index, and waist to hip ratio were assessed. A paired t-test and bivariate analysis were conducted between the sleep quality and body composition indices of the participants.

Results: Body weight (102.33±15.80 < 96.47±15.36, *P=0.000*), body mass index (33.55±2.56 < 31.61±2.55, *P=0.000*), visceral fat (10.23±3.03 <8.47± 2.20), (*P=0.003*), and waist to hip ratio (0.86±0.04 < 0.83±0.05, *P=0.000*) decreased significantly while sleep quality (*P=0.000)* improved significantly after *ampe* exercise programme. The relationship between sleep quality and body composition indices was not significant.

Conclusion: *Ampe* exercise programme potently improved body weight, body mass index, visceral fat, waist to hip ratio, and sleep quality in obese female adolescents. It is an effective and inexpensive therapeutic exercise programme suggested for individuals with non-communicable diseases and mental health. Further, comprehensive clinical trial studies on cardiovascular disease patients will ascertain the clinical efficacy of *ampe* exercise programme.

Key words: Sleep quality, Sleep latency, Sleep duration, Visceral fat, Waist-to-hip ratio.

INTRODUCTION

Obesity, sleep quality, and physical activity are interrelated factors that contribute significantly to overall health and wellbeing. Obesity is frequently influenced by genetic predisposition, dietary choices, a sedentary lifestyle, and a lack of physical activity. Multiple physiological and psychological processes require enough restorative sleep [(1)]. However, poor sleep quality can have negative effects on several aspects of health, such as metabolic function, appetite regulation, and energy balance [(2)]. Participating in regular physical exercise is essential for achieving and sustaining a healthy weight, increasing one's mood, lowering the chance of acquiring chronic illnesses, and promoting cardiovascular health [(3,4)].

Inadequate sleep quality has been linked to an increased risk of obesity and weight gain[(2)]. Sleep deprivation disrupts hormonal regulation, resulting in changes in appetite-regulating hormones such as ghrelin and leptin, which can contribute to increased hunger and appetites, especially for high-calorie foods[(5)]. Obesity, notably abdominal obesity, can cause obstructive sleep apnea, sleep disorder characterised by repetitive partial or complete obstruction of the upper airway during sleep [(6)]. The importance of physical activity in mitigating the negative effects of obesity and poor sleep quality cannot be overstated. Regular exercise promotes weight loss and maintenance, enhances sleep quality, and lessens the severity of sleep disorders like obstructive sleep apnea[(7)]. Wiklund[(8)] opined that exercise regulates appetite, balances energy expenditure, and improves metabolic function, thereby contributing to improved overall health and a reduced risk of obesity.

Obesity has attained the worldwide epidemic proportions, and now roughly 25 percent of adults in industrialised countries are obese [(9)]. In Ghana, the national prevalence of obesity was estimated as 17.1% (95% CI = 14.7–19.5%) with higher prevalence of obesity (20.6% vs 8.0%) estimated for urban than rural dwellers [(10)]. Prevalence of obesity (21.9% vs 6.0%) were also significantly higher in women than men [(10)]. At the regional level, about 43.4%, 36.9%, 32.4% and 55.2% of residents in Ashanti, Central, Northern and Greater Accra region, respectively were overweight or obese [(10)]. Studies by Mohammed and Vuvor [(11)], (2012), and Oduwole et al., [(12)] indicate the prevalence of obesity in Ghana among adolescents is as high as 10.9%.

Physical inactivity prevalence for Ghanaian adolescents aged 11–17 years was 87.9%, as seen in the 2014 global status report on NCDs [(13)]. With the onset of the COVID-19 pandemic, physical activity levels continue in the downward trend globally, with reports showing low adherence to the WHO physical activity guidelines. Stay-at-home programmes during COVID-19 have been implicated in accounting for the downward trend and changes in physical activity patterns (e.g., decreased physical activity and increased sedentary behaviour), despite being vital to stopping the disease's spread [(14)]. According to Hall et al., [(15)], sedentary time may have replaced transportation-related and occupational physical activity during the pandemic due to stay-at-home initiatives and unemployment, as well as a disruption of people's daily routines and the widespread closure of exercise facilities. Emerging self-reported [(16-18)] and device-measured data [(19-20)] suggest that physical activity may have indeed decreased because of the stay-at-home orders among healthy-weight, overweight, and obese individuals, even in developing countries such as Ghana with a high physical inactivity rate.

Encouraging and experimenting with a variety of physical activities to accommodate various interests and fitness levels should be one of the multidimensional and multifaceted approaches required to address the endemic challenges posed by a high physical inactivity rate in developing nations such as Ghana. Based on the poor economic status of the average

Ghanaian, experimenting with ampe, a cheaper, friendly, and motivating indigenous physical activity, might be helpful in reducing the burden of obesity and increasing sleep quality. Ampe is a traditional Ghanaian leisure time activity that is performed by two or more individuals (teams) recognised as Ohyiwa and Opare [21]. Although the only previous study [21] on the efficacy of *ampe* exercise programme (AEP) reported that participation in the AEP showed improvement in the body composition, blood pressure and heart rate characteristics of youngsters, AEP effectiveness on sleep quality and body composition indices in obese female adolescents is yet to be determined. This study will hence be the first report to establish and confirm that AEP improves sleep quality and body composition indices in obese female adolescents.

Material and Methods

Research Design

The effect of *AEP* on the sleep quality and body composition of fifteen obese female adolescents was determined by using a pretest-posttest experimental study design. The participants were relatively healthy, without any significant medical conditions or diseases, had normal blood pressure, falls within age range 18-65 years, had body mass index (BMI) of 30 or higher, and had the ability to participate in the AEP.

Experimental procedure

Individuals who initially showed interest were screened to indicate whether they were eligible suing the inclusion and exclusion criteria. Individuals who were female between the ages of 18 to 25 years, having a BMI of 25 and above, being apparently healthy, have not been diagnosed of any medical condition, being physically inactive, i.e. engaging in ≥ 3 sessions of planned physical activity or exercise per week, and Answer "NO" to all the questions of the Physical Activity Readiness Questionnaire plus (PAR-Q+) and have signed the informed consent form were included in the study. However, obese women who either less than 18 or more than 25years, pregnant or lactating, on any dietary restrictions or chronic medications with the aim to lose weight, or undesirable alcohol consumption (>2 drinks per day) and smoking (> 5 cigarettes per day), living with any form disability or musculoskeletal conditions that can limit or prohibit safe participation exercise participation were also excluded. In addition, volunteers who were living with any reported acute illness, chronic disease or any other medical problems such as of CVD, renal, hepatic and endocrine disorders, as well as intestinal and gastrointestinal surgery during the health screening session that did not necessarily exclude them from physical activity by the PAR-Q+ or have been diagnosed with any of the metabolic disorders (such as hypo- or hyperthyroidism) were excluded.

After meeting the inclusion criteria, the experimental procedure and objectives of the study were explained to the participants. They were given the ability to ask questions and form their own decisions as to whether they want to join the study or not. Following this, those who formed the decision to join the study were given the informed consent to read and sign. On their second visit to the study site, their baseline body composition parameters such as visceral fat, body mass index and waist to hip ratio were measured while quality of sleep was assessed. Participants then underwent a 6-week ampe exercise program after which the baseline data was repeated. The 'ampe' exercise programme took place between the hours of 16h00 and 18h00 GMT every day at the KNUST Exercise Physiology laboratory.

The 'ampe' exercise programme

AEP was administered to the participants for a duration of forty minutes per session, three times in a week for six consecutive weeks. The

AEP took place during the second week of the study period through to the 7 weeks. To control other confounding effects and the metabolic state, the participants were standardized during all the exercise sessions. Participants were not required to eat for at least two hours before swimming sessions; must not take caffeinated drinks and alcohol at least 12 hours before session; and not do vigorous activities (rating of perceived exertion more than (>) 12 on the Borg scale) or any unusual exercise at least 24 hours before each session and testing. Each section of the exercise program began with a warm-up and ended with a cool down. The 'ampe' exercise sessions was conducted in the evening between 16h00 and 18h00 each day of the session. Participants were strictly and closely monitored and made sure no one get hurt. All exercise sessions took place under the guidance and supervision of the researchers.

Measurements

Body composition

Standardised procedures were used to measure height and weight[22]. Using a single, previously standardised portable weighing scale, weight was measured without shoes to the nearest 0.1 kg. With the use of a height rod mounted on a wall, height was measured without shoes and recorded to the nearest 0.1 cm. Total body fat, visceral fat, muscle mass, and waist-hip ratio were measured using the Omron Body Composition Body Composition Monitor HBF-375. The body mass index (BMI) of each of the individual was calculated as weight in kilograms divided by height in metres squared. The BMI classes adopted are the same as those used by the International Obesity Task Force for the international overweight and obesity [23].

Sleep Quality

Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI) developed by Buysse et al., [24]. Subjective sleep quality index, sleep latency, duration of sleep, habitual sleep efficiency, sleep disturbances, usage of sleep medicine, and daytime dysfunction are the seven categories along which the PSQI, a 24-items scale, assesses sleep disorders. Total score is established by adding the scores from these seven categories. Responses were anlysed based on most days (and nights) of the previous month. This scale was modified as question 10 (A-E) of the PSQI was excluded because no roommates/partner of the adolescents was involved in the assessment.

Data Analysis

Microsoft Excel and Statistical Package for Social Sciences version 26.1 were used for data entry and analysis. Descriptive statistics were used to examine anthropometric characteristics and sleep quality. Bivariate analysis (paired t-test) of the Pearson correlation was used to test correlation between anthropometric variables, sleep quality and demographics of respondents. Due small sample size of the participants, tests of normality was conducted (table 1) which ascertained that the data was normally distributed with most of the *P values* greater than 0.05.

Table 1: Tests of Normality

Variables df = 15	Kolmogorov-Smirnov[a]		Shapiro-Wilk	
	Pre (Pvalue)	Post (Pvalue)	Pre (Pvalue)	Post (Pvalue)
BMI	-0.176 (0.200*)	0.180(0.200*)	0.928 (.254)	0.960(.693)
Visceral Fat	0.135 (0.256*)	0.224 (0.142*)	0.957(0.914)	0.632 (0.157)
WHR	0.160(0.200*)	0.142(0.200*)	0.894(.078)	0.966(.796)
Subjective Sleep Quality	0.145 (0.036)	0.105 (0.012)	0.603(0.072)	0.350(0.000)
Sleep Latency	0.114(0.200*)	0.123(0.200*)	0.868 (0.000)	0.514(0.000)
Sleep Duration Score	0.119 (0.002)	0.174 (0.131*)	0.758 (0.000)	0.763 (0.000)
Habitual Sleep Efficiency	0.140(0.200*)	0.198 (0.200*)	0.801(0.000)	0.561(0.002)
Sleep Disturbances	0.067(0.200*)	0.199 (0.200*)	0.497(0.007)	0.790 (0.014)
Use of Sleep Medication	0.183 (0.102)	0.161 (0.144*)	0.499(0.012)	0.694 (0.072)
Daytime Dysfunction	0.066 (0.200*)	0.163 (0.200*)	0.643(0.006)	0.763(0.511)

*. This is a lower bound of the true significance. a. Lilliefors Significance Correction.

Ethical Consideration

Ethical approval was sought from the research ethics committee at Kwame Nkrumah University of Science and Technology. Participants were notified that participation is voluntary and that they have the prerogative to withdraw their participation during the study without having to provide reasons. Participants were made to sign the informed consent form before they partake in the study.

Results

The research had fifteen participants ranging in age from 18 to 25, with a mean age of 21.80±2.24 years and height of 174±11.48 cm. Body weight considerably decreased from 102.33±15.80kg to 96.47±15.36 kg and BMI from 33.55±2.56 kg/m2 to 31.61±2.55 kg/m2. There was a decrease in visceral fat from 10.27±3.03 to 8.47±2.20, waist to hip ratio from 0.86±0.04 to 0.83±0.05, and sleep quality scale from 11.13±2.03 to 6.47±1.64 (Table 2).

Table 2: Paired t-test Results on Pre-Post analysis of age and body composition parameters

Variable	Pretest Mean ± SD	Posttest Mean ± SD	95% CI		Mean Diff.	P-Value
			Lower	Upper		
Weight (kg)	102.33(15.80)	96.47(15.36)	4.316	7.403	5.86	0.000*
Height (cm)	174.20(11.48)	174.40(11.51)	-0.429	0.029	-0.20	0.082
BMI (kg/m^2)	33.55(2.56)	31.61(2.55)	1.390	2.476	1.93	0.000*
Visceral fat	10.23(3.03)	8.47(2.20)	0.708	2.891	1.80	0.003*
Waist-Hip Ratio	0.86±0.04	0.83±0.05	0.015	0.042	0.03	0.000*

Body Mass Index-BMI; mean ± standard deviation; *P<0.05, significant difference.

Table 3 revealed that participants had a mean of 2.53±0.516 and 0.53±0.516 for pre and post-test respectively in Subjective Sleep Quality component. In Sleep Latency participants had a mean of 2.33±0.488 for the pre-test and 0.73±0.458 respectively. For the sleep duration score, participants had a mean of 2.73±0.458 for the pre-test and mean score of 0.27±0.458 for that of the post-test. For the Habitual Sleep Efficiency, participants had a mean score of 2.13±1.125 for the pre-test and 0.27±0.458 for that of the posttest. Participants had a mean score of 2.87±0.352 for the pre-test and 1.07±0.258 for the post of that of the Sleep Disturbances. Respectively, participants had a mean of 2.73±0.458 for the pre-test and 0.73±0.458 for that of the pro test for the Use of Sleep Medication. Participants had a mean of 2.80±0.414 for the pre-test and 0.87±0.352 for the pro test respectively for Daytime Dysfunction. For the Global PSQI Score, the participants had a mean of 18.13±1.995 for the pre-test and 4.47±1.125 for the post-test respectively. Significant values were recorded

for Sleep quality, sleep latency, sleep duration score, habitual sleep efficiency, sleep disturbances, use of medication, daytime dysfunction, and that of the Global PSQI score.

Table 3: Components of Sleep Quality

Components	Pre (Mean ± SD)	Post (Mean ± SD)	*t*	*P-value*
1: Subjective Sleep Quality	2.53±0.516	0.53±0.516	10.120	0.000
2: Sleep Latency	2.33±0.488	0.73±0.458	12.220	0.000
3: Sleep Duration Score	2.73±0.458	0.27±0.458	14.929	0.000
4: Habitual Sleep Efficiency	2.13±1.125	0.27±0.458	7.299	0.000
5: Sleep Disturbances	2.87±0.352	1.07±0.258	16.837	0.000
6: Use of Sleep Medication	2.73±0.458	0.73±0.458	09.110	0.000
7: Daytime Dysfunction	2.80±0.414	0.87±0.352	29.000	0.000
Global PSQI Score	18.13±1.995	4.47±1.125	29.000	0.000

A Pearson correlation was conducted to assess the correlation between the body composition parameters and sleep quality. Table 4 revealed that there was no significant relationship between the body compositional parameters and sleep quality. Body mass index and waist to hip ratio showed a positive correlation with sleep quality even though it was not significant while visceral fat had a negative relationship with sleep quality.

Table 4: Correlation between Body composition and Sleep Quality

Body composition Indices	Pittsburgh Sleep Quality Index	Pvalue
Body mass index	0.311	0.259
Waist-to-hip ratio	0.123	0.661
Visceral fat	-0.296	0.284

Pvalue < 0.05.

Discussion

The study established the effects of *AEP* on sleep quality and body composition indices. It also looked at the correlation between body composition and sleep quality. The six-week ampe programme had positive effects on all body compositions: body weight, BMI, visceral fat, and waist to hip ratio, except for height as evidenced by reduction in all post-tests means as compared to the pre-test means of almost all variables. This means that *ampe*, another physical activity/form of exercise can significantly improve body weight, BMI, visceral fat, and waist to hip ratio especially among obese people. The findings of this study are in conformity with Moses et al., [21], who reported that a 4-week 'ampe' exercise programme reduced Weight, BMI, Waist-to-hip ratio by a percentage change of 0.31, 0.58 and 0.31 respectively. The study findings also agree with the US Department of Health and Human Services [25], (2018) who found that physical activity can help reduce the risk of excessive weight gain and the incidence of obesity. Moreover, when compared with other forms of exercise, it was also like the findings of Adams et al., [26] who found out that jogging exercise programme reduced the amount of visceral fat in obese individuals significantly. According to Powell-Wiley, et al., [27], a high correlation exists between high adiposity and cardiovascular disease risk and as such reducing visceral body fat, waist circumference and body mass reduces, and individuals risks level.

Sleep quality assessment found that, Sleep challenges were improved after the ampe exposure. +Respondents had better sleep as compared to their initial sleep experiences. They slept early, had reduced sleep latency (taking less time to fall asleep), improved sleep efficiency (higher percentage of time in bed

sleeping) and improved sleep quality. This is consistent with findings by the U.S. Department of Health and Human Services [25] who found that exercise reduced sleep latency (taking less time to fall asleep), improved sleep efficiency (higher percentage of time in bed actually sleeping), improved sleep quality, and more deep sleep among obese persons [25]. All other sleep challenges such as waking up at the middle of the night or early morning, getting up to use the bathroom, inability to breathe comfortably, cough or snore, feeling of too cold or too hot, trouble staying awake were all significantly improved. The majority rated their overall sleep to be good. Good quality sleep has been found to help reduce obesity by decreasing energy intake by decreasing hunger. Sleep deprivation may alter the hormones that control hunger [28]. Spiegel et al., [29] found that young men who were deprived of sleep had higher levels of the appetite-stimulating hormone ghrelin and lower levels of the satiety-inducing hormone leptin, with a corresponding increase in hunger and appetite-especially for foods rich in fat and carbohydrates.

Results from this study showed no significant relationships between obesity and sleep quality ($p > 0.259$). Contrary to this study's findings, studies by Mahfouz et al., [30], Erlacher et al., [31] and Wang et al., [32] found significant associations between sleep quality and obesity ($p < .001$). The difference in findings could be due to the use of different classifications on the PSQI which can give different relationships between BMI and sleep quality, which suggests that different classifications of PSQI may influence the study of sleep quality and should be chosen carefully in studies. However, the sleep quality reported in this study is similar to the work of Wang et al., [32], who reported the sleep quality among university adolescents to be 4.91±2.67. Even though this study found no relationship between obesity and sleep quality, it is important to understand that sleep deprivation due to self-induction, insomnia, untreated sleep apnea, or other sleep disorders may lead to metabolic dysregulation [33-34]. Poor sleep is associated with increased oxidative stress, glucose (blood sugar) intolerance (a precursor to diabetes), and insulin resistance [35]. Extra time spent awake may increase the opportunities to eat, and sleeping less may disrupt circadian rhythms, leading to weight gain [35-36].

Conclusions

AEP potently improves quality of sleep, body weight, body mass index, visceral fat, and waist to hip ratio quality in obese female adolescents. *AEP* is an effective and inexpensive therapeutic exercise programme suggested for individuals with non-communicable diseases and mental health. Further comprehensive clinical trial studies on cardiovascular disease patients will ascertain the clinical efficacy of *AEP*. Efficacy of *AEP* on biochemical and cardiovascular risks and other confounding factors such as diet and energy expenditure will also present viable findings.

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Assessment Of Healthcare Workers' Knowledge About Vaccines In Al-Najaf Primary Health Care Centers

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Abstract

Background: Immunization performed an important role in enhancing global health through decreased transmission of infectious diseases. Numerous aspects within healthcare facilities including supervision, cold-chain management, immunization session procedure, and reporting, must be thoroughly examined to ensure the effective delivery of immunization service. **The study aims to** evaluate the knowledge of healthcare workers working in the immunization unit in randomly selected primary healthcare centers at Najaf Province. For s**ubjects and method**, a cross-sectional research descriptive study took place at 26 healthcare facilities at six districts of Najaf, by using simple random sampling. The study involved a total of 143 healthcare personnel, including 122 healthcare workers working in the immunization units and 21 doctors. A questionnaire was used to evaluate the vaccine knowledge of healthcare workers. Data collecting began on December 2nd, 2022, and ended on March 2nd, 2023. The statistical program Statistical Package for Social Sciences/version 26 was used to examine and achieve the desired findings. Analytic statistics of Chi-square test (X2) was used to establish the statistically significant relationship between variables. **Results:** The study's findings revealed that healthcare workers have moderate degrees of overall vaccine knowledge (mean of score =2.23). Furthermore, a statistically significant link was discovered between the place of residence of healthcare workers and their knowledge (P=0.007), indicating that those live-in urban regions had greater knowledge levels than those living in rural areas. **Conclusion:** Healthcare workers possess good knowledge regarding vaccine types, doses, and schedules, moderate knowledge about contraindications and causes of postponement, and their knowledge was substantially associated with their place of residence.

Keywords: Primary health care, Immunization, Al-Najaf, Governorate, Knowledge.

INTRODUCTION

World Health Organization (WHO) defined immunization as a key health service that maintains and protects the health and well-being of populations, and so becomes critical for the effective functioning of governments and economies. Immunization activities should be maintained to ensure optimum continuity during periods of major disruption in the supply of services or consumption(1). It is a method for eradicating and controlling infectious diseases that threaten life, affecting an estimated two to three million children deaths to be avoided every year. Routine vaccination is cost-effective and the most

important public health measure for children(2).

In Iraq, the "Expanded Program on Immunization" was founded in 1985 and has been providing vaccination services for its target groups since that time. Measures of health status have been increasing for two decades, particularly in terms of controlling Vaccine Preventable illnesses, and this represents the high standards of the EPI program's successes(3).

Vaccinations have significantly enhanced world health by limiting the transmission of infectious diseases. Worldwide health organizations such as the World Health Organization (WHO), place a high value on developing and implementing effective immunization programs(4,5).

Despite a large drop in vaccine-preventable diseases in the country, there is a huge gap in vaccination rates and an impressive percentage related to the children who are not vaccinated below one year of age in Iraq, raising the danger of transmission and maintenance of infectious illnesses(6).

Despite evidence indicating that vaccination is among the most successful strategies for avoiding mortality and morbidity from diseases that can be prevented by vaccines throughout the world, vaccination percentages in several countries continue to be low due to the lack of complete knowledge, incorrect beliefs, concerns about side effects, along with vaccine hesitancy among the general public(7).

Vaccinations are normally safe, although they can carry certain risks, and negative reactions to immunization can occur on a few occasions. The public's trust in the safety of vaccinations is seen as vital to the success and efficacy of any immunization programs(8) .

Vaccination processes require health care providers to obtain and maintain the greatest level of competency. Yet, due to a shortage of resources and the constant demand on professionals' time, this procedure is becoming increasingly complex. Knowledge is essential for maintaining complete vaccination programs and improving best practices in everyday work, and the aim is to use this information to enhance immunization session procedures and build vaccinators' skills(9).

Aim of study

The present study aims to assess health workers' knowledge about vaccines in primary healthcare centres (PHCCs) and to determine the association of this knowledge with sociodemographic characteristics.

Materials and Methods

A descriptive, cross-sectional study was carried out at a simple sample of 26 Primary Health Centers selected at random in Najaf Province. Najaf has 52 primary healthcare centers spread across six primary healthcare sectors. The 26 primary healthcare centers (52 % of the total), selected from all sectors at random by using a simple sampling procedure, include: Al-Abbasia, Al-Atebbaa, Al-Jameaa, Al-Naser, Al-Moalemin, Al-Qudus, Misan, Kendah, Al-Qadesiyah, Khula Zowin, Al-Emam Alhasan, Al-mushkhab, Al-noaman, Al-Marasheda, Al-Radhawiyah, Ali Al-Ramahy, Alfaw, Said Al-shohadaa, Al-Emam Al-Jawad, Al-Wafaa, Al-Jamiyah, Mahdy Al-Attar, Al-mutanaby, Hussain Naji, Al-huriyah and Al-Manatherah.

Period of the study

The data collection began on December 2nd , 2022, and to March 2nd, 2023. For each center, 3 days were provided for data collection, which took place on average 5 days per week.

Data collection technique

The data were collected by a **Convenience Sampli**ng Method using a questionnaire that included information from the guideline of Expanded Program Immunization of "World Health Organization" and "The Ministry of Health in Iraq", as well as the advice and

approval from experts, to evaluate the knowledge of health workers about vaccines. The questionnaire consists of the following information:

1- Healthcare worker (HCW) demographic information.
2- Checklist for the knowledge of healthcare workers (HCW) which includes four domains:

•Type of vaccines.

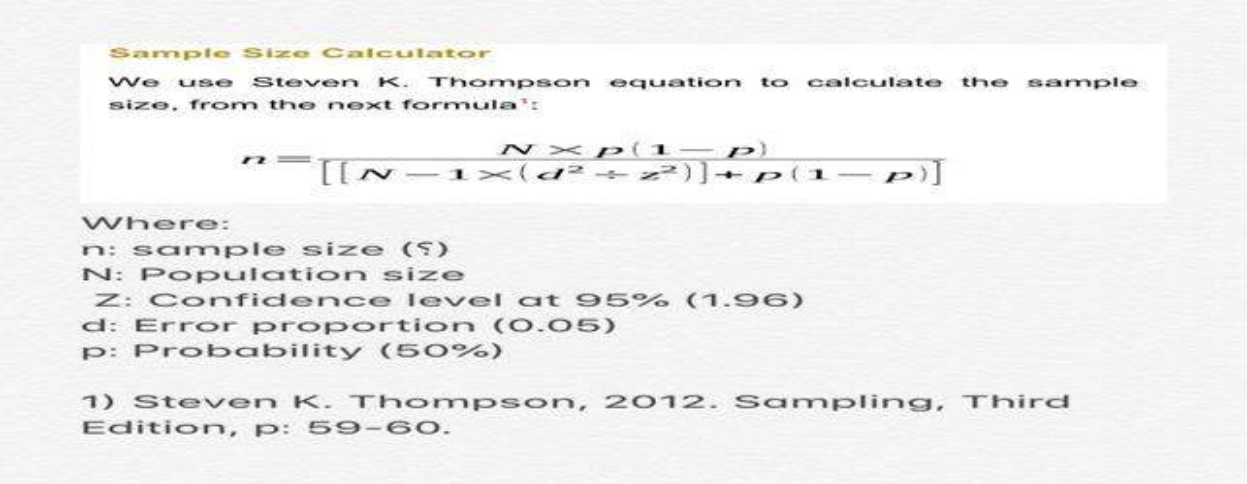
•The number of doses recommended for routine vaccines in the national schedule and the interval between doses.

•General rules for dealing with vaccination dates for children who are late for vaccination.

•Reasons for postponement and contraindication of vaccination

Population of the Study

The population includes all health workers from both genders who work in immunization units, as well as primary healthcare physicians. The sample size for healthcare workers was (143) persons, including (122) vaccinators and (21) doctors. The sample size was selected Depending on the attached equation to choose the appropriate sample size.


Sample Size Calculator

We use Steven K. Thompson equation to calculate the sample size, from the next formula[1]:

$$n = \frac{N \times p(1-p)}{[[N-1 \times (d^2 \div z^2)] + p(1-p)]}$$

Where:
n: sample size (؟)
N: Population size
Z: Confidence level at 95% (1.96)
d: Error proportion (0.05)
p: Probability (50%)

1) Steven K. Thompson, 2012. Sampling, Third Edition, p: 59-60.

Stephen Thompson equation (10).

Inclusion Criteria

Firstly, at the time of research, the sample includes all the healthcare workers working in the immunization units and the primary healthcare doctors who work in the healthcare centers. Secondly, both genders and all age ranges are represented.

Exclusion Criteria

The staff who refused to be interviewed and all healthcare workers who did not have an administrative order to work in the immunization units were excluded.

Statistical Analysis

The SPSS-26 was employed in data analysis, the data were presented in simple measures of percentage, frequency, standard deviation, and mean, and analytic statistics of Chi-square Test (X2) was used to establish the statistically significant relationship between variables, with findings regarded statistically significant when

a p-value was (<0.05). The differences between observations were judged significant at p≤0.05.

Ethical considerations

The research proposal was submitted to the An-Najaf Al-Ashraf Health Department, Iraq, before beginning data collecting, to acquire the approval. A cover letter with an information sheet outlining the aims of the study and the time necessary to complete the questionnaire was given to all primary healthcare sectors in Najaf Province with an attached consent.

Results

1- Sociodemographic characteristics of healthcare workers

Table 1 presents the sociodemographic characteristics of the studied group, indicating that the majority of workers were between the ages of 20 and 30 years, accounting for 67.8%. In terms of residency, a significant proportion of respondents (73.4%) lived in urban areas. Furthermore, nearly half of the participants (51.7%) held a diploma degree. Among the healthcare workers in the immunization unit of Najaf Province, females constituted 64.3%, whereas males accounted for 35.7%. Regarding experience in the field of vaccination, most healthcare workers (37.8%) had served for 1 to 12 months. Lower percentages were observed for other time periods, including 23.1% for both 13 to 36 months and 61 months and above, and 16.1% for 37 to 60 months. A significant majority of health workers (76%) had participated in the training program on immunization standards. More than one third (38%) of healthcare workers were medical assistants.

Table (1): Sociodemographic characteristics of healthcare workers

Variable (N=143)		F	%
Age in years	20-30	97	67.8
	31-40	18	12.6
	41-50	21	14.7
	51 and above	7	4.9
Gender	Female	92	64.3
	Male	51	35.7
Resident	Urban	105	73.4
	Rural	38	26.6
Level of educational	Diploma	74	51.7
	High school	32	22.4
	PhD	2	1.4
	B.Sc.	28	19.6
	High Diploma	7	4.9
Specialty	Technical Nurse	20	14.0
	Skilled Nurse	31	21.7
	Medical Assistant	55	38.5
	Doctor	21	14.7
	Medical Technologist	16	11.2

Training on immunization	Yes	109	76.2
	No	34	23.8
Experience (months)	1-12 M	54	37.8
	13-36 M	33	23.1
	37-60 M	23	16.1
	61M and above	33	23.1

Evaluation of Knowledge Regarding the Type of vaccines

Table 2 shows the evaluation of healthcare workers in health centers about the types of vaccines, from which the heights average was awarded to question (4) (Measles vaccine is a live-attenuated viral vaccine.) with a mean of 2.50 and std. deviation 0.77, followed by question (5) (Diphtheria and tetanus vaccines are bacterial toxoid vaccines) with a mean of 2.49 and std. deviation 0.80, reading percentages of 67.1% and 67.8% respectively. While the lowest average was awarded to the question (7) (HepB-containing vaccine is a Recombinant DNA or plasmaderived.) with a mean of 2.13 and std. deviation 0.82 , followed by question (10) (Pneumococcal vaccine is a "Conjugate" ("pneumococcal polysaccharide bound to a carrier protein"; does not contain any live bacteria) with a mean of 2.15 and std. deviation 0.80, reading percentages of 40.6% and 39.9% respectively.

A weighted average of the knowledge regarding types of vaccine was 2.36 and std. deviation 0.40 which indicates the trend of (Assessment of Knowledge about Type of vaccines) is high as a general trend according to 3-point Likert scale since 2.36 lie in the interval { 2.24-3.00}. it has been found that most of healthcare workers have high knowledge about the type of vaccines.

Table (2): Types of vaccine

Q	(N=143)	Rating						Mean of Score	Standard Deviation	Assessment
		Disagree		Not sure		Agree				
		F	%	F	%	F	%			
1	There are different types of vaccines, including live and killed ones. There are also bacterial and viral vaccines, and there are also the live attenuated viral and bacterial vaccines	31	21.7	13	9.1	99	69.2	**2.48**	**0.829**	Agree
2	live attenuated vaccines include oral polio vaccine (viral)	29	20.3	16	11.2	98	68.5	**2.48**	**0.812**	Agree
3	injectable polio is killed vaccine	27	18.9	26	18.2	90	62.9	**2.44**	**0.793**	Agree
4	The vaccine for measles is a live attenuated vaccine (viral)	24	16.8	23	16.1	96	67.1	**2.50**	**0.768**	Agree
5	Vaccines for Tetanus and diphtheria are bacterial vaccines (toxoid).	27	18.9	19	13.3	97	67.8	**2.49**	**0.795**	Agree
6	combination vaccines include pentavalent vaccine.	29	20.3	41	28.7	73	51.0	**2.31**	**0.789**	Agree

7	HepB vaccines are manufactured using recombinant DNA or plasma.	40	28.0	45	31.5	58	40.6	**2.13**	**0.821**	Not sure
8	BCG vaccine is a bacterial vaccine that is alive.	34	23.8	19	13.3	90	62.9	**2.39**	**0.848**	Agree
9	The vaccine for rotavirus is a live weakened vaccine. (viral vaccine)	23	16.1	31	21.7	89	62.2	**2.46**	**0.758**	Agree
10	the vaccine for pneumococcal is conjugate vaccines	36	25.2	50	35.0	57	39.9	**2.15**	**0.796**	Not sure
11	The Mumps vaccine is a viral vaccine that has been live attenuated	33	23.1	40	28.0	70	49.0	**2.26**	**0.811**	Agree
12	Rubella is a viral vaccine that has been live attenuated	34	23.8	21	14.7	88	61.5	**2.38**	**0.846**	Agree
13	The pertussis vaccination is acellular or cellular vaccine (bacterial vaccine)	39	27.3	40	28.0	64	44.8	**2.17**	**0.833**	Not sure
	Overall							**2.36**	**0.40**	**high**

*"3-Point Likert Scale { high range (2.24-3.00), moderate range (1.67-2.23), low range (1.00-1.66)}"

Evaluation of the Health Worker's Knowledge of Vaccine Doses in the Routine Schedule of Children's Vaccinations

Table 3 shows the knowledge about the number of doses recommended for routine vaccines in the national schedule and the interval between doses. Out of which the heights average was awarded to the question(8) (Measles vaccine is given in the routine schedule in a single dose at the age of nine months, and it is not given above the age of one year) with a mean of 2.75 and std. deviation 0.63, followed by question (9) (The MMR vaccine is given in the routine schedule in two doses, the first dose at the age of 12 months and the second at the age of 18 months, and it is not given at the age of less than a year), with a mean of 2.73 and std. deviation 0.65, reading percentages of 85.3 % and 84.6 % respectively. While the lowest average was awarded to the question (2) (The hepatitis B vaccine is given in four doses (the birth dose within 24 hours of childbirth and a dose at the age of two months, four months and six months with the pentavalent vaccine, at an interval of no less than four weeks) with a mean of 2.23 and std. deviation 0.94, reading a percentage of 58.0%. A weighted average of section 2 was 2.52 and std. deviation 0.45 which indicate the trend that (Assessment of Knowledge About the Number of Doses Recommended for Routine Vaccines in The National Schedule and The Interval Between Doses) is high as a general trend according to 3-point Likert scale since 2.52 lie in the interval { 2.24-3.00}.

Table (3): Knowledge of Vaccine Doses in the Routine Schedule of Children's Vaccinations

Q	(N=143)	Rating						Mean of Score	Standard Deviation	Assessment
		Disagree		Not sure		Agree				
		F	%	F	%	F	%			
1	BCG is administered within the 1st week of life, and not given after one	20	14.0	3	2.1	120	83.9	2.70	0.702	Agree

	year of the child's age									
2	The vaccine of hepatitis B is administered in four doses (24 hours after birth as well as at 2,4, and 6 months,(The minimum period between vaccines doses is 4 weeks.)	50	35.0	10	7.0	83	58.0	2.23	0.940	Not sure
3	oral polio vaccine (OPV vaccine) is administered in 6 doses (zero dose at the first week of life and 3 administrations at the ages of 2,4, and 6 months,(The minimum period between vaccines doses is 4 weeks), plus two booster doses given at the ages of 4-6 years and 18 months.	31	21.7	6	4.2	106	74.1	2.52	0.829	Agree
4	The vaccine of injectable polio is administered at 4 and 6 months of life (The minimum period between vaccines doses is 4 weeks)	28	19.6	7	4.9	108	75.5	2.56	0.802	Agree
5	pentavalent vaccine is administered at 2,4, and 6 months ,(The minimum period between vaccines doses is 4 weeks)	29	20.3	8	5.6	106	74.1	2.54	0.812	Agree
6	The pneumococcal vaccine is administered at 2,4, and 6 months ,(The minimum period between vaccines doses is 4 weeks)	30	21.0	26	18.2	87	60.8	2.40	0.815	Agree
7	Rotavirus vaccine is administered in 2 or 3 doses, according to the type of vaccine administered.	39	27.3	13	9.1	91	63.6	2.36	0.884	Agree
8	The measles vaccine is administered in a single dose at age of 9 months	15	10.5	6	4.2	122	85.3	2.75	0.633	Agree
9	The MMR vaccination is provided in two doses at ages of 12 months and 18 months.	16	11.2	6	4.2	121	84.6	2.73	0.649	Agree
10	trivalent vaccine administered at the ages of 4-6 years and 18 months.	34	23.8	17	11.9	92	64.3	2.41	0.850	Agree
	Overall							**2.52**	**0.45**	**high**

*"3-Point Likert Scale { high range (2.24-3.00), moderate range (1.67-2.23), low range (1.00-1.66)}"

Evaluation of Knowledge regarding Reasons for Postponement and Contraindication

Table 4 provides an overview of healthcare workers' knowledge regarding reasons for delaying vaccines and contraindication. The weighted average for this domain was 2.11, with a standard deviation of 0.39. These figures suggest that the assessment of knowledge concerning contraindications and reasons for postponing vaccines is moderate, according to the 3-point Likert scale, as 2.11 falls within the range of 1.67-2.23.

Table (4): Reason for Postponement and Contraindications of Vaccination

Q	(N=143)	Rating						Mean of Score	Standard Deviation	Assessment
		Disagree		Not sure		Agree				
		F	%	F	%	F	%			
1	Vascular shock or acute allergy caused by a previous injection of an exact vaccine.	22	15.4	14	9.8	107	74.8	2.59	0.743	Agree
2	Fever after the previous dosage is not considered a contraindication to vaccination.	68	47.6	9	6.3	66	46.2	1.99	0.971	Not sure
3	Contraindications include hypersensitivity to a specific component in the vaccine.	26	18.2	11	7.7	106	74.1	2.56	0.784	Agree
4	Otitis media with no fever is not considered a vaccine contraindications	87	60.8	16	11.2	40	28.0	1.67	0.886	Not sure
5	A family history of bad reactions to pertussis vaccine doses is not a contraindication to vaccination.	45	31.5	37	25.9	61	42.7	2.11	0.857	Not sure
6	Minor diseases, like upper respiratory infection and diarrhea, not prevent vaccination.	79	55.2	17	11.9	47	32.9	1.78	0.915	Not sure
7	A serious side effect of certain vaccines in the previous dose consider a contraindication to that vaccines	33	23.1	22	15.4	88	61.5	2.38	0.839	Agree
8	well-controlled epilepsy is not regarded as a contraindication to vaccination.	64	44.8	30	21.0	49	34.3	1.90	0.886	Not sure
9	If the child's temperature increases above 38.5 C , vaccinations will be delayed.	27	18.9	8	5.6	108	75.5	2.57	0.792	Agree
10	The immunization is postponed if a kid has a serious or neutral acute sickness.	21	14.7	18	12.6	104	72.7	2.58	0.736	Agree
11	Live attenuated vaccination is not provided in the case of immunodeficiency illnesses.	23	16.1	24	16.8	96	67.1	2.51	0.759	Agree
12	Asthma, allergies, or allergic symptoms, as well as Hey fever, are not regarded contraindications to vaccination.	73	51.0	27	18.9	43	30.1	1.79	0.879	Not sure
13	Premature newborns (babies born before 37 weeks of age) can receive the vaccine.	47	32.9	20	14.0	76	53.1	2.20	0.908	Not sure
14	Malnutrition is not a reason to avoid	70	49.0	27	18.9	46	32.2	1.83	0.888	Not sure

	a vaccine.									
15	seizures in family history are not a contraindication to receiving a vaccination.	53	37.1	36	25.2	54	37.8	2.01	0.868	Not sure
16	low-dose corticosteroids ,antibiotics, , or short-acting steroids are not considered contraindications to vaccination.	44	30.8	36	25.2	63	44.1	2.13	0.858	Not sure
17	Eczema, dermatitis, or a topical infection of the skin are not regarded as contraindications to vaccination.	89	62.2	14	9.8	40	28.0	1.66	0.889	Disagree
18	Chronic lung , heart, kidney, as well as liver problems are not considered contraindications to vaccination.	77	53.8	18	12.6	48	33.6	1.80	0.916	Not sure
19	Down syndrome or cerebral palsy , do not prevent vaccination.	73	51.0	28	19.6	42	29.4	1.78	0.873	Not sure
20	Jaundice shortly after birth is not considered a contraindication to immunization.	64	44.8	17	11.9	62	43.4	1.99	0.942	Not sure
21	Children with low birth weight are not regarded as contraindications to vaccination.	51	35.7	27	18.9	65	45.5	2.10	0.898	Not sure
22	In the case of using steroids for 14 days or getting blood or its derivatives, the immunization will be delayed for three months.	18	12.6	41	28.7	84	58.7	2.46	0.710	Agree
	Overall							**2.11**	**0.39**	**moderate**

*"3-Point Likert Scale { high range (2.24-3.00), moderate range (1.67-2.23), low range (1.00-1.66) }"

Relationship of Overall Knowledge Regarding Vaccination with Sociodemographic Characteristics.

Table 5 provides insights into the relationship between demographic variables and the levels of knowledge observed in the sample. Statistical analysis revealed no significant association with age (P=0.719), gender(P=0.257), and educational level (P=0.266). The variables examined also included specialization level, years of experience in the field of vaccination. According to the findings, there is no significant relationship between these occupational characteristics including (years of experience at the immunization unit and specialization level) and overall knowledge of healthcare workers. In terms of residency, the findings show that a higher percentage of healthcare workers from urban areas (27.3%) displayed good knowledge compared to those in rural areas (3.5%). This difference has been determined to be statistically significant (P-value equal to 0.007).

Table (5): Relationship of Sociodemographic Characteristics of Participants with Overall Knowledge on Vaccines

Variables		Rating						Chi square ($\chi 2$)	P. value	Sig
		F	Disagree (%)	F	Neutral (%)	F	Agree (%)			
Age (year)	30-20	1	0.7%	69	48.3%	27	18.9%	3.686	0.719	Non-Significant
	31-40	0	0.0%	11	7.7%	7	4.9%			
	41-50	0	0.0%	12	8.4%	9	6.3%			
	51 and above	0	0.0%	6	4.2%	1	0.7%			
Gender	Female	0	0.0%	66	46.2%	26	18.2%	2.719	0.257	Non-Significant
	Male	1	0.7%	32	22.4%	18	12.6%			
Resident	Urban	0	0.0%	66	46.2%	39	27.3%	**9.836a**	**0.007**	**Significant**
	Rural	1	0.7%	32	22.4%	5	3.5%			
Level of Educational	Diploma	1	0.7%	46	32.2%	27	18.9%	9.982	0.266	Non-Significant
	High school	0	0.0%	20	14.0%	12	8.4%			
	PhD	0	0.0%	1	0.7%	1	0.7%			
	B.Sc.	0	0.0%	24	16.8%	4	2.8%			
	High Diploma	0	0.0%	7	4.9%	0	0.0%			
Specialty	Technical Nurse	0	0.0%	12	8.4%	8	5.6%	9.371a	0.312	Non-Significant
	Skilled Nurse	0	0.0%	19	13.3%	12	4.8%			
	Medical Assistant	1	0.7%	35	24.5%	19	13.3%			
	Doctor	0	0.0%	19	13.3%	2	1.4%			
	Medical Technologist	0	0.0%	13	9.1%	3	2.1%			
Training on Immunization	Yes	1	0.7%	72	50.3%	36	25.2%	1482a	0.477	Non-Significant

	No	0	0.0%	26	18.2%	8	5.6%			
Experience (months)	1-12 M	0	0.0%	37	25.9%	17	11.9%	6.393[a]	0.381	Non-Significant
	13-36 M	0	0.0%	21	14.7%	12	8.4%			
	37-60 M	1	0.7%	17	11.9%	5	3.5%			
	61M and Above	0	0.0%	23	16.1%	10	7.0%			

Discussion

In this study, it has been observed that the majority of primary healthcare employees in Najaf were young and newly appointed. Additionally, most participants held a diploma degree. The study has also revealed that the majority of healthcare workers in the immunization units of Najaf were females (64.3%) while the males have accounted for 35.7%. This may be attributed to the fact that dealing with women, especially in Najaf, is simpler in the context of bringing their children to the health center, considering societal characteristics. Furthermore, a significant percentage (76%) of healthcare workers had participated in a training program on immunization standards. This can be attributed to ongoing training provided by the state's public health department. In terms of specialization, most healthcare workers were in the medical assistant specialty. Regarding knowledge about types of vaccines, the study has found that most healthcare workers had a high level of knowledge. This was due to several reasons, including Health workers undergo formal education and training in medical or nursing schools, which includes comprehensive coursework on vaccines and immunization, Health workers engage in continuous professional development activities, such as attending workshops, seminars, and conferences focused on vaccines and immunization, Primary health care centers typically have standardized protocols and guidelines for vaccine administration, Health centers often have quality assurance mechanisms in place, including regular supervision and monitoring.

The present findings are similar to a study conducted by Hashim et al. (2020) who found that the knowledge of health center workers about vaccines was good. The study, which was conducted in Iraq, involved 308 health center workers who were interviewed using a questionnaire. The results showed that the majority of the health center workers had good knowledge about vaccines, including their types, indications, and adverse effects (11). Regarding the knowledge about the number of doses recommended for routine vaccines in the national schedule and the interval between doses, healthcare workers have high knowledge about this subject. This may be due to Availability of the schedule of routine vaccinations hanging inside the room of the immunization unit and the abundance of training on it, in addition to the continuous practice of vaccination. This finding is consistent with previous studies that have also assessed the knowledge of healthcare workers about vaccines in different countries and settings. For instance, a study by Al Khaldi et al. (2019) found that healthcare workers in Saudi Arabia had good knowledge about vaccines, with over 90% of them being able to correctly identify the vaccines included in the national immunization program(12). However, when it came to knowledge about handling late vaccination dates for children, healthcare workers had a moderate level of knowledge. This finding is consistent with a study conducted in Ghana, which found that healthcare workers' knowledge about handling children who were late for vaccination was moderate [12]. Health care workers have a moderate level of knowledge regarding the reasons for postponement and contraindication of vaccination. This may be due to a lack of resources or time, as well as a lack of awareness of the importance of this topic as

well as Direct dependence on the doctor regarding this matter. This result is similar to a recent study by Al-Obaidi et al. (2020) which aimed to assess the knowledge of healthcare workers in Iraq about the side effects of vaccines. The study involved 300 healthcare workers from different healthcare settings across Iraq, who were surveyed using a structured questionnaire. The results showed that the overall knowledge of healthcare workers about the side effects of vaccines was moderate. While most of the healthcare workers had a good understanding of the benefits of vaccines, their knowledge about the side effects was only moderate(13). Another study by Abdulrazzaq et al. (2014) found that healthcare workers in Iraq had moderate knowledge about the immunization schedule and the side effects of vaccines(14). The general final assessment of overall knowledge of the healthcare workers was moderate. This suggest that the health care worker is not familiar with the comprehensive guide to the expanded program for immunization, or maybe due to weak training program. These findings are consistent with another study conducted by Metwali, F., et al.(2019) in El-Hossania City at Sharkia Governorate, it shows not adequate knowledge about vaccination; this result may be due to weakness in training program content (15). Higher percentage of healthcare workers from urban areas displayed good knowledge compared to those in rural areas, It is likely due to the majority of health workers in the health care centers in rural areas are residents of the same rural area and because of the remoteness of these centers and their presence in remote areas and the difficulty of their access to training centers that are always in the city center. The present findings are similar to a study conducted by Mohamed Zayed et al.,(2022) which included 150 healthcare worker in 16 primary healthcare centers in Egypt, for the assessment of the knowledge of healthcare workers. The study found a significant association between healthcare workers knowledge levels and Residents (16). Another study that disagrees with the results of the present study was conducted in primary healthcare centers of Nigeria by Adebimpe, et al.,(2021); it found those practicing in rural areas were found to have better knowledge than those in urban areas (17). Another study agreed with the recent findings about the number of years in the vaccination field was conducted in Benin City, Edo State, Nigeria by Uwaibi, N. E. (2018) for the evaluation of the implementation of routine childhood immunization services at the primary health care centers, the study found that there is no significant relationship between health care workers knowledge about immunization and years of experience in the field of immunization(18).

Conclusion

Healthcare workers possess good knowledge regarding vaccine types, doses, and schedules, moderate knowledge about contraindications and causes of postponement, possibly due to their lack of familiarity with the comprehensive guide to the expanded program of immunization. Additionally, the knowledge of healthcare workers was strongly related to their residences place.

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Pregnancy Rate In Non-Azoospermia With Normal Or Suboptimal Semen Parameter Versus Azoospermic Male Treated By IVF-ICSI Cycle

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Abstract

Background: Intracytoplasmic sperm injection (ICSI) opens the gate for many cases of male factor infertility to be the biological fathers of their sibling since 1992. Most of cases were non-obstructive azoospermia and different levels of oligoastheno-teratozoospermia. Nowadays many cases of reduced semen parameter or female factor infertility are treated by IVF-ICSI Cycle for better pregnancy rate, biochemical and clinical, and live birth rate.

Aim of the study: The study aims to compare biochemical, clinical pregnancy rate and outcome of pregnancies in the group with ejaculated sperm with normal or suboptimal semen parameter and group with non-obstructive azoospermia in whom sperm retrieved by TESE, using ICSI.

Method: A retrospective cohort study was conducted between January, 2016 and February, 2023 in the fertility center of Al-Sader Medical City, a total of 372 couple, 90 of the males gave semen sample by masturbation and 282 of the males were non-obstructive azoospermia and their sperms were retrieved by TESE; all are treated by ICSI, all of their female partner were under age of 37 year, the maternal medical condition and obstetric history were not included in this study. Simple random sampling was depended, SPSS version 26 was used to perform the statistical analysis processes.

Results: There was a highly significant difference in pregnancy rate by β.HCG between ejaculate group (43.3 %) and azoospermia (26.6 %) with p. value =0.003. A significant difference in clinical pregnancy rate by ultrasound between the ejaculate group (31.1%) and azoospermia (20.9%) with p. value =0.047. There was no statistically significant difference in live birth rate between ejaculate group as (24.4 %) and azoospermia as (17.4 %) with p.value=0.137.

Conclusion: Freshly ejaculated sperm with normal or suboptimal semen parameter gave a better biochemical and clinical pregnancy rate than obtained from NOA by TESE, while live birth rate was not largely different in both groups

Keywords: ICSI, TESE, Ejaculate, Non-obstructive azoospermia

INTRODUCTION

Most literature supports the fact that male factor infertility can be responsible for about half of cases of infertility among couples and can even reaches 70% of all cases of infertility [(1)]. It is estimated that 1 out of 100 healthy men is azoospermic, the sole treatment till now is the testicular sperm retrieval and ICSI [(2)]. According to the way that testis produce sperm, azoospermic men are divided into obstructive azoospermia (OA) and non-obstructive azoospermia (NOA); the second type is more common and can be responsible for more than 60% of cases[(3)]. Testicular sperm extraction (TESE) and ICSI nowadays regards as the gold standard for most of non-obstructive azoospermia management; and enable them to have their biological children, despite retrieval rate nearly half of cases[(4)]. The new technique for sperm retrieval which is microscopic TESE (m.TESE) is regarded as the most effective technique for high sperm retrieval rate and minimal postoperative complication[(5)]. However, clinical pregnancy by using testicular sperm recorded by many research paper, some researchers like (Bernardini *et al.*,) [(6)] and (Rodrigo *et al.*,) [(7)] found an increment in chromosomal aberration in sperm retrieved from NOA patients. So, concerns about the risk of congenital anomaly in children born after ICSI with testicular spermatozoa are pertinent. Up to date, the neonatal health of children born after ICSI using testicular spermatozoa from patients with NOA is not well documented. Sperm donation for many years was the only hope for azoospermic men to have children, but ethical, legal, religious and psychological issues had limited the use of sperm donation in many countries, nowadays it becomes more acceptable for couples specially in the western countries[(8)]. Some men with varying degrees of oligozoospermia, asthenozoospermia, and teratozoospermia, who cannot conceive naturally are best treated by ICSI, which, since its invention at 1992, makes revolutionized management in male factor infertility; it involves insertion of single morphologically normal live spermatozoon into oocyte by fine glass micropipette and the resulting embryos are transferred to the uterine cavity or cryopreserved [(9)] [(10)].

MATERIAL AND METHOD

The Study Design

This study is a retrospective cohort type which was held in the fertility center of Al-Sader Medical City between January, 2016 and February, 2023. It included a total number of three hundred seventy-two (372) couples with random sampling method; all reside at middle Euphrates region in Iraq. 90 male partners were non-azoospermia with normal or mild suboptimal semen parameter, isolated oligozoospermia, isolated asthenozoospermia or isolated terarozoospermia, who gave the semen sample by masturbation and 282 were azoospermia (non-obstructive type) whom diagnosed by urologist according to history, clinical examination, testicular size by ultrasound and hormonal levels (FSH, LH, testosterone and prolactin) in which the sperm retrieved from testis by TESE. A simple random sampling was depended in which each couple came to the center were assigned a unique number and “computer-generated lists used for random selection”. All the couples were residing at middle Euphrates region in Iraq. The range of age of all male partner was (21-58) year and the median of age of all male partner was 34 year irrespective to groups. The range of age of female partner was (16-38) year and the median age was 29 year. All the data were collected from patient's files and records. The maternal medical condition, obstetric history and type of stimulation protocol were not included in this study. All the results of biochemical pregnancy (by β.HCG), clinical pregnancy (by ultrasound) and live birth were taken. Biochemical pregnancy test (β-hCG) was performed 10-14 days after embryo

transfer. Clinical pregnancy was regarded by visualization of one or more gestational sacs by U\S during 4th to 5th week, the ectopic pregnancy also included, live birth was regarded as clinically viable newborn according to Zegers-Hochschild *et al.'s* [11] definitions.

Ethical approval

This study obtained the ethical approval from the internal ethical committee of the Urology Department/Faculty of Medicine, University of Kufa and the health directorate in Najaf Province.

Statistical Analysis

A statistical analysis was carried out by using SPSS version 26 (Inc. Chicago, IL, USA). Categorical variables were presented as frequencies and percentages. Chi square, Mann–Whitney and Pearson correlation were applied. A P-value < 0.05 is considered as significant and P-value< 0.01 is considered as highly significant.

RESULTS

The total number of the 372 couples were divided according to male partner, either ejaculate or azoospermia. The ejaculate group were 90 (24.2%) of the cases and the azoospermia group were 282 (75.8%). Median ± IQR for the age of ejaculate group was 34±10 years, while Median ± IQR for the age in the azoospermia group was 34± 8 years. Median ± IQR for the age of female partner in both groups was 29±8 years. Median ± IQR for retrieved oocyte in ejaculate group was 8.5 ± 8 oocytes, while Median ± IQR for retrieved oocyte in azoospermia group was 10 ± 6 oocytes. Median ± IQR for injected oocyte in ejaculate group was 7 ± 7 oocytes, while Median ± IQR for injected oocyte in azoospermia group was 8 ± 5 oocytes as shown in Table.1 There was a highly significant difference in the pregnancy rate by β.HCG between ejaculate group (43.3 %) and azoospermia (26.6 %) with P-value=0.003. A significant difference in clinical pregnancy rate by ultrasound between the ejaculate group (31.1 %) and azoospermia (20.9 %) with P-value=0.047. There was no statistically significant difference in live birth rate between ejaculate group (24.4 %) and azoospermia (17.4 %) with P-value=0.137 as shown in tab.2.

Table NO.1: A Comparison of variable characteristics between the two study groups.

	Ejaculate	Azoospermia
Number (Percentage)	90 (24.2%)	282 (75.8%)
Age (years) Median ± IQR for male partner	34 ± 10	34 ± 8
Age (years) Median ± IQR for female partner	29 ± 8	29 ± 8
Median ± IQR for retrieved oocyte	8.5 ± 8	10 ± 6
Median ± IQR for injected oocyte	7 ± 7	8 ± 5

Table NO.2: Comparison between the studied groups regarding biochemical pregnancy, clinical pregnancy and live birth rate.

	Ejaculate	Azoospermia	P. value
Pregnancy rate by β.HCG	43.3 %	26.6 %	**0.003 Group 1>group 2
Pregnancy rate by ultrasound	31.1 %	20.9 %	*0.047 Group 1>group 2
Live birth rate	24.4 %	17.4 %	0.137

P value< 0.05: significant* P value< 0.01: highly significant**

More details about the positive and negative pregnancy by β-HCG, clinical pregnancy and live birth are summarized in figures 2,3 and 4 respectively.

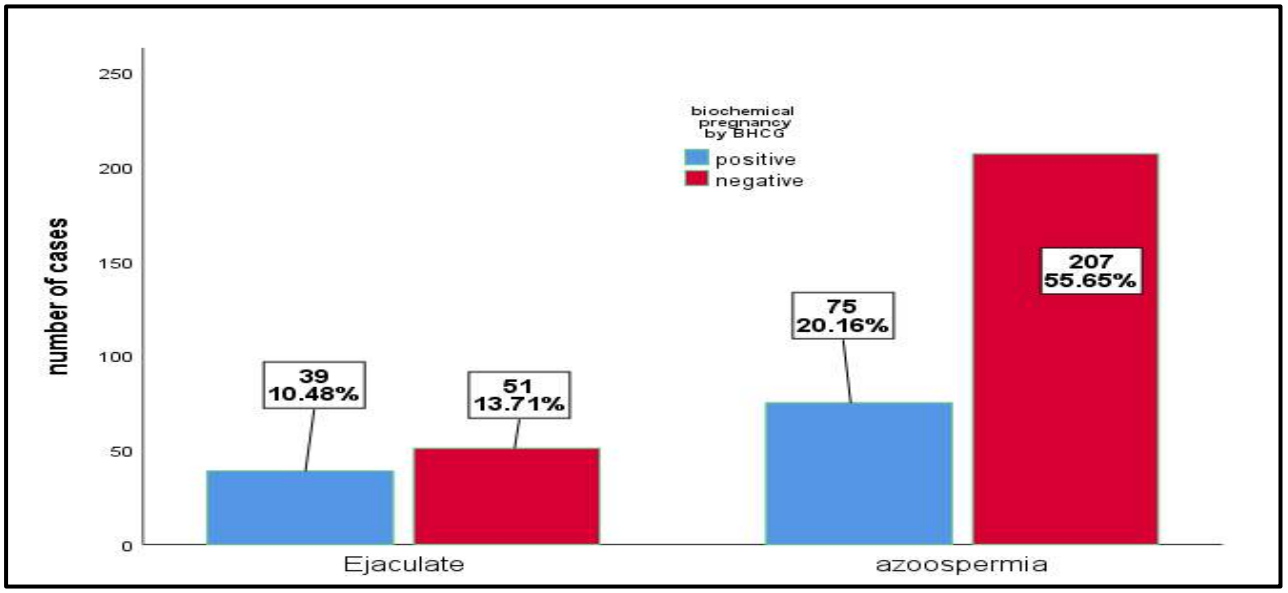

Figure NO.1: The distribution of cases according to β-HCG test result between the two studied groups.

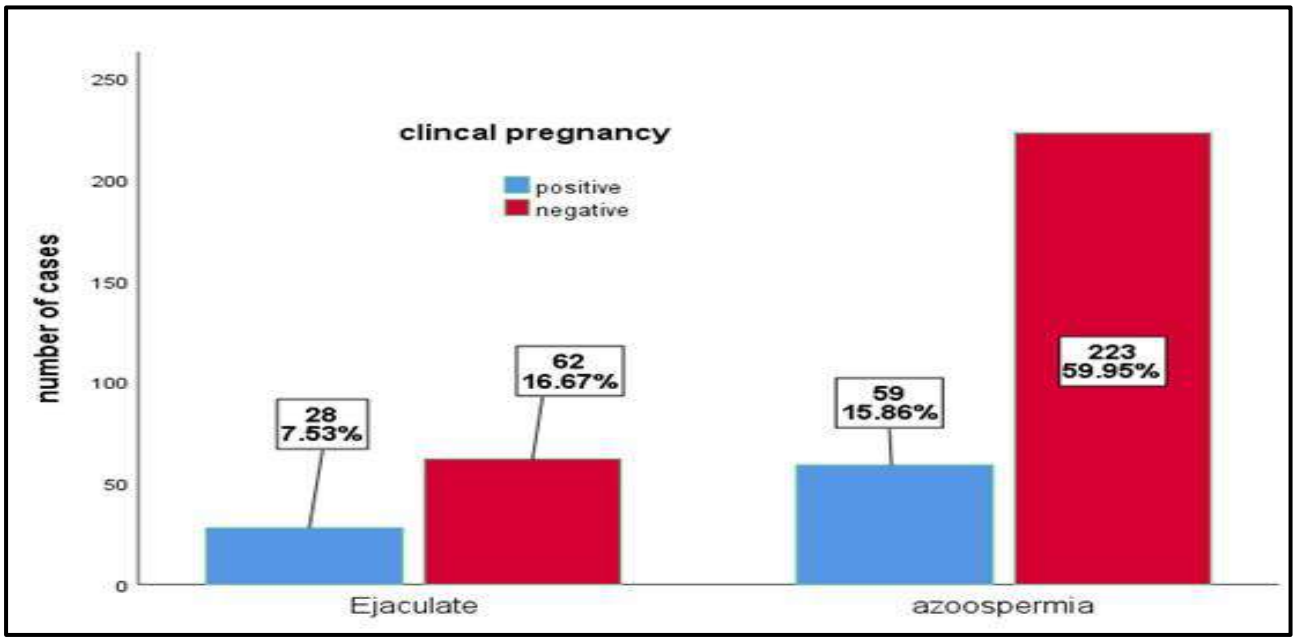

Figure NO.2: The distribution of cases according to clinical pregnancy result between the two studied groups.

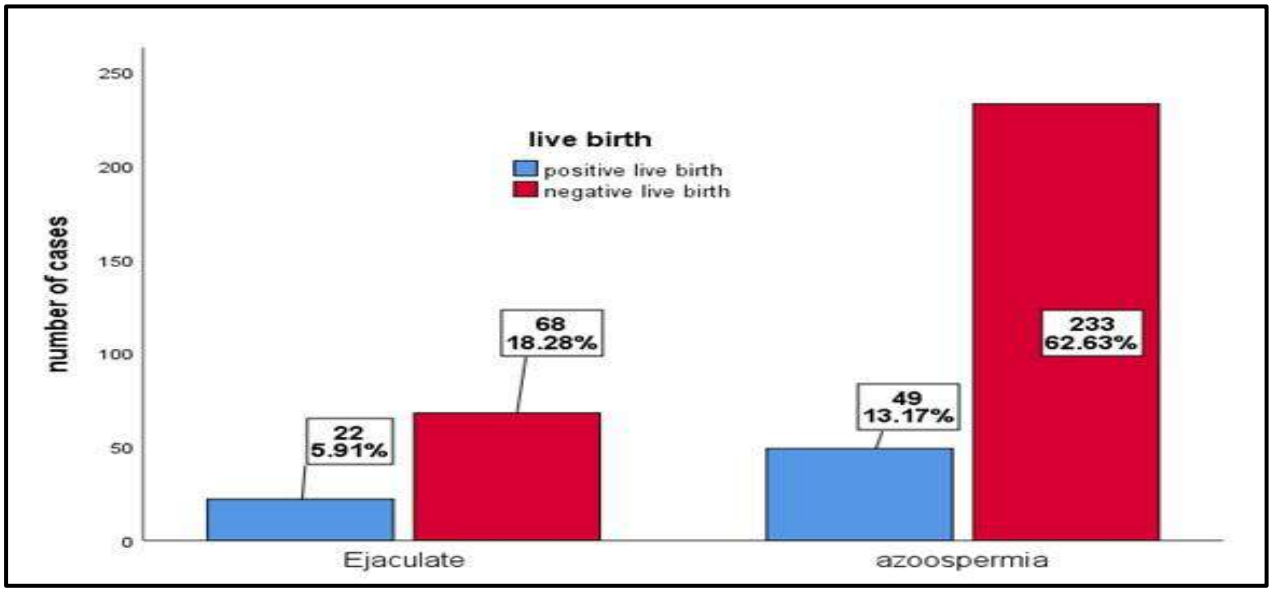

Figure NO.3: The distribution of cases according to live birth result between the two studied groups.

DISCUSSION:

Since the invention of ICSI, a dramatic improvement in cases of sever male factor infertility happened; nowadays, it became clear that ICSI could be used for male infertility with reduced semen parameter in which sperm had limited number or poor motility or poor morphology[12] [13]. The present study shows significantly a higher pregnancy rate, biochemical and clinical, in the ejaculate group rather than azoospermia group, while no significant difference regarding live birth rate between the two groups. This is supported by Göker et al.[14] who found similar results. Magli et al. [15] agreed with the study and found mosaicism and chromosomal aneuploidy in NOA patients that make embryos genetically abnormal and lead to decrement in clinical pregnancy when comparing them to normozoospermia. Bernardini *et al.* [6] reported that testicular germ cells had higher rates of sperm aneuploidy and diploidy than ejaculated sperm. It is important to note that neither sperm morphology nor chromatin condensation of testicular sperm from NOA patient can predict pregnancy outcome [16].

A study done by Yu et al., [17] in China used sperm from NOA patients by TESE and ejaculated sperm from donors and concluded that testicular sperm from NOA patients negatively affect clinical pregnancy while donor sperms were not, it also found no significant difference regarding live birth rate in both groups. In contrast, Ghazzawi et al.[18] found no significant difference regarding pregnancy rate and live birth rate between ejaculated sperm and testicular sperm of NOA patients. It is well known that in addition to surgical complications of TESE, the retrieval rate did not exceed 60% in best situation [19] [20].

CONCLUSION:

Freshly ejaculated sperms with normal or suboptimal semen parameter gave better biochemical and clinical pregnancy rate than obtained from NOA by TESE, while live birth rate was not largely different in both groups.

RECOMMENDATION: it is recommended that paternal genetic testing before ICSI cycle in NOA patients or use of pre-implantation genetic diagnosis (PGD) in the embryos.

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Serum levels of Interleukin-6 in patients with Idiopathic Carpal Tunnel Syndrome: A case control study in Najaf Province

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Abstract

Background: Carpal Tunnel Syndrome (CTS) is a disease caused by a compression of the median nerve at the wrist within carpal canal that lead to multiple symptoms as paraesthesia, numbness and pain sensation in the median distribution fingers. If untreated, it leads to sensation loss, thenar muscle weakness and atrophy. It is most frequent peripheral neuropathy of upper limbs and is most predominant in female gender. The pathogenesis of CTS is yet unknown, and the majority of conditions are idiopathic.

Interleukin 6 is a cytokine that has multiple functions including pro-inflammatory and anti-inflammatory or regenerative actions. The impact of serum inflammatory cytokines on incidence and severity of CTS is still unclear.

Aim of the study: this study aims to correlate the clinical severity of CTS and the serum interleukin 6 concentrations.

Patients and methods: This is a case control study which involved 140 participants who were categorized into 70 patients with CTS and 70 healthy persons according to clinical assessment and nerve conduction study results. After that, the participants were divided to normal, mild, moderate and severe groups according to Boston carpal tunnel questionnaire (BCTQ). Then, a blood sample was taken from each participant to assess serum interleukin 6 levels. A statistical analysis by SPSS was done for the collected data.

Results: The study has shown that there was no significant correlation between serum interleukin 6 levels and the clinical severity score of CTS (P value >0.05).

Conclusion: It has been concluded that serum interleukin 6 levels did not have an impact on incidence and clinical severity of CTS and that its role in CTS is yet unclear.

Key words: Carpal tunnel syndrome, clinical severity score of CTS, Interleukin 6.

INTRODUCTION

Carpal Tunnel Syndrome (CTS) is the most frequent upper limb compression neuropathy encountered clinically. It takes place when the median nerve is entrapped as it enters the tunnel [(1)]. In general, 2–3% of people suffer from carpal tunnel syndrome [(2)]. It is

more predominant in females, more frequent in persons between 40-60 years old, and its severity increases with increment of age [3]. The majority of conditions of CTS are idiopathic, but there are numerous predisposing factors linked with increased CTS incidence, including pregnancy, obesity, systemic disease such as diabetes mellitus, hypothyroidism, and rheumatoid arthritis, space-occupying lesions such as hematoma, tumors, or ganglion cysts, repetitive use injuries, wrist fracture or surgery, hereditary disorders such as abnormal muscles, inherited small tunnel, smoking, and alcoholism [4]. The pathophysiology of CTS is thought to be a mechanical compression of the median nerve which leads to ischemic changes inside the nerve. This decrement in the intraneural blood flow, and thus oxygen flow, result in defects in axonal transport and nerve tissue fibrosis. This causes atypical impulse production, slowness of conduction gradually and lastly axonal injury [5]. Initially, sensory fibers are damaged, then motor fibers. As well as autonomic fibers, may be damaged [6]. Clinical manifestations of CTS involve disorders of sensation and motor weakness. Sensory disorders localized to the median innervated digits like first, second, third and lateral side of fourth digit and involved intermittent tingling, numbness, and pain. The symptoms exacerbate during activities that involve hand extension or flexion for a long time and are calmed by hand shaking [5]. The characteristic feature of CTS is nocturnal tingling that awakens the patient from sleep. In more advanced conditions, the intermittent tingling and numbness turn into persistent, and the nerve dysfunction may lead to thenar muscle weakness and atrophy. CTS diagnosis is dependent on the history and physical examination. It is assured by electrophysiological studies [7]. Boston carpal tunnel questionnaire (BCTQ) is valid and reliable to assess the severity of symptoms and functional impairment in patients with CTS. The symptoms severity scale (SSS) and functional status scale (FSS) are the two sections of the questionnaire. There are eleven questions in the SSS, and answers are graded between one and five points, 1=normal, 2=slight, 3=medium, 4=severe, and 5=very serious. Besides, there are eight questions in the FSS to gauge how hard it is to carry out particular tasks, and answers are graded between one and five points, grades of 1=no difficulty, 2=little difficulty, 3=moderate difficulty, 4=intense difficulty, and 5=very severe difficulty that indicate patients cannot do the activity at all [8]. Peripheral immunity maintains homeostasis and has neuroprotective functions on the damaged nervous system, and it can potentially increase neuropathic pain sensitivity at the same time [9]. IL-6 is a multifunctional cytokine that is formed by immune cells such as T-cells, B-cells, macrophages, and microglia, and non-immune cells such as endothelial cells, muscle cells, fibroblasts, adipocytes, and neurons [10].

Patients and methods

In this case-control study, the total number of participants was 140. Patients were collected from the Neurophysiology Unit at the Middle Euphrates Center for Neurological Sciences/ Al-Sader Teaching Hospital in Al-Najaf city from the beginning of November 2022 until June 2023. The inclusion criteria were participants' age (18–50 years), clinical and electrodiagnostic confirmation of CTS in the patient group, and body mass index (BMI < 30) while the exclusion criteria were history of diabetes mellitus, thyroid dysfunction, polyneuropathy, rheumatoid arthritis, acromegaly, pregnancy, systemic lupus erythematosus, cervical radiculopathy, wrist fractures, hand trauma, and any upper limb trauma or surgery for CTS.

All participants involved in the research were subjected to full history and physical examination, Boston Carpal Tunnel Syndrome Questionnaire (BCTQ), nerve conduction study

of the upper limbs, and body mass index calculation. A venous blood sample of 2.5 milliliters was collected from each participant and put in a gel tube, then serum interleukin-6 levels were measured using a human interleukin-6 ELISA kit (Sunlong, China). A patient group composed of seventy patients (11 males and 59 females) came with clinical and electrophysiological findings of CTS, and then they were classified into mild, moderate, and severe subgroups according to Boston Carpal Tunnel Syndrome Questionnaire (BCTQ). The total score of the SSS was classified into asymptomatic (11 points), mild (12–22 points), moderate (23–33 points), severe (34–44 points), and very severe (45–55 points). The total score of FSS was categorized into no difficulty (8 points), little difficulty (9–16 points), moderate difficulty (17–24 points), severe difficulty (25–32 points), and very severe (33–40 points) [11]. The control group was composed of seventy healthy participants (10 males and 60 females); they had no clinical or electrophysiological manifestations of CTS, and their age, gender, BMI, and geographical distribution were similar to the patients.

Ethical Approval

This study obtained the ethical approval from the internal ethical committee of the Medical Physiology Department/Faculty of Medicine, University of Kufa and the Health Directorate in Najaf Province. Further, a verbal voluntary consent was taken from the all patients and controls who were involved in this study.

Statistical Analysis

The data analysis was performed by the utilizing Statistical Package of Social Science (SPSS) software program version 26. Categorical variables were expressed as frequency and percentage and analyzed by using Chi-square test to measure the significance level of difference and the relationships between them. Continuous variables were stated as means and standard deviation (SD) and analyzed by using an independent t-test to compare between patient and control groups. However, utilizing ANOVA and Post Hoc test to measure the significance level of difference for continuous variables for comparing the four groups. The correlations were assessed by Bivariate Pearson Correlation (r: correlation coefficients). P value < or =0.05 was regarded significant.

Results

The participants were divided into three age groups, and the most frequent age group was 40–50 years (45.7%) for both the patient and control groups. There were 11 (15.7%) males and 59 (84.3%) females among the patient group, demonstrating that females are more commonly affected than males. Most of the patients 55 (78.6%), and controls 52 (74.3%), were overweight (BMI = 25–29.9 kg/m2). Concerning the patients' jobs, all of the patients were working in high-risk manual jobs. The female patients: 53 (89.8%) of them were housewives, and 6 (10.2%) of them were employed. The male patients: 9 (81.8%) of them were unemployed, and 2 (18.2%) were employed (Table 1). The gender had no significant effect on serum IL-6 levels in the patient group (P value= 0.4). So male and female patients are counted as one group in this study (Table 2). Independent T- test was used to compare the mean and standard deviation of serum interleukin-6 between the patient and control groups; there was no significant difference between the two groups (P value >0.05) (Table 3). According to the symptom severity score and functional status score, there was no significant difference in the mean IL-6 levels between CTS severity groups (P values = 0.76, and 0.81, respectively). When we compared the mean IL-6 of each group with the other groups, there was no significant difference between the groups (P value >0.05) (Table 4). There was no significant correlation between the CTS scales (SSS and FSS) and

serum IL-6 (Table 5) (Figure 1 & 2). There was no significant correlation between age of patients and serum interleukin-6 (P value= 0.13, r =0.18) (Figure 3).

Table 1. Demographic Data for Patient and Control Groups.

Variables	Patient group n (%)	Control group n (%)	P value
Age group			
18-28	15 (21.4)	16(22.9)	0.97
29-39	23 (32.9)	22(31.4)	
40-50	32 (45.7)	32(45.7)	
Occupation			
housewife	53(75.7)	51(72.9)	0.40
employed	8(11.4)	13(18.6)	
unemployed	9(12.9)	6(8.6)	
BMI status			
normal	15(21.4)	18(25.7)	0.55
overweight	55(78.6)	52(74.3)	
Dominant hand			
right hand	63(90)	65(92.9)	0.55
left hand	7(10)	5(7.1)	
Involved hand			
right hand	25 (35.7)		
left hand	11(15.7)		
both hands	34(48.6)		
Gender			
male	11(15.7)	10(14.3)	0.81
female	59(84.3)	60(85.7)	
Severity of CTS			
mild	24(34.3)		
moderate	23(32.9)		
severe	23(32.9)		

Table 2. The Relationship between Gender and IL-6 Levels in the Patient Group.

Variables	Gender	N.	Mean ±SD	P-value
IL-6 (pg/ml)	Male	11	31.55±10.92	0.4
	Female	59	28.58±7.22	

Table 3. A Comparison of Serum Interleukin 6 between CTS Patient and Control Groups.

Variables	NCS groups		P value
	Patient group N=70 mean±SD	Control group N=70 mean±SD	
IL-6 (pg/ml)	29.05±7.89	28.92±7.93	0.92

NCS: Nerve conduction study.

Table 4. Relationship of Clinical CTS Scales (SSS and FSS) with Serum IL-6.

IL_6 (pg/ml)	Scale	Normal mean±SD	Mild mean±SD	Moderate mean±SD	Severe mean±SD	P value
	SSS	28.92±7.93	27.74±2.79	28.94±8.74	30.15±9.84	0.76
	FSS	28.79±7.8	28.01±2.61	30.19±10.67	29.18±8.13	0.81

SSS: Symptom Severity Scale, FSS: Functional Status Scale.

Table 5. The Correlation between Interleukin-6 and CTS Clinical Scales.

Variables	Symptom Severity Scale SSS		Functional Status Scale FSS	
	Correlation Coefficients (r)	P-value	Correlation Coefficients (r)	P-value
IL_6(pg/ml)	0.06	0.48	0.06	0.47

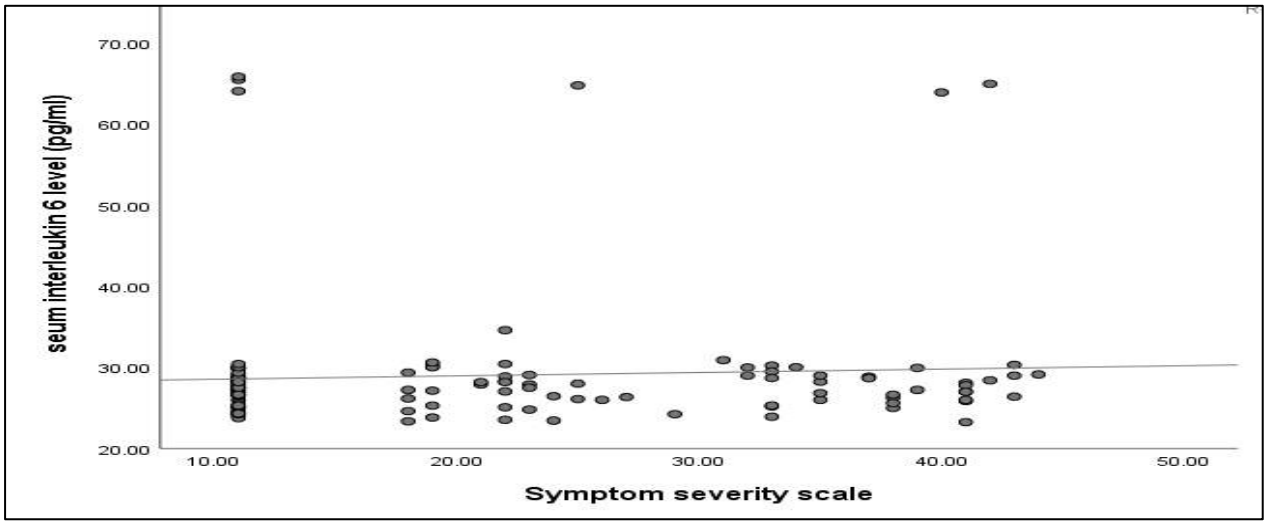

Figure 1. The Correlation between Serum Interleukin 6 and Symptom Severity Scale of CTS.

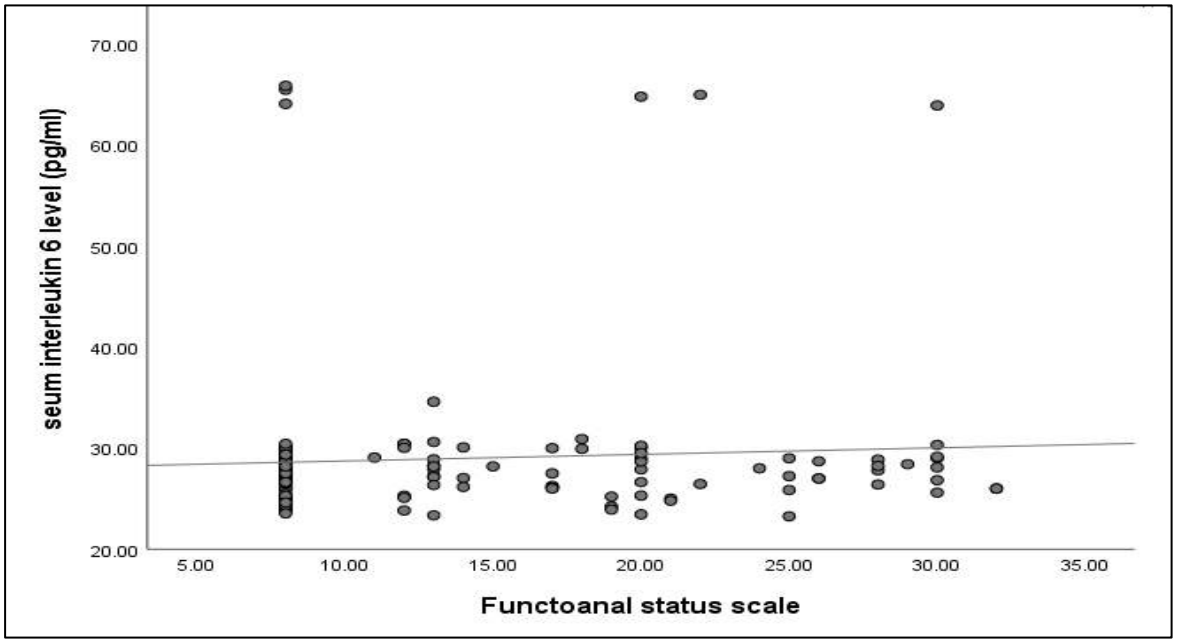

Figure 2. The Correlation between Serum Interleukin 6 and Functional Status Scale of CTS.

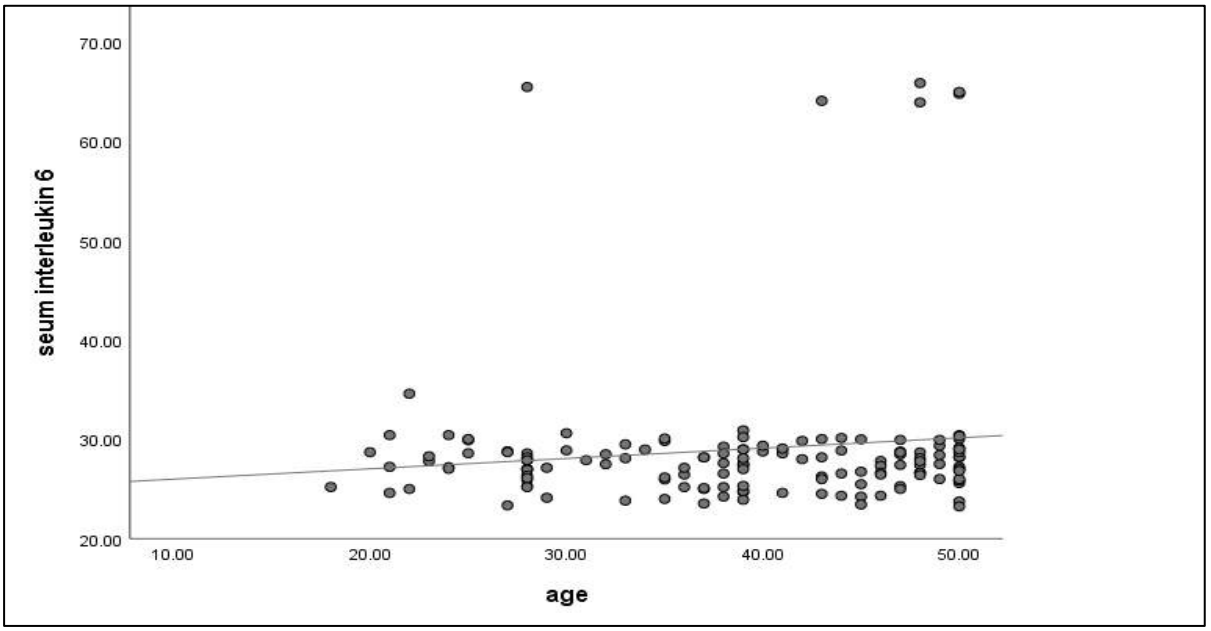

Figure 3. Correlation between Serum IL-6 Levels and Age of Patients.

Discussion

In this study, most of the patients were middle-aged (Table 1); this appears logical due to the fact that the likelihood of developing CTS is higher among working-age people than the general population, possibly due to degenerative changes resulting from repeated hand activities [(12).] Similar results were reported by numerous researches [(13,14)]. 84.3% of the patients in this study were female (Table 1); this was consistent with other researches [(15,16)], which may be a result of the fact that females have a smaller wrist canal than males [(17)]. Moreover, a woman's everyday activities inside the house might worsen her condition, and hormonal variations during pregnancy and the menstrual cycle have been found to contribute to the development of CTS [(18)]. In this research, 89.8% of the female patients were housewives. This is in agreement with another research, which showed that

housework was likely a contributing factor to CTS among women under the age of 45[19]. In this research, there was no statistical effect of gender on serum IL-6 levels (Table 2), as the increment in inflammatory mediators is associated with the progression of disease regardless of gender [20]. This research showed there was no statistically significant difference in serum interleukin-6 concentrations between the patient group and the control group (Table 3). Besides, there was no statistically significant difference in serum interleukin-6 concentrations between CTS clinical severity groups (Table 4). These findings were consistent with those of Karimi et al. (2020), who reported that blood levels of inflammatory cytokines (IL6, IL1, IL10, and TNF) did not significantly vary in persons with carpal tunnel syndrome in comparison with healthy participants and were not significantly associated with SSS and FSS of CTS [9]. According to research by Freeland et al. (2002) and Sud et al. (2005), there is no variation in the level of IL1 in the blood or tenosynovium among individuals with CTS and the control subjects. Also, the serum concentrations of PGE2 and IL-6 showed no significant difference between cases and controls. However, PGE2 and IL-6 tenosynovial concentrations were elevated in the carpal tunnel syndrome group. These studies stated that IL-6 has a local role in the pathophysiology of CTS. The researchers suggested that these changes could be due to oxidative damage resulting from repetitive ischemia and reperfusion injuries [21,22]. Taylor et al. (2017) found that individuals with CTS had higher serum concentrations of a number of cytokines, including IL-12, IL-4, and IL-9, than healthy persons while they found no significant difference in serum IL-2, IL-6, IL-7, IL-10 or IL-13 between CTS cases and controls. Taylor's study suggested that neuroinflammation had important role in the development of CTS. However, there was no correlation between plasma cytokine concentrations and the severity of the symptoms. They measured serum concentrations of twenty-seven chemokines and cytokines; so, they noted a significant difference in serum concentrations of some cytokines between CTS cases and controls [23]. While this study assayed serum concentrations of interleukin-6 only, a significant difference was not observed in IL-6 between CTS cases and controls. Ajeena et al (2021) showed that the levels of Regulated on Activation, Normal T Cell Expressed and Secreted (RANTES chemokine) were significantly elevated in CTS patients in comparison to healthy persons. Although there was no notable variance in levels of RANTES between CTS severity groups [24]. Another research found that individuals with herniated intervertebral disks and CTS had elevated levels of IL-6 and TNF in their serum compared to healthy individuals [25]. Magrinelli et al. (2015) focused on the connection between serum proinflammatory cytokine levels and the damage of both small and big nerve cells in diabetic polyneuropathy patients. It stated that there was an association between IL6, IL10 serum concentrations and large nerve fiber axonal lesions, whereas these abnormalities are not linked to neuropathic pain or the destruction of tiny nerve fibers [26]. Although the fact that CTS is a large nerve fiber lesion, unpredictably, our study didn't notice any noteworthy dissimilarity in the blood IL-6 concentrations in cases of CTS. For Magrinelli et al. (2015), diabetic patients' serum cytokine concentrations were measured [26]. Diabetes mellitus may be related to changes in cytokine concentrations in the blood of the patients. According to research by Kawamoto et al. (2020), CTS patients with comorbid trigger finger had considerably higher levels of IL-6 released by fibroblasts originating from the tenosynovium than CTS patients without trigger finger. This could be a possible explanation for the commonly observed correlation between CTS and trigger finger [27].

Conclusions

Neither the functional status of patients with carpal tunnel syndrome nor the severity of their symptoms are significantly correlated with the levels of the inflammatory cytokine interleukin 6 in their serum. Interleukin-6 doesn't appear to have an important impact on the incidence and clinical severity of CTS among Iraqi patients.

Recommendations

A measurement of other inflammatory cytokines and finding their correlation with incidence and severity of CTS is recommended.

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Self-Esteem Of Caregivers Of Child With Developmental Dysplasia Of The Hip

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Abstract

Background: self-esteem could have a negative impact on caregivers and it is important for caregivers to take care of their own mental and physical health to provide the best care for their children.

Aims of the Study: the present study aims to assess the level of self-esteem among caregivers of children with DDH and to find out the relationships between self-esteem among caregivers of child with DDH and different socio-demographic characteristics.

Methods: A descriptive cross-sectional research design was used in this study which was conducted in Najaf city hospitals. A non-probability, convenience, technique was used to collect the data. The study subjects included 50 caregivers who have been selected from Najaf Province. The questionnaire is adapted and modified by the researcher to achieve the goals of the study.

Results: The results of the study revealed that caregivers of children with DDH have low levels of self-esteem. There is a significant relationship ($P<0.05$) between self-esteem and the socio-demographic characteristics marital status.

Keywords: caregiver, children, Developmental dysplasia of the hip (DDH), self-esteem.

INTRODUCTION

Self-esteem is a term used to express a person's general feeling of value or self-worth. It may also be defined as how people view themselves, how they feel they contribute to the world, and how important they believe they are to others (1). Self-esteem is influencing factors of mental health problems; the occurrence of life events decrease the level of self-esteem. It may work as a mediator between life events and mental health status It is reported that family function and life events correlate with each other. Self-esteem is an important psychological resource that contains values and abilities; it is at the core of

individual mental health which influences the psychological health state of the individual (2). The formation of self-esteem is a long process that is linked to the development of self-image and self-conscience. Because self-esteem is usually related with psychological conditions, it appears to be highly and adversely associated with both state depression and state anxiety (3). James (1890) established the first significant definition of self-esteem as the relationship between success and aspirations in the primary areas of life. James focused on the individual factors that influence self-esteem, while subsequent symbolic interactionism techniques highlighted how society affects self-esteem (4). Developmental dysplasia of the hip (DDH) is a term that describes the abnormal form of the newborn hip's acetabula, which can cause early osteoarthritis, increased wear, and severe functional gait impairment if a hip dislocation goes unnoticed (5). DDH refers to a variety of situations that have an impact on hip development and frequently affects infants and young children. It involves aberrant acetabular and/or proximal femoral growth and can vary from mild capsular laxity to frank dislocation (6).

Caregivers play a critical role since they are the primary source of information regarding their child's health status (7). The caregivers of handicapped children had impacts in all areas of quality of life and were at the risk for sadness, rage, and high levels of stress (8)(9). However, in reality, families that care for a family member with a handicap endure a decline in self-esteem as a result of the difficulties they face. Low self-esteem sets up a vicious cycle whereby a person is unwilling to seek for assistance and reduces their social circle, both of which increase the burden of care. Contrarily, a person with high self-esteem is less stressed because they have a greater ability to defend themselves from psychological difficulties and are able to react to conditions in a more positive way (10). Self-esteem has been recognized as one of the mediators and moderators that might affect the health and quality of life of caregivers of disabled children(11). Therefore, it is very important to find ways to help the families improve self-esteem.

Methods and Materials

The Study Design:

A quantitative descriptive cross-sectional design was used in the current study to assess the level of self-esteem among caregivers of children with DDH and to find out the relationships between self-esteem among caregivers of child with DDH and different socio demographic characteristics.

Ethical Considerations:

Prior to conducting the study, the researcher adhered to the National Research Ethics Committee's standards and obtained an approval from the relevant government entity to ensure ethical considerations. After describing the goal of the study to each participant, the researcher assured to keep the caregivers' information private and only used for this study. In addition, to obtain the informed consent, the researcher told each participant that this was a voluntary role and that they might leave at any time.

Sample and sampling technique:

A non-probability sampling technique, convenience sampling, was used to choose a sample of fifty caregivers of children with DDH who were selected from, Al-Sadder Medical City, Al- Najaf Al-Ashraf Teaching Hospital, Al-Hakeem General Hospital, and Al-Furat Al-Awsat Teaching Hospital in Najaf Province.

Inclusion Criteria :

1. The ages of all caregivers above 18 years.
2. Both sex (male and female).
3. caregivers with no history of mental health problems. This problem is recognized with a particular question in the Socio-demographic section. All

caregivers stated that they had no history of mental health problems.

Criteria for Excluding from the Sample:

1. Caregivers who have been included in the pilot study sample,
2. Caregivers of children with DDH under 18 years old,
3. Respondents who did not completely answer the questionnaire

Study Instruments:

In addition to an assessment, the researcher constructed a self-administrative questionnaire, the final research instrument is divided into two parts:

Part I: Socio-Demographic Characteristics :

Caregiver characteristics

This part consists of the Socio-demographic characteristics sheet consisting of (13) items, including who the caregiver are, their gender, age, mothers' age at child's birth, number of children, marital status, level of education, Primary knowledge about DDH, job, monthly income, residency area, family history of DDH, and if there is any psychiatric disorders.

Child Characteristics

This included a socio-demographic characteristics sheet of (5) items: gender, age, birth order of the child in the family, types of delivery, type of treatment

Part II: The Rosenberg Self-Esteem Scale (RSES):

This is the most widely used measure of global self-esteem for research purposes but it is not a diagnostic aid for any psychological issues of states. It is a 10-item questionnaire; five of them have positively worded statements and the other five have negatively worded ones, Four response categories are used (strongly disagree, disagree, agree, strongly agree)

Data Collection

Participants were caregivers of children with a diagnosis of DDH, The researcher visited every caregiver separately, and after getting a verbal consent from the caregiver to participate, he demonstrates the contents of the questionnaire to them, and then to all individuals in the current study. The data were collected by using the designed questionnaire and the self-reported technique in the Arabic version of the questionnaire for the subjects included in the study.

Statistical Analysis

After the data was prepared for statistical analysis, the descriptive and inferential statistics was applied to the data analysis by using the Statically Package of the Social Sciences (SPSS), version (IBM 21) as follows:

Descriptive statistics.

The study used frequency and percentage tables and mean and standard deviation.

Inferential statistics

Cronbach's alpha, Analysis of Variance (ANOVA), is conducted for determining the difference in the study variables such the relationship between self-esteem overall scores and socio-demographic data.

The Results

Table (1) below shows the socio-demographic data of the caregivers in the study within mother caregiver (86%), female caregivers (90%), caregivers between the ages 18-27 and 28-37 with percentage (42%) , mother's age at child birth was the ages <= 27 (58%), those with number of children less than 3 (66%), those who are married (96%), those with primary level of education (37%); those who were not trained for DDH (96%) ; those who are housewives (66%); those with barely sufficient monthly income (56%); those who live in urban areas (62%); those with no family history of DDH(62%); those with no psychiatric disorder (100%). Child Characteristic has the highest percentage of: female gender (84%), while age of 2 years with percentage (34%), order of the child's birth being the first (32%) ; those with caesarean section of delivery (64%) and those with surgical treatment (58%) .

Table (1) A Statistical Summary of the Socio-Demographic Data related to the Study Sample

Socio -demographic data	Ranking and Interval	Freq.	%
Who are caregiver	Father	5	10.0
	Mother	43	86.0
	Sister	2	4.0
Gender	Male	5	10.0
	Female	45	90.0
Age	<= 27	21	42.0
	28 – 37	21	42.0
	38+	8	16.0
	Mean	30.26	
	SD.	6.369	
Mothers Age at Child's Birth	<= 27	29	58.0
	28 – 35	14	28.0
	36+	7	14.0
	Mean	28.6	
	SD.	5.53	
Number of children	<= 3	33	66.0
	4 – 6	16	32.0
	7+	1	2.0
Marital status	Married	48	96.0
	Divorced	2	4.0
Level of Education	Literate	11	22.0
	Primary	19	38.0
	Secondary S.	10	20.0
	College /High Education	10	20.0
Primary knowledge about DDH	Not Once	48	96.0
	The once	2	4.0
Working	Employed	9	18.0
	Free Work	6	12.0
	Unemployed	33	66.0
	Student	2	4.0
Monthly Income	Sufficient	14	28.0
	Barely Sufficient	28	56.0
	Insufficient	8	16.0
Residency area	Urban	31	62.0
	Rural	19	38.0
Family history of DDH	Yes	19	38.0
	No	31	62.0
Do you have any psychiatric disorders	Yes	0	0.0
	No	50	100.0
Child characteristics			

Gender of the Child	Male	8	16.0
	Female	42	84.0
Age of the Child	<= 1	15	30.0
	2	17	34.0
	3	14	28.0
	4	2	4.0
	5+	2	4.0
	Mean	2.10	
	SD.	1.16	
Birth order of the child in the family	1	16	32.0
	2	10	20.0
	3	8	16.0
	4	9	18.0
	5	5	10.0
	6	2	4.0
Types of delivery	Normal Vaginal Delivery	18	36.0
	Caesarean Section	32	64.0
Type of treatment	Surgical	29	58.0
	Non-Surgical	21	42.0

Table (2) below, however, provides the overall assessment of self-esteem among caregivers of children with DDH according to Rosenberg's self-esteem scale; it shows that the overall assessment of RSE is (low) at mean of scores equals to 1.882.

Table (2) Overall Assessment of Self-Esteem among Caregivers of Children with DDH

Levels	**Freq.**	**%**	**Ms.**	**Asses.**
Strongly Disagree	30	60.0	1.882	Low
Disagree	13	26.0		
Agree	6	12.0		
Strongly Agree	1	2.0		

Freq : Frequency ; MS : Mean of Scores ; Low: MS = 1-1.99 ; Moderate: MS = 2-2.99 ; Good: MS 3-4

Table (3) below illustrates the relationship between the overall assessment of self-esteem among caregivers of children with DDH and the different socio-demographic characteristics. It exposes that there is no significant relationship between the assessment of the Rosenberg's self-esteem scale for caregivers and their socio-demographic data (P>0.05); however, the marital status has a significant relationship (p value =0.03) .

Table (3) ANOVA table for the relationships between self- esteem among caregivers of child with Developmental dysplasia of the hip and different socio-demographic characteristics

Socio-Demographic Data	Ranking and Interval	Mean	SD.	F	Sig.
Who are caregiver	Father	2.00	0.42	0.78	0.46
	Mother	1.89	0.49		
	Sister	1.50	0.00		
Gender	Male	2.00	0.42	0.33	0.57
	Female	1.87	0.49		
Age (Years)	<= 27	1.98	0.58	0.75	0.48
	28 – 37	1.83	0.43		
	38+	1.76	0.28		
Mothers Age at Child's Birth (Years)	<= 27	1.98	0.51	1.64	0.20
	28 – 35	1.81	0.48		
	36+	1.64	0.13		
Number of children	<= 3	1.95	0.53	0.98	0.38
	4 – 6	1.74	0.36		
	7+	1.90	.		
Marital status	Married	1.85	0.42	5.06	0.03*
	Divorced	2.60	1.41		
Level of Education	Literate	1.80	0.23	0.81	0.50
	Primary	1.85	0.53		
	Secondary S.	1.82	0.42		
	College /High Education	2.09	0.62		
Participation in Trainings dealing with child having DDH	Not Once	1.89	0.49	0.30	0.59
	The once	1.70	0.14		
Working	Employed	1.99	0.53	0.40	0.75
	Free Work	1.82	0.29		
	Unemployed	1.88	0.51		
	Student	1.60	0.14		
Monthly Income	Sufficient	1.85	0.43	0.04	0.96
	Barely Sufficient	1.89	0.54		
	Insufficient	1.90	0.36		
Residency area	Urban	1.96	0.56	2.49	0.12
	Rural	1.75	0.27		
Family history of DDH	Yes	1.85	0.31	0.16	0.69
	No	1.90	0.56		
Child Characteristics					
Gender of the Child	Male	1.90	0.54	0.01	0.91
	Female	1.88	0.47		
Age of the Child (Years)	<= 1	1.96	0.55	1.44	0.23
	2	1.70	0.09		

	3	2.06	0.65		
	4	1.85	0.07		
	5+	1.60	0.00		
Birth order of the child in the family	1	1.88	0.51	0.61	0.70
	2	2.03	0.50		
	3	1.95	0.62		
	4	1.67	0.12		
	5	1.94	0.61		
	6	1.75	0.21		
Types of delivery	Normal Vaginal Delivery	1.91	0.52	0.07	0.80
	Caesarean Section	1.87	0.46		
Type of treatment	Surgical	1.93	0.53	0.72	0.40
	Non-Surgical	1.81	0.39		

*** Significant at P<0.05 ; ** "Do you have any psychiatric disorders" is a constant Variable**

Discussion

In Table (1), the analysis of findings revealed that most of the sample were married mothers of children with DDH, fall in the age group (<= 27) years old and age group (28-37). The highest percentage of the study sample is of primary school level of education with barely sufficient monthly income. These findings have revealed that parenting of DDH children fell overwhelmingly on the hands of mothers more than fathers; it was observed that more mother had responsibility of caring in the family as mothers play greater roles in their children's care than fathers, while fathers role is in business life, or sometimes no role at all . This finding was backed up by Rodrigue and his colleagues, who found that mothers accounted for 74% of all parents and also this agrees with a study of (12) whose results indicate that the more caregiver is the mother (93.9%)

The results showed that the majority of the subjects' job (66%) are housewives. In the point of view that is majority of research participants did not complete their education, and mother are in charge of the household and children care all the time. This result goes in line with (13) who found that (70%) of the sample are housewives. Supplementary support was found by (14) who found that (62.4%) of participants in the study were housewives.

In regards to the primary knowledge about DDH, according to the findings in current study, caregivers who have no primary knowledge about DDH represent the largest proportion than those with knowledge. This result agrees with (15).This study found that the majority had a low knowledge level regarding DDH. As for the family history, the study states that it is not found in most of the sample study (62%); this finding comes along with the study of (16) which found that most of participant are negative in the results of family history in (77.8%). The characteristics of children revealed that most of the children were girls. Such finding could be explained by the incidence ratio of DDH, which reflects that the incidence rate of DDH is higher in female than male because of the effects of more estrogen generated by the female. A study presented a supportive evidence to this result by (17) who found that the gender of child is girls (92.6%) and by (18) who showed (77%) of the children to be females.

The distribution of DDH children according to their age indicated that the majority of them fall in the age of two years old (34%). This results agrees with (19) who found that the majority of children with DDH

were 1-2 years old. Regarding the birth order of the child, the first order of child in family is highest (32%). This results is similar to (20) who found that the first child was higher than the second and later. Because when the mothers birth the first child the uterus and abdominal wall tightened and the pelvis is not exposed to pressure, it is more flexible and subject to deformation.

Table (1) showed that most of the study sample were delivered through caesarean section (64%). This result is similar to a study done by (21) who find that most (63.1%) of them delivered through caesarean section. These results can be interpreted by the abnormal baby position during pregnancy. In relation to the type of treatment, the study has shown that the surgical treatment of most of the children was the highest percentage (58%). These findings with (22) who found that the sample was treated surgically (52%). These results may be due to the delay in the diagnosis of DDH and due to the lack of awareness of DDH and neglecting the child.

Table (2) asserts that the majority of caregivers have low RSE Scale assessment; these results are similar to a study (23) which found that parents have low level of self-esteem to parenting of children.

Table (3) displays that there is a significant relationship between self-esteem among caregivers of DDH children and marital status; there is a significant relationship between the overall assessment of RSE scale and marital status; caregivers with married (48of total 50) have low self-esteem of RSE. There is no study found to support the result, but the researcher assumes such reasons according to the results of the research: married caregivers have low level of self-esteem because the many responsibilities and life burden affect the quality of the marital relationship, as the nature of the tasks of providing care for the variety of children (24) (25). Married caregivers may also face additional pressures within their marital relationship, which could exacerbate stress and affect their self-esteem, as suggested by the possible explanations for the observed relationship between low self-esteem and marital status among caregivers of children with DDH (26).

Conclusion

The results of the current study showed that most of caregivers were to have low level of self-esteem**,** Marital status is statistically significant with self-esteem, while other socio-demographic characteristics of caregivers are not significant. All of the caregivers were under the age of fifty, and more than fifty percent of the caregivers' children were females (mothers). The highest percentage of the subjects were married, unemployed job, had a primary degree of education, and had a barely monthly income .The present study showed that DDH is more common among girls with highest percentage child's age of two years; children with DDH were treated with surgical treatment and had first birth order is highest percentage.

Recommendations

- Designing educational program for caregivers to improve the knowledge of parents of how to deal with their children
- Provideing DDH-related scientific books, articles, and journals and Caregivers who participate in social activities and caregiver support groups are more confident and have higher levels of self-esteem.

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A Comparison of ICSI Outcomes and Reactive Oxygen Species Levels in Seminal Plasma between Normozoospermia and Sperm Abnormalities Groups for Infertile Men

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Abstract

Background: Social life and the healthcare systems are affected by infertility. Infertility could be primary or secondary; secondary infertility is the inability to conceive after one successful pregnancy while primary infertility is the inability to conceive at all. As sperm abnormalities cause male infertility, Intracytoplasmic Sperm Injection (ICSI) is a particular type of in vitro fertilization (IVF) used to treat severe male-factor infertility. Free radical oxygen derivatives are reactive oxygen species (ROS). Reactive oxygen species may cause 30% to 80% of male infertility. **Aims of the study:** the present study aims to determine the reactive oxygen species level in seminal plasma and to study the Intracytoplasmic Sperm Injection outcomes for Normospermia group and compare it with Oligozoospermia, Asthenozoospermia and the Teratozoospermia Groups. **Material, and Methods:** a cross-sectional study was conducted between January 2023 to June 2023 in Najaf, on a non-random sampling including 50 couples who suffered from a minimum of 12 months of primary fertility with regular unprotected sexual intercourse and who had attended the fertility center in Najaf requesting fertility treatment. A gynecological examination and assessment were done for the female participants while the urologists examined and assessed the male subjects; then, a semen analysis was carried out followed by macroscopic and microscopic examinations. After the preparation of the sample for ICSI and performing ICSI, pregnancy was assessed and the outcomes of the different groups were compared. At the same time, reactive oxygen species levels were assessed by using the Human Reactive Oxygen Species ELISA kit. Then, the SPSS version 26 was used to perform the statistical analysis. **Results:** Among the twenty-one patients with Normozoospermia, seven with Asthenospermic, seven with Oligozoospermia and fifteen with Teratozoospermia, there was a significant difference among the four groups regarding sperm concentration, progressive motility, and sperm normal morphology. There was no significant difference among the type of sperm, Normo, Astheno, Tearato, and Oligozoospermia, regarding birth rate and ICSI outcomes. Males with higher progressive motility showed a higher pregnancy rate. **In conclusion**, despite the presence of reactive oxygen species, Intracytoplasmic Sperm Injection was advantageous and effective for all four groups. reactive oxygen species had no significant effect on Intracytoplasmic Sperm Injection outcomes, however Normozoospermia was associated with greater pregnancy rates. Despite the presence of reactive oxygen species, Intracytoplasmic Sperm Injection was advantageous and effective for all four groups. ROS had no significant effect on Intracytoplasmic Sperm Injection outcomes, however Normozoospermia was associated with greater pregnancy rates.

Keywords: Infertility, Intracytoplasmic Sperm Injection, Najaf, Reactive Oxygen Species.

INTRODUCTION

Infertility is a clinical and public concern as it affects both social life and the health system [1]. According to the World Health Organization 2020, infertility is "a condition of the reproductive system characterized as a couple's failure to conceive after twelve months of unprotected sexual intercourse in the fertile phase of the menstrual cycle among women younger than 35 and the failure to conceive after six months of regular unprotected sexual intercourse in women aged 35 or older" [2]. Infertility is either primary or secondary [3]. Primary infertility is when a pregnancy has never been achieved by an individual, while secondary infertility is the inability to conceive after at least one prior successful conception [4]. Infertility in men is typically brought on by issues with the ejection of semen, a lack of sperm or low sperm counts, or poor sperm shape (morphology) and motility [5]. Environmental, occupational, and lifestyle habits can degrade semen quality and cause male infertility [6].

Semen analysis continues to be the cornerstone investigation for male infertility, regardless of its weakness [7]. It is performed with high standards to evaluate the ejaculate's descriptive parameters [8]. Normospermia is characterized by having normal seminal fluid analysis values across all ejaculate parameters according to WHO's 2021 semen normalcy guidelines. Men with normal sperm parameters, often known as normospermia, may have infertility due to idiopathic, endocrine, or hormonal reasons, congenital or acquired urogenital abnormalities, or extramarital sexual dysfunction [9].

Sperm abnormalities are an essential factor in male infertility. Low sperm count is known as "oligozoospermia" (15 million sperm/mL) [10]. Teratozoospermia refers to an abnormal morphology of spermatozoa in more than 85% of the sperm. The term "monomorphic teratozoospermia" is used when all the spermatozoa exhibit a distinct abnormality [11].

Asthenozoospermia is a term referring to poor sperm motility or an absence of sperm motility in the analysis of semen samples. It is considered a major factor in men's infertility [12]. Abnormalities related to sperm motility are another type of sperm issue that causes infertility. Rapid progressive motility of a minimum of 25 m/s plays a significant role in the effective passage of spermatozoa through the cervical mucus.

Reactive oxygen species (ROS) are oxygen derivatives and free radical-containing molecules. Free radicals are molecules that are not paired with electrons and are extremely reactive, attempting to reach an electronically stable form. It has been reported by Wagner et al. that reactive oxygen species might be a causative factor in 30% to 80% of infertility cases in men's cytoplasm [13].

Many studies suggested oxidative stress, a condition characterized by an imbalance between reactive oxygen species (ROS) production and antioxidant defense systems, as a new emerging factor in unexplained male infertility [14,15,16,17].

Spermatozoa and polymorph-nuclear leukocytes produce the most reactive oxygen species in semen. DNA fragmentation in spermatozoa is linked to low-quality semen. The fraction of spermatozoa with fragmented DNA negatively affects IVF and ICSI fertilization rates. Infertile men fragment sperm DNA for unknown reasons. However, reactive oxygen species (ROS) are known to cause somatic cell DNA damage, therefore they may be linked to germ cell DNA fragmentation [13].

Intracytoplasmic Sperm Injection (ICSI) is a specially designed form of in vitro fertilization (IVF) used mainly to manage severe cases of male-factor infertility; it involves the injection

of a single sperm that has been surgically retrieved from the epididymis or testis into a mature egg (10). According to WHO 2021 standards for normal sperm, Normospermia is defined by having normal seminal fluid analysis values for all ejaculate parameters. Men with normal sperm parameters, known as normospermia, might suffer from infertility that can be either idiopathic, endocrine, hormonal, congenital or acquired urogenital abnormalities or sexual dysfunction extra [(9)].

This study aimed first to determine the reactive oxygen species level in seminal plasma and to study the ICSI outcomes for the Normospermia group and compare it with Oligozoospermia, Asthenozoospermia, and the Teratozoospermia Groups. Secondly, it aims to study the relationship between ROS, sperm parameters and the ICSI outcomes.

Material and Methods

Study design and sample collection

This cross-sectional study was performed at the Fertility Centre/ Al Sadr Medical City / Najaf for six months, from Jan 2023-June 2023. Patients with Normospermia, Oligozoospermia, Asthenozoospermia, and Teratozoospermia, in line with WHO standards 2021, were included in the study. The study included 50 couples who suffered from a minimum of 12 months of primary fertility with regular unprotected sexual intercourse and infertility factors related to males who had attended the fertility centre requesting fertility treatment. Gynecological examination and assessment were done for the female participants while the male subjects were examined and assessed by the urologists.

The inclusion criteria for male participants include Normospermia, Oligospermia, Asthenospermia and Teratozoospermia *while inclusion criteria for the female partners of the participants*: healthy female partners, Young female partners 21<age< 43 years old).

The exclusion criteria for male participants include: severe Oligozoospermia, Severe Asthenozoospermia , Severe Teratozoospermia while the exclusion Criteria for the Female Partners of the Participants: > 43 years old, & <21 years old), Overweight (BMI ≥ 30 kg/m²), Underweight female partners (BMI < 18.5 kg/m²), Female partners with polycystic ovarian syndrome (PCOS) and Female partners with Ovarian hyper-stimulation syndrome (OHSS).

Sperm classification diagnosis for males was reached by performing two seminal fluid analysis tests of two to three months' intervals depending on the (WHO criteria 2021). The participant's hormonal profiles (FSH, LH, testosterone, & Prolactin) were retrieved from the case records. No exclusion criteria were implemented regarding previous fertility treatment outcomes. Then ROS levels, ICSI outcomes ((Retrieved oocytes, MII oocytes, 2PN, Fertilisation rate, Cleavage rate and Pregnancy Ratio) for Normospermia and Oligozoospermia, Asthenozoospermia and Teratozoospermia patients.

Semen sample processes and Techniques:

The participants received oral instructions regarding the method of sample collection and preparation advice, such as abstinence from sexual activity for a minimum of two to seven days. The fresh ejaculate was collected from the participants in a sterile container (wide-mouthed) by masturbation in a laboratory room isolated for privacy and ethical purposes. Each container has the participant's identification details, such as name, age, and the sample collection time, as they were instructed that the sample must be complete. Semen from each participant included in the study was obtained from the participants' ejaculated samples.

Then macroscopic examinations of the seminal fluid, including liquefaction, viscosity, appearance, volume, and PH, were performed, followed by microscopic examinations of

concentration, motility, and morphology of the sperm. Then cells other than sperm that were present in the ejaculate were separated and counted, depending on WHO 2021 (Sunder & Leslie, 2021

Next, the sperm sample was prepared for ICSI by using the centrifugation swim-up technique for sperm preparation. These have been summarized by the following steps:

- The tube was centrifuged at 3000 rpm for 10 minutes,
- the supernatant was aspirated without disturbing the pellet, and then
- a resuspension took place in 0.3–0.5 mL of media.
- The conical tube was put in the incubator at a 45° angle for 30 minutes at 37°C to allow the sperm to swim up.
- Following the incubation period, an aspiration of the supernatant was done without disturbing the upper layer that accommodates the highest amount of motile sperm.
- Slide analysis was performed by taking a slight drop.
- After that, ROS were by assessed using an ELISA kit. Following manufacture instructions

Preparation for ICSI:

An inverted microscope, type Olympus Optical Co Ltd., Japan, which is provided by micro-injectors, a magnificent lens, with a capability of 200x and 400x, micromanipulators ("RI, UK"), and a three-dimensional maneuverer for both coarse and refined movements were employed for the process. The temperature was maintained at 37 °C by a heating surface on the inverted microscope.

Sperm immobilization:

Sperms that looked motile and had normal morphology were selected for immobilization. An aspiration of the selected sperm took place by injection pipette "Cook, Australia" to the PVP droplet for immobilization.

Oocyte Injection:

The oocyte was placed in a suction connected to the attached pipette (Cook, Australia). The immobilized spermatozoa were pushed inside the cytoplasm of the mature oocyte MII at 3 o'clock. Lastly, a small suction of the ooplasm was done after the introduction of the oocyte to guarantee that the injector pipette was inside the cytoplasm.

Incubation of injected oocytes:

The preparation of the culture dish took place 24 hours before using the oocyte injection. Then, the injected oocytes were moved to droplets through an automatic pipette and stored in a CO2 incubator until the next day to assess fertilization.

Fertilization Assessment:

This assessment took place on the morning of the next day before the injection of the mature oocytes. Injected oocytes that manifested two pronuclei and two polar bodies were deemed to have been fertilized successfully, while others were neglected.

Embryo selection and transfer:

Morphological evaluation of the embryos took place 24–48 hours after the oocytes had been retrieved. The morphological assessment included the existence of the first cleavage, the symmetry of blastomeres, and the magnitude of fragmentation. Good-quality embryos, grade I, selected for transfer have symmetrical blastomeres with no trivial cytoplasmic fragments. Grade II followed the good-quality embryos for transfer as they also have symmetrical blastomeres but with a minimum amount of cytoplasmic fragments. Finally, grade III embryos were transferred that have asymmetrical blastomeres and fragmentation, which is not greater than 50%. Other embryos that displayed higher grading should have been addressed. The maximum number of transferred embryos was three to four; the best-

selected embryos were transferred 48 to 72 hours after the retrieved oocyte.

Pregnancy examination:

Pregnancy was confirmed by an elevation in serum HCG hormone concentrations, known as a positive pregnancy test. The pregnancy test was done at least 12 days after the embryo selection and transfer.

Statistical analysis:

Version 26 of SPSS was used for the statistical analysis (Inc., Chicago, IL, USA); mean and standard deviation were used for parametric data; one-way ANOVA was used to compare between categorical independent and numerical dependent variables; and Chi-Square was used to compare between categorical variables. A P value of 0.05 was considered statistically significant.

Ethical approval

This study obtained ethical approval from the internal ethical committee of the Urology-Clinical Embryology department/Faculty of Medicine/University of Kufa and the Health Directorate in Najaf province. Additionally, verbal consent was obtained by all of the included patients or their parents prior to participation, as they gave their approval to participate in this study by giving their samples and providing the information that is needed.

Results

The study included 50 couples; the male participants were classified into four groups (Normospermia, Oligospermia, Teratozoospermia, and Asthenospermia) according to their seminal fluid analysis(SFA). The mean age of the Normo group was 38 ± 11 years, while their female partners' mean age was 32 ± 5 years old. The mean age of the Oligo group was 36 ± 4 years, while their female partners' mean age was 32 ± 5 years old. The mean age of the Astheno group was 40 ± 9 years, while their female partners' mean age was 31 ± 6 years old. The mean age of the Terato group was 35 ± 8 years, while their female partners' mean age was 33 ± 6 years old. There was no significant difference in the age of the four groups (*P* value = 0.6), Table no. 4.1.

Regarding sperm parameters variables among the four groups (Normo, Oligo, Astheno, Terato), a One-way ANOVA test was performed. It has shown that there is a significant difference in Sperm concentration (*P* value = 0.006), Progressive sperm motility (*P* value <0.001), and Sperm normal morphology (*P* value <0.001) among the four groups, Table no. 4.1.

Table 1: Demographic variables analysis & Sperm Parameters in Normo, Oligo, Astheno, and Terato samples of patients who underwent the ICSI program.

Variable	Normo (N=21) Per cent 42%	Oligo (N=7) Per cent 14%	Astheno (N=7) Percent 14%	Terato (N=15) Per cent 30%	*P* value
Age years	Mean ± SD 38 ± 11	Mean ± SD 36 ± 4	Mean ± SD 40 ± 9	Mean ± SD 35 ± 8	0.6
Height cm	176 ± 6	177 ± 6	178 ± 5	176 ± 6	0.8
Weight Kg	83 ± 11	91 ± 17	86 ± 10	89 ± 8	0.3
Infertility duration	5 ± 3	9 ± 7	7 ± 4	8 ± 5	0.4

Infertility type	Primary = 10 Secondary =11	Primary = 4 Secondary = 3	Primary = 1 Secondary = 6	Primary = 11 Secondary = 4	0.07
Testicular varicocele	Yes = 6 No =15	Yes = 4 No = 3	Yes = 7 No = 0	Yes = 8 No = 7	**0.01****
Smoking	Yes = 12 No = 9	Yes = 6 No = 1	Yes = 6 No = 1	Yes = 9 No = 6	0.3
Wife's age/year	32 ± 5	32 ± 5	31 ± 6	33 ± 6	0.9
Abstinence period	3 ± 0.6	4 ± 0.8	3 ± 0	3 ± 0.4	0.2
Sperm concentration million/ml	59.8 ± 24.5	7.5 ± 5.6	46.6 ± 31.7	32.7 ± 21.8	**0.006***
Progressive sperm motility%	57 ± 17	30 ± 33	14 ± 13	26 ± 15	**<0.001***
Sperm normal morphology %	38 ± 20	28 ± 37	22 ± 11	4 ± 2	**<0.001***
P value ≤ 0.05 is significant for the one-way ANOVA test*. P value ≤ 0.05 is significant for the Chi-square test**.					

There was no significant difference in ROS levels among the two groups (Astheno & Normo) (*P* value = 0.6. There was no significant difference in ROS levels among the two groups (Terato & Normo) (*P* value = 0.2). as shown in Table2

Table 2: ROS levels in the seminal fluid samples of oligospermia, Asthenospermia, & Teratospermia patients compared to the samples of Normospermia patients.

Variable	Sperm classification	Number	Mean	P value
ROS	Normospermia Oligospermia	21 7	400.4 505.5	0.7
ROS	Normospermia Asthenospermia	21 7	400.4 506.2	0.6
ROS	Normospermia Teratozoospermia	21 15	400.4 259.8	0.2

Pearson's rank correlation coefficient test was consulted to investigate the relationship between ROS and (sperm concentration, progressive sperm motility, Normal Sperm Morphology, number of oocytes, and mature oocytes) in the studied samples. It has been found that there is no relationship between ROS and five other parameters as follows: (P value = 0.5, r = 0.09), (P value = 0.9, r = 0.009), (P value = 0.9, r = 0.003), (P value = 0.09, r = 0.243) and (P value = 0.07, r = 0.261) regarding sperm concentration, progressive sperm motility, Normal Sperm Morphology, number of oocytes, and mature oocytes respectively, as shown in Table. 3.

Table 3: The relationship between ROS & sperm parameters and oocytes numbers.

First variable	Second Variable	R value	P value
ROS	Sperm Concentration	0.09	0.5
ROS	Progressive Sperm Motility	0.009	0.9
ROS	Normal Sperm Morphology	0.003	0.9
ROS	Number Of Oocytes	0.243	0.09
ROS	Mature Oocytes	0.261	0.07
P value ≤ 0.05 is significant for Pearson's rank correlation coefficient test*.			

Pearson's rank correlation coefficient test was consulted to investigate the relationship between ROS and (the fertilized oocyte (2pn), the fertilization rate, the total number of embryos, and the number of transferred embryos) in the studied samples (50 participants). It was found that there is no relationship between ROS & the four comparison groups) (P value = 0.4, r = 0.130), (P value = 0.2, r = - 0.183), (P value = 0.5, r = 0.096) and (P value = 0.4, r = 0.134) regarding the fertilized oocyte (2pn), the fertilization rate, the total number of embryos, and the number of transferred embryos respectively as shown in Table 4

Table 4: The relationship between ROS & (fertilized oocyte (2pn), fertilization rate, number of embryos).

First variable	Second Variable	r value	P value
ROS	Fertilised Oocyte (2pn)	0.130	0.4
ROS	Fertilisation Rate	- 0.183	0.2
ROS	Total Number of Embryos	0.096	0.5
ROS	The Number of Transferred Embryos	0.134	0.4
P value ≤ 0.05 is significant for Pearson's rank correlation coefficient test*.			

Pearson's rank correlation coefficient test was performed to investigate the relationship between ROS and ICSI outcomes, the number of good embryos, the cleavage rate, the pregnancy ratio, and the oocyte number, in the studied samples. It has been found that there is no relationship between ROS & ICSI outcomes as follows (P value = 0.07, r = 0.257), (P value = 0.7, r = 0.052), (P value = 0.4, r = 0.118) and (P value = 0.4, r = - 0.111) regarding the number of good embryos, the cleavage rate, the pregnancy ratio, and the oocyte number respectively, as shown in Table. 5

Table 5: The relationship between ROS & the number of good embryos and cleavage rate.

First variable	Second Variable	r value	P value
ROS	Number of Good Embryos	0.257	0.07
ROS	Cleavage Rate	0.052	0.7
ROS	Pregnancy Ratio	0.118	0.4
P value ≤ 0.05 is significant for Pearson's rank correlation coefficient test*.			

Table.6 illustrates the primary ICSI outcomes among the four groups included in the study according to sperm classification (Norm (N=21), Oligo (N=7), and Astheno (N=7), Terato (N=15)). ANOVA test was done, and there was no significant difference in the retrieved oocytes among the four groups (*P* value=0.3). Similarly, there was no significant difference in the MII oocytes for (Normo mean ± SD=8.9±5.6), (Oligo 5.9±2.5), (Astheno 8.3±6.8), and (Terato participants as (*P* value =0.6). Likewise, there was no significant difference in the fertilization rate (*P* value =0.2), cleavage rate (*P* value =0.8), and 2PN (*P* value =0.6) among the four groups (Norm, Oligo, Astheno, Terato).

A chi-square test was done to investigate the difference in the pregnancy ratio between the four groups, and it was found that there was no significant difference in the pregnancy ratio (*P* value =0.5). Participants with Normospermia samples who underwent ICSI procedure yielded 18 positive pregnancies out of 21 participants. In comparison, participants with Oligospermia had four positive pregnancies out of 7 participants. Participants with Asthenospermia who underwent ICSI had only two positive pregnancies out of seven participants. Finally, patients with Teratozoospermia who underwent an ICSI procedure had seven positive pregnancies out of 15 participants,

Table. 6.: ICSI outcome in Normo, Oligo, Astheno, &Terato patients.

Variables	Normospermia N=21	Oligospermia N=7	Asthenospermia N=7	Teratozoospermia N=15	P value
Retrieved oocytes	11.5±6	6.3±2.4	10±9	9.5±6.8	0.3
MII oocytes	8.9±5.6	5.9±2.5	8.3±6.8	7.8±5	0.6
2PN	4.8±3.1	3.4±1.6	3.7±2.5	3.8±2.7	0.6
Fertilisation rate	72.9±19	88.6±18.6	86±13	78±21	0.2
Cleavage rate	84.4±22.7	94±10.3	85.7±37.8	88±16.5	0.8
Pregnancy Ratio	Pregnancy:61.9%	pregnancy:57.1%	Pregnancy:28.6%	Pregnancy: 46.7%	0.5

P value ≤ 0.05 is significant for the one-way ANOVA test*.

P value ≤ 0.05 is significant for the Chi-square test**.

Discussion

ICSI was introduced in the early nineties (1992) and has drastically changed the treatment of advanced cases of male infertility. The performance of ICSI procedures has expanded and revolutionized worldwide to treat infertile couples and not merely treat male infertility, which was initially developed for it [19]. Therefore, the development of the

procedure makes it necessary to investigate the efficacy, safety, and factors that might influence ICSI outcomes, such as ROS, which are the main concern in the current study.

Couples included in the study have similar sociodemographic variables, such as weight, age, partners' age, and years of infertility, and similar ovarian reserve features, the total number of retrieved oocytes, number of transferred oocytes, mature MII oocytes, and the various grades embryos were similar among the participants, and that was done to limit the effects of any confounding factors that might affect ICSI outcome and concentrate mainly on male factors of infertility.

In the current study, ICSI outcomes were compared according to the results of SFA, which were divided into four main groups (Normospermia, Oligospermia, Asthenospermia, & Teratospermai). It is worth mentioning that there was a significant difference in sperm features among the four groups: 1- sperm concentration (P value = 0.006) 2- progressive sperm motility (P value <0.001) 3- normal sperm morphology (P value <0.001).

The study aims to investigate the relationship between ROS and sperm features, the results of the present study have shown that there are ROS levels in the semen of the participants did not affect the sperm parameters (sperm concentration (P values = 0.5), progressive sperm motility (P values = 0.9), and normal sperm morphology (P values = 0.9)) and it is almost the same among the four included groups (Normospermia, Oligospermia, Asthenospermia, Teratospermia).

However, the results from the present study contradict a prospective clinical study that investigated the relationship between (ROS) production and sperm morphology among infertile men [20]. The prospective clinical study has concluded that sperm ROS production was inversely related to the proportion of normal sperm morphology and borderline morphology. Additionally, ROS production was related directly to the proportion of sperm amorphous heads, faulty acrosomes, and mid-piece defects.

The prospective study has concluded that high ROS concentration is associated significantly with reduced sperm concentration and the percentage of motile sperm in semen. This result disagrees with the present study results that show no association between ROS and sperm features. The present study included only 8 participants (16%) with high ROS levels (≥ 400) and 42 participants (84%) with low ROS levels (≤ 400), while in the prospective study, 84% of the included individuals had high ROS levels, and 85% of included individuals had low ROS levels. These differences might explain the contradiction in the results of the two studies due to the lower sample size recruited in the current study.

According to a study conducted by (Agarwal), reactive oxygen species are inversely connected with classical sperm characteristics such as concentration, motility, and morphology. This is not the same result as the current study, which found no significant association between ROS and sperm parameters (see Table3). This disparity could be attributed to (Agarwal's) usage of a lower ROS cut-off level of 91.9 RLU/s.

A study was performed by [21] to compare the concentration of reactive oxygen species (ROS) and total antioxidant (TAS) in seminal plasma among two groups of IVF and ICSI patients to determine these effects on sperm quality and IVF/ICSI outcome. The study included 48 participants (26 underwent IVF, & 22 underwent ICSI), while the present study included 50 couples who underwent ICSI procedures only. The sperm parameters were evaluated one-hour post ejaculation (sperm morphology, maturity, & DNA strand breaks). Some of the interesting findings, there was a negative correlation between seminal plasma ROS concentration and sperm vitality (r =

−0.111, P = 0.453) and morphology (−0.141, P = 0.340) [13]. However, in this study, we measured sperm concentration in a million/ml, progressive sperm motility%, & sperm morphology % for sperm parameters. It was found that there is no relationship between ROS and sperm parameters (P value = 0.5), (P value = 0.9), (P value = 0.9), respectively.

The present study compared sperm parameters according to normal ROS distribution (400 was the cut-off point, 42 participants ≤ 400, & 8 Participants ≥ 400), and there was no difference between the two groups in all measured sperm parameters sperm concentration million/ml (P value = 0.3), progressive sperm motility % (P value = 0.1), & sperm normal morphology % (P value = 0.4). The contradiction in this result can be explained by the fact that the collected semen was washed before the ICSI procedure, which diminishes ROS concentration from the sperm. In contrast, in the mentioned study, ROS concentration might refer to the unwashed seminal plasma (before washing the samples). Furthermore, in the mentioned study, the fertilization rates were comparable in both groups (IVF & ICSI) (67. 26 vs 67.26), while the relationship between ROS concentration and fertilization rate was n. In contrast, (r = − 0.029, P = 0.045) contradicts our findings as we found no correlation between ROS and the fertilization rate (P value = 0.2, r = - 0.183). Despite the differences in the methodologies and some findings from the two studies, it was concluded in the mentioned study that ROS concentration hurts spermatozoa quality but doesn't affect the fertilization rate in IVF/ICSI, which is a comparable result to the present study.

This may have been due to the small sample size; a study with a larger sample size and longer duration could have produced meaningful results.

There were some limitations that countered the current study and resulted in a lower sample size: first, since we were collecting semen samples from patients who were attending the fertility center/Al-Sader Medical City sometimes the center was shut down due to financial issues, thus lower sample size was collected. the second limitation is the short duration of the study (6-9 months only).

Conclusion

The current study concluded that: The Normozoospermia patients group had a higher pregnancy rate than the other three groups. The ICSI technique is a successful way to overcome the ROS presented in the semen plasma. There was a negative correlation between ROS and (the motility of Sperms, Fertilization rate) .

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Association Of IL-6, And IL-10 Gene Snps In Childhood Febrile Seizure

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Abstract

Background: Febrile seizure are typically defined as convulsions=that-occur in children, between/6 months to 5years, who have a fever of more,,than"38 degrees Celsius, that is not associated with an intracranial' reason such as an infection, ,head .injury, or epilepsy. It is also known as the immature brain's response to fever, which is age-dependent. As a child's brain develops, there is an increase in neuronal excitability which puts the child at the risk of febrile seizures.

Aims: the aim of the present study is to find out the association of Inflammatory cytokines (IL-6, IL-10) SNP with the onset of childhood febrile seizure. **Method-** Blood samples from patients with childhood febrile seizure will be collected in a sterile condition, and the association of SNP for both IL-6 (-597) G/A, and IL-10 (-819) C/T with disease susceptibility will be studied by using allele specific PCR. **Results:** The case-control study of 40 patients with Febrile seizure and 40 control without Febrile seizure has revealed that a substantial difference in the frequency distribution of IL-6 genotypes between the patient group and the control group where ($p = 0.041$). Besides, there was no discernible variation in the frequency distribution of IL-10 genotypes and alleles. ($p > 0.05$); therefore, none of genotypes or alleles can be regarded as risk factor or protective factor. **Conclusion:** The present study has concluded that IL-6(-597) G/A, (rs:1800797) single nucleotide polymorphism (SNP) was associated with Febrile seizure susceptibility, and GG, genotype considered as, risk factor, while genotype GA act as protective factor. However, it refers that the IL-10-819C/T (rs:1800871), genes may not represent the Febrile-seizure-associated genetic risk factor.

Keywords: FSE'febrile status epilepticus, SNP'Single nucleotide polymorphisms, SCN1A' Voltage-gated sodium channel alpha subunit 1, GABA'Gamma-aminobutyric acid receptor, IL-1RA'IL-1 receptor antagonist, LE'Limbic encephalitis, COX2' Cyclooxygenase2, BBB'Blood-brain-barrier, SFS'Simple febrile seizure , CFS'Complex febrile seizure.

INTRODUCTION

Febrile seizures (FSs) are typically defined as convulsions observed in children, between the ages of 6 months and 5 years, who are experiencing a fever of more than 38 degrees Celsius, and which are not linked to an intracranial cause such as infection, head injury, or epilepsy(1). The occurrence of FSs is observed in the community, ranging between 2% and 5%, with a recognized family history. An

epilepsy diagnosis is made in a small number of individuals(2). The majority of FSs occur in children aged 12 to 18 months. It is hypothesized that the developing brain possesses a low seizure threshold during this early age and is particularly susceptible to sudden increases in body temperature. The likelihood of experiencing FSs increases when combined with specific environmental factors and genetic predisposition(3). FSs are considered a significant neurological phenomenon in children under the age of five in Western Europe and the United States, with an assumed prevalence of 2-5% among children aged 6 months to 5 years(4). While FSs can develop in any ethnic group, they appear to be more common in Asian children, with prevalence rates of 5-10% among Indian children and 6-9% among Japanese children(5). In addition to spontaneous seizures and epilepsy, induced seizures are notably common in resource-limited regions within tropical areas, largely due to the high incidence of diseases affecting the central nervous system, such as neurocysticercosis, cerebral malaria, TB, schistosomiasis, and HIV(6). Children possessing the HLA-B5 antigen have a 4.4 times higher likelihood of experiencing febrile convulsions compared to those lacking the antigen, reflecting a substantially elevated relative risk (7).

The IL-6 gene's promoter and coding regions display a variability that may influence the cytokine's secretory response and become associated with elevated serum IL6 concentrations under specific clinical conditions(8). The Interleukin-6 gene is located on chromosome 7 (p21-24) and might contribute to the risk of febrile seizure development by promoting increased IL-6 secretion, resulting in an imbalance between pro- and anti-inflammatory cytokines and ultimately leading to febrile convulsions (9). The most notable SNPs in the IL-6 gene include -174G/C (rs1800795), -597G/A (rs1800797), and -572G/C (rs1800796). Certain SNPs have been identified as impacting the transcriptional regulation of the IL-6 gene (10). While the human IL-10 gene is situated on 1q31-32, a genomic region associated with various autoimmune disorders, including FSs, IL-6 plays a critical role in the host's response to infection by inducing fever, leukocytosis, and the production of acute-phase proteins (12).

Therefore, the aim of the present study is to investigate the association between single nucleotide polymorphisms (SNPs) in the inflammatory cytokines IL-6 and IL-10 and the occurrence of childhood FSs.

Patient and Methods

A case control study was conducted on 40 patients with FSs and 40 control children whose ages ranged from 5 months to 5 years to determine the association of SNP for both IL-6 (-597) G/A(rs1800797), and IL-10-819C/T(rs1800871) with FS. The sociodermographic data are age, gender and family history of babies.

Under the supervision of a specialist pediatrician, samples were taken from Al-Zahra Maternity and Pediatric Hospital and outpatient clinics for the time period of 8 October 2022 to 5 February 2023. In these locations, cases were diagnosed by pediatricians. The control group has been selected due to their regular calcium levels, normal complete blood counts, and general health. About 2 mL blood sample was collected from each group by sterile syringe under aseptic condition; the blood was collected in

EDTA tube, then after the total DNA have been extracted, and allele specific PCR have been done, the SNP of IL-6 and IL-10 have been studied in both group

1. **Genomic DNA Extraction:** The blood samples' genomic DNA was extracted by using Frozen Blood by FavoPrep DNA kit extraction /Korea. It is done according to the instruction manual. The purity of the DNA was determined by reading 260 and 280 nm absorbance measured with a Nano-drop spectrophotometer (THERMO, USA).
2. **ARMS PCR Technique:** an amplification-refractory mutation system polymerase chain reaction technique (ARMS-PCR) assay was performed for genotyping and detection of IL-6 and IL-10 gene SNP in FS patients and control group. This method was done according to the procedure described by Qian *et al.*, (2017); Ahmed *et al.*, (2019) as in the following steps:
3. **Preparation The Primers Suspension:** The lyophilized primers were dissolved in deionized distilled water to create a stock solution with a concentration of 100 pmol/l, as directed by the manufacturer, to make the primers**,** as shown in **Table-(1**)

Table (1) Sequences of primers used for allele specific PCR.

Gene	S	P
IL-6(-597) C	**F** **F** **R**	**4**
IL-10(-819) C	**F** **F** **R**	**2**

4. **ARMS- PCR Master Mix Preparation**

An ARMS-PCR master mix was prepared by using (**GoTaq® G2 Green Master Mix kit**); it has done two reactions for each samples according to company instructions as in the following tables:

1- IL-6-597G/A (rs1800797) ARMS- PCR reaction Mix as show in table (2):

Table (2): IL-6-597G/A (rs1800797) ARMS- PCR reaction Mix

ARMS PCR Master mix	V
DNA template	8
Forward primers (10pmol)	2
Common Reverse Primer (10pmol)	2
G2 Green Master Mix	1
Total volume	2

2- IL-10-819C/T(rs1800871)ARMS- PCR reaction Mix as show in table (3):

Table (3): IL-10-819C/T(rs1800871)ARMS- PCR reaction Mix

ARMS PCR Master mix	V
DNA template	8
common Forward primer (10pmol)	2
Reverse Primers (10pmol)	2
G2 Green Master Mix	1
Total volume	2

Following that, the PCR master mix components mentioned in the table above were moved to an Exispin vortex centrifuge and centrifuged at 3000 rpm for 3minutes. The samples were then put in a PCR thermocycler (BioRad. USA).

Results

The frequency distribution of IL-6 genotypes was significantly different between the patient group and the control group.(*p* =0.041). Genotype GG was more common in the patient compared to the control group., 28 (70.0 %) versus 18 (45.0 %), respectively, thus it acts as a risk factor with an etiologic fraction of 0.40 and odds ratio of 2.85. Genotype GA was less common in the patient group than in the control group, 10 (25.0 %) versus 21 (52.5 %), respectively, thus it acts as a protective factor with a preventive fraction of 0.43 and odds ratio of 0.30,Genotype AA was equally prevalent in both the patient and control groups; hence, it cannot be a risk or protective factor. Moreover, there was no discernible variation in the frequency distribution of alleles between the patient group and the control group (p= 0.092), they cannot constitute risk or protective factors, as shown in **Table (4) below:**

Table(4): Comparison of IL-6 frequencies of genotypes and alleles in the patient group versus the control group

IL-6 G/A	**Patients group *n* = 40**	**Control group *n* = 40**	***P***	**OR**	**95 % CI**	**EF**	**PF**
Genotypes							
GG, *n* (%)	28 (70.0 %)	18 (45.0 %)	0.041 C *	2.85	1.14 -7.15	0.40	---
GA, *n* (%)	10 (25.0 %)	21 (52.5 %)		0.30	0.12 -0.78	---	0.43
AA, *n* (%)	2 (5.0 %)	1 (2.5 %)		2.05	0.18 -23.59	0.34	---
Alleles	**Patients group *n* = 80**	**Control group *n* = 80**	***P***	**OR**	**95 % CI**	**EF**	**PF**
G, *n* (%)	66 (82.5 %)	57 (71.3 %)	0.092 C NS	1.90	0.90 -4.04	0.25	---
A, *n* (%)	14 (17.5 %)	23 (28.8 %)		0.53	0.25 -1.12	---	0.25

significant at $p \leq 0.05$

Figure-1. Image of IL-6, SNP G/A, and 597 gene polymorphisms analysed by ARMS-PCR run on 2% Agarose gel electrophoresis, where stand for marker (1500- 100bp).

■ comparison the genotype and allele frequencies of IL-10 in the patient group and the control group is shown in **table-5**.Between the patient group and the control group, there was no discernible variation in the frequency of Genotype distribution and alleles.($p > 0.05$); therefore, none of genotypes or alleles can be regarded as risk factor or protective factor

Table-5: Comparison of IL-10 frequencies of genotypes and alleles in the patient group and the control group

IL-10 C/T	**Patients group *n* = 40**	**Control group *n* = 40**	***P***	**OR**	**95 % CI**	**EF**	**PF**
Genotypes							
CC, *n* (%)	2 (5.0 %)	1 (2.5 %)	0.539C NS	2.05	0.18-23.59	0.34	---
CT, *n* (%)	36 (90.0 %)	38 (95.0 %)		0.47	0.08 -2.75	---	0.35
TT, *n* (%)	2 (5.0 %)	1 (2.5 %)		2.05	0.18-23.59	0.34	---
Alleles	**Patients group *n* = 80**	**Control group *n* = 80**	***P***	**OR**	**95 % CI**	**EF**	**PF**
C, *n* (%)	40 (50.0 %)	40 (50.0 %)	1.000 C NS	1.00	0.54 -1.86	0.00	0.00
T, *n* (%)	40 (50.0 %)	40 (50.0 %)		1.00	0.54 -1.86	0.00	0.00

NS: **not significant**

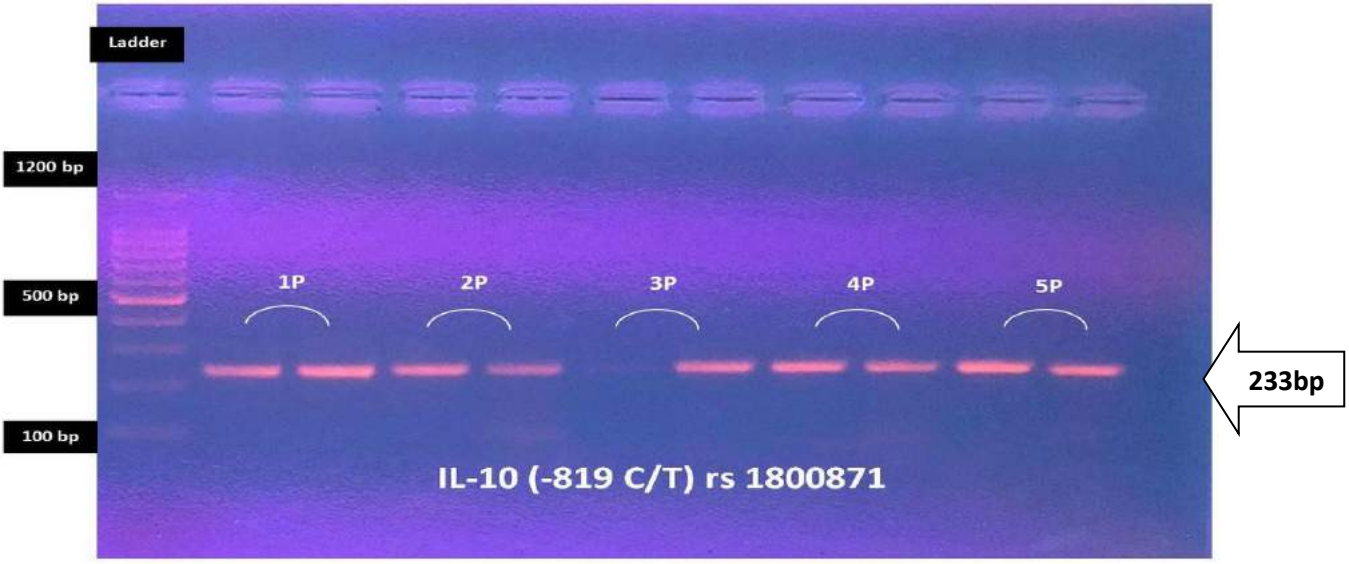

Figure 2. Image of IL-10, SNP C/T, and 819 gene polymorphisms analysed by ARMS-PCR run on 2% Agarose gel electrophoresis. Where stand for marker (1500-100bp).

Correlations of IL-10 and IL-6 genotypes to serum levels of IL-10 and IL-6 are shown in table-6. There was no significant correlation (p>0.05).

Table -6: Correlations of IL-10 and IL-6 genotypes to serum levels of IL-10 and IL-6

Characteristic	ELISA IL-10		ELISA IL-6	
	R	***P***	***R***	***P***
IL-10 C/T	-0.015	0.895 NS	0.068	0.547 NS
IL-6 G/A	-0.122	0.280 NS	-0.072	0.528 NS

NS: not significant

Discussion

The current results have shwonhthat the **IL-6-597G/A(1800797)** polymorphism may be significantly associated with susceptibility to FS. They were concordant with those of Nur et al (13) who reported that the presence of the G allele or the GG genotype at −174 and the GG genotype at −572 positions of the interleukin-6 promoter regions constituted risk factors for developing FSs in Turkish children. These findings support the hypothesis that a positive genotype predisposes individual to febrile seizure.

On the contrary, Shahrokhi et al. [14] studied IL-6 gene (−174 and +565) SNPs on genomic DNAs of 90 Iranian children with FSs, compared to 139 healthy subjects. They reported that the presence of the G allele or the GG genotype at +565 position reduced the risk of FS, while the A allele at +565 position of the promoter regions was a constituted risk factor for developing FS.

Concerning IL-10 SNP and disease susceptibility, IL-10 acts through suppression of pro-inflammatory cytokine production. Ishizaki et al reported that the frequencies of the IL-10 592C allele and 1082A/819C/592C haplotype were significantly decreased in patients with febrile seizure. Their hyperthermia-induced seizure models in immature animals showed that administration of IL-10 increased the seizure threshold temperature, and the authors concluded that IL-10 is genetically associated with

febrile seizure.(15). In previous study reported that the -592C allele and ACC haplotype in the promoter region of the *IL10* gene are significantly associated with resistance to FS. In experimental hyperthermic seizures in immature rodent models, IL-10 plays an anticonvulsant role(16).

Furthermore, the current study detected that IL-10 and IL-6 genotypes were not significantly correlated with IL-10 and IL-6 serum levels, (p>0.05), Such a result does not exclude the impact of SNP on serum level of standard cytokines**.**

Conclusion

1- The current study has concluded that there was a positive association of IL-6 SNP in patient group with febrile seizure.

2- There are also a significant difference in the distribution frequency of genotypes between the patient group and the control group, (p =0.041), and IL-6 SNP Genotype GG acts as a risk factor, while Genotype GA acts as a protective factor in FS.

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The Effects of Intraoperative Placement of Tetracycline, Tetracycline + Gelatin Sponge, and Placebo on Postoperative Dry Socket Incidence After Mandibular Molar Extraction: (A Comparative Prospective Study)

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Abstract

Background: The aim of the study evaluation 0f tetracycline, tetracycline plus gelatin sponge efficacy in lowering dry socket incidence among patients experienced extraction procedure for mandibular molars compared to control group..

Material and Methods: The sample was divided into three groups each group have 30 patients (34 male and 56 female) :

- Group A (patients dealt without intra-socket tetracycline) in which only applying figure of 8 suturing and dressing adhesive material for sockets.
- Group B (patients managed with intra-socket tetracycline alone) in which patients managed after extraction with tetracycline solution, figure of 8 suturing and dressing adhesive material.
- Group C (patients managed with intra-socket tetracycline plus gelatin sponge complex) in which patients managed after extraction with tetracycline-gelatin sponge vehicle, figure of 8 suturing and adhesive dressing material.

Results: Dry socket following extraction was encountered in 4 female patients, with an incidence of 4.4%. Group A reported the highest number.

Conclusions: In spite of the limits of this clinical trial, the placement of tetracycline as intra-socket medicament serve in a good choice for treating extracted socket, by reducing bacterial load that will result in lowering the possible chances of infection thus relieving pain, on the other hand the Ora-aid dressing material serve a good way accompanied with suturing in avoiding dry socket occurrence.

- **(Thai Clinical Trial Registry TCTR20230724006).**

Keywords: Dental extraction, dry socket, dental pain, mandibular molar extraction

INTRODUCTION

Tooth extraction is considered to be the most used procedure which is done by dentists; it is often associated with trismus, swelling and pain. As a result of extraction it will cause pain which differs from one patient to another and it differs in the same patient among his or her other teeth [1].

Complications are events that tend to increase the morbidity, beyond what could be expected from procedure under normal situations. They could range from common ones, like dry socket, to uncommon and serious ones [2]. postoperative complications, like mouth opening limitation, swelling, dry socket, pain and inferior alveolar nerve injury, however, may be associated with the extraction of an impacted third molar [3]. Further, dry socket is a post-extraction socket where some or all of the bone within this socket, or around it, are exposed in the days following the dental extraction, because the bone having not been covered by an initial and persistent blood clot or having not been covered by a layer of vital, persistent, healing epithelium [4].

The basic treatment for dry sockets is to irrigate out the food particles or bacterial material by using normal saline solution or chlorhexidine and then occupy the socket with a medicament [5]; the operator might suture the lesion for retaining the medicament or blood clot. The objective of treating a dry socket is to optimize the lesion so that the socket could optimally be capable of forming an enduring layer of epithelium that covers the exposed bone inside the socket and around the socket occlusal perimeter [6].

Dressings the sockets is the most useful healing medicaments including broad spectrum antibiotics specifically tetracycline and clindamycin. Gelatin-sponge, are used as clot stabilizing sockets [7]. Tetracycline is a bacteriostatic antibiotic which acts active against Gram + and Gram – bacteria, by blocking the protein synthesis and binding to the ribosomal subunit [8].

The gelatin sponge (Gelfoam), as an effective and economical clot stabilizer, is purified porcine skin gelatin without which the sponge would simply slough from the socket [9]. However, as an attachable intraoral wound dressing, the Ora-aid presents a reasonable advantage as the manufacturer illustrates that it:

1. protects intraoral wounds from food, bacteria, and cigarette smoking,
2. aids in hemostasis,
3. protects suture thread from tongue irritation,
4. is a self-adhesive with saliva and strong adhesion,
5. is easy to cut into different shapes\sizes, and
6. contains vitamin E.

MATERIAL AND METHODS

This clinical prospective comparative study was conducted from December 2021 to August 2022 in the College of Dentistry Teaching Hospital, Department of Oral and Maxillofacial Surgery/oral surgery Unit/ University of Baghdad and Al-Shaab Specialized Dental Center. A total of 90 Iraqi patients aged 18-60 years (56 females and 34 males) met the eligibility criteria and enrolled in this study. The sample was divided into three groups:

- Group A includes patients treated without intra-socket tetracycline and to which only was a figure of 8 suturing and dressing adhesive material for sockets applied.
- Group B includes patients treated with intra-socket tetracycline alone and dealt after extraction with tetracycline solution, a figure of 8 suturing and dressing adhesive material.
- Group C includes patients treated with intra-socket tetracycline plus gelatin sponge complex and managed after extraction with tetracycline-gelatin sponge vehicle, a figure of 8 suturing and adhesive dressing material.

Ethical Approval

The Research Ethics Committee at the College of Dentistry, University of Baghdad approved the protocol of this study, protocol reference number 416121, and every patient signed an informed consent to participate in

this study. The Thai Clinical Trial Registry (TCTR) assigned this study registration number **TCTR20230724006**.

Eligibility criteria

These criteria include:

1. patients over 18 years of age.
2. absence of general medical contraindications for oral surgery procedures like jaws pathology, uncontrolled diabetes, uncontrolled hypertension).
3. mandibular molar teeth indicated for extraction.

Exclusion criteria

These criteria include:

1. patients who were immune-compromised with systemic disease, pregnant or lactating women.
2. patients with acute, chronic infection.
3. teeth with peri-apical cyst.
4. patients allergic to tetracycline.
5. poor compliance.
6. mandibular molars requiring surgical extractions (either sectioning or flap releasing).
7. impacted mandibular third molar.

Preoperative assessment, clinical and radiological examinations

History

Patients were inquired in details about medical, dental and family history to see if they had any systemic diseases that might affect pain intensity.

Clinical examination

Extraoral

A clinical examination was performed for the patients to evaluate regional lymph nodes, facial profile.

Intraoral

The intraoral examination assessed mouth opening, oral hygiene, and periodontal status. All teeth are inspected for caries and gingival condition, and checking the accused tooth who met the criteria of the study.

Radiographical, periapical radiograph

For some patients, a periapical radiograph was taken for the accused tooth in order to exclude the presence of any lesion patient's preparation. First of all, the extraction procedure was explained to the patients in simple words with the possible intra-operative and post-operative complications. Following the verbal approval of the patients to participate with the current study, they signed a special consent form. This was followed by the application of disposable sterile surgical drapes.

The Extraction Procedure

Block anesthesia for the inferior alveolar nerve along with buccal infiltration for the long buccal nerve was established. After few minutes the anesthetic effect will be secured, a dental probe is utilized to separate the tooth from the surrounding soft tissue, after that the extraction procedure started by mandibular molar forceps for teeth that had grasp with forceps or elevator / chisel for retained roots. Those elevators\ chisels were used to luxate the unrestorable severly damaged tooth / root and gain an reasonable mobility; this is followed by using the lower mandibular molar forceps for extraction if needed and squeezing the socket.

Group A

In the control group, the attached gingiva surrounding the socket was sutured with a figure of 8 suturing technique at the extraction site by using 3\0 black silk sutured via a needle holder followed by dryness of the soft tissue around the extraction site in order to apply the Ora-aid dressing material.

Group B:

In the first study group, the preparation of the tetracycline solution is conducted by the powder of 250 mg tetracycline cap in a disposable cup mixed with 0.5cc of saline solution which are mixed together and converted into a yellowish solution that is drained into a disposable syringe.

After the extraction, a 3\0 black silk is used to close the socket with a figure of 8

suturing technique, followed by the insertion of the previously made tetracycline into the socket by applying it directly to the socket of the extracted molar; following this step a small piece of gauze is used to dry the soft tissue around the extraction site in order to apply the Ora-aid dressing material:

- No tetracycline solution was used to be inserted inside the socket, this mixture was so thick that it could retain inside the socket, along with the sutures and dressing material.
- It was retained for the first day, strictly the first 2 hours after extraction as the Ora-aid retained 2 hours and then they slough. From the 2 hours to the rest of the first day, the patient does not spit/rising the mouth.
- the new thing in this technique is to eliminate the usage of systemic antibiotics as well as pain killers. Although, the uses of broad spectrum tetracycline locally to the supposed source of pain and decreasing the chances or percentage of inflammation. Group C:

In the 2nd study group, the preparation of the tetracycline-gelatin sponge complex is prepared by putting a 0.5 cc of saline solution in a disposable cup then adding the powder of 250 mg tetracycline capsule, after mixing both of them the gelatin sponge is added to the tetracycline solution and mixed until the gelatin sponge is fully saturated with the tetracycline solution.

The empty socket was dried by using a small piece of cotton, then the application of the previously made tetracycline-gelatin sponge, after that figure of 8 suturing technique is although used followed by drying the soft tissue at the extraction site in order to apply the Ora-aid dressing material.

Instructions and Postextraction Care

1. The patient is instructed not to remove the Ora-aid dressing material neither disrupt the sutures.
2. The patients were instructed not to rinse their mouth at the day of extraction, starting in the second day with gently rinsing with warm salty water for 30 seconds every morning after breakfast. During the daytime rinsing every 3 hours for 3 days with approximately teaspoonful of salt dissolved in a cup of warm water.
3. The patients were informed not to eat for 2 hours after extraction to allow blood clotting not to be disturbed. Then, they should begin with a liquid diet, always cool and not to take any hot foods or liquids during the first 24 hours.
4. Begin brushing of teeth one day following extraction, it is important to brush all the teeth and gently near the extraction site for proper healing that plaque and food are not allowed to collect near the extraction field.
5. after the 7th day the patient instructed to attend for suture removal.

Follow up and Data Collection (the answers will be below the questions)

When the patients had signs and symptoms of dry socket, which is dedicated by clinical examination, they were treated by conventional protocol (socket debridement, irrigation with normal saline solution, since it`s already sutured, a dressing material (Ora-aid) is used over the sutures to protect the blood clot from dislodgment, and take medications:

1. Co-amoxiclav 625 mg tablet three times per day for 5 days.
2. Azythromycine 500 mg tablet one time per day for 3 days for those who have pencilline allergy.
3. Metronidazole 500 mg tablet three times per day for 5 days.
4. Acetaminophen 500 mg taken on need.
5. 3.1 Results

Ninety patients aged from 18-60 years with an average of 30.88 years and standard deviation (SD) ± 9.82 contributed to this study.

Patients enrolled in the study were 45 patients < 30 years and the same number was ≥ 30 years was with no significance for age with a P-value of 0.875. This study included 32 male and 58 female patients (35.56% and 64.44% respectively) with no significance the day before extraction.

Table (1): Distribution of teeth among groups.

Tooth number	Group No. (%)			Total No. (%)	P-value
	A	B	C		
#6	7 (23.33%)	8 (26.67%)	12 (40%)	27 (30%)	0.585
#7	10 (33.33%)	10 (33.33%)	6 (20%)	26 (28.89%)	
#8	13 (43.33%)	12 (40%)	12 (40%)	37 (41.11%)	

Dry socket following extraction was encountered in 4 female patients, with an incidence of 4.4%. Group A reported the highest number (2 cases).

Table (2) : Distribution of dry socket incidence among groups.

Groups	D	T
A	2	#
B	1	#
C	1	#
Total percentage and number	4	4

Discussion

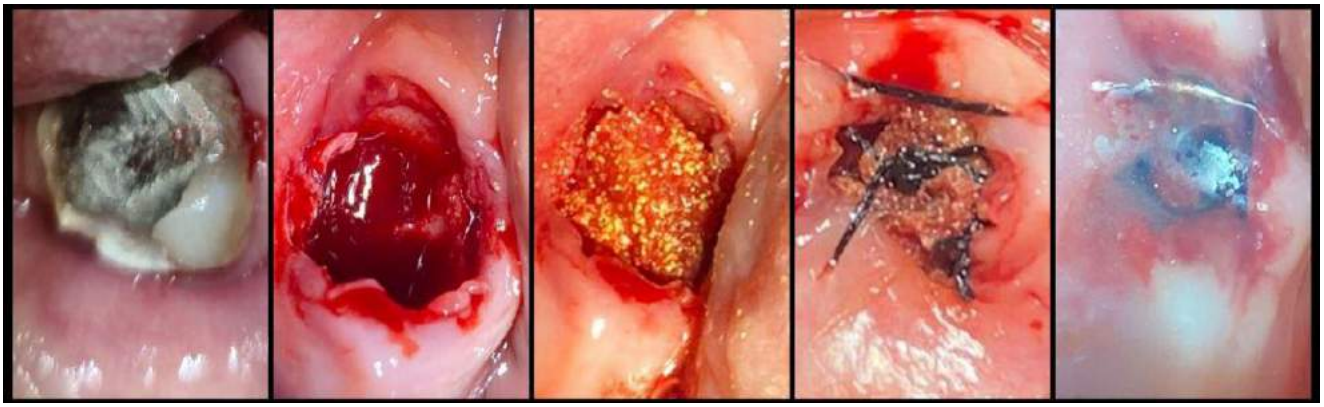
The research has registered a **significant difference** in group C compared to group A (**0.018**) and group B (**0.014**); these findings may be explained by the presence of gelatin sponge material which aim to stabilize the blood clot with the aid of both suturing material and Ora-aid dressing material, tetracycline bacteriostatic effect on bacterial load and the closure of the wound with figure of 8 suture. **No significant difference** scored between group B compared to group A (1.00); this may contributed to the tetracycline low effect in changing the results.

Patil et al., 2021 declared the same findings of this study, the comparison between tetracycline and gelatin sponge and control group showed statistically **significant difference** between the groups (0.009, 0.001, and 0.017) respectively, and the comparison between tetracycline alone and control group demonstrated **no significant difference** (0.031 and 0.017) respectively [10].

However, the delivery of tetracycline as powder and/or suspensions, may be transported via gauze or gelatin sponge, although it has been suggested that practically adding anything into the alveolus, including plain gelatin sponge, will result in the improvement in dry socket symptoms which pain is one of these symptoms [11].

Conclusion

Age does not affect the dry socket incidence, but gender seems to be influenced, four dry socket cases among female patients while 0 cases for male patients.



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Association of Interleukin-17 and ACCP levels with Rheumatoid arthritis patients and Control Groups

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Abstract

Background: Rheumatoid arthritis (RA) represents the prevailing form of chronic inflammatory polyarthritis, characterized by an autoimmune response directed against citrullinated antigens and subsequent synovial joint destruction. The susceptibility to RA appears to be influenced by a complex interplay between a specific immune response to various environmental factors and a favorable genetic predisposition. IL-17 Association with Diseases found to be elevated in various chronic inflammatory conditions including RA especially in cases resistant to anti-TNF therapy.
Aim : To investigate the value of IL-17 and ACCP levels with study groups as well as the association of chronic periodontal disease as an environmental risk factor of RA.
Methods : This case-control study involved a total of 140 participants were enrolled, with 70 individuals meeting specific criteria and serological testing confirming their RA diagnosis, while the remaining 70 served as healthy controls.The study involved the collection of blood samples from the participants. Various measurements and tests were conducted, including the assessment of disease activity using the Disease Activity Score (DAS28-ESR) and erythrocyte sedimentation rate (ESR), detection of RF through latex agglutination, quantification of anti-cyclic citrullinated peptide (ACCP) and interleukin-17 (IL-17) levels via enzyme-linked immunosorbent assay (ELISA).
Results : RA patients exhibited substantially higher values for ESR, RF, ACCP compared to the control group. Also IL-17 substantially higher values for RA patients Notably, the p-values for ESR, ACCP, and IL-17 were 0.0001, 0.02, and 0.0001, respectively, indicating strong statistical significance. patients who had gum problems were 43(61.4 %) while the control group was 9 (12.5%) had a gum problem Statistically, parameter had significant differences (p.value=0.0001).

Keywords: Anti-cyclic citrullinated peptide (ACCP), Disease Activity Score 28 (DAS28), Interleukin-17 (IL-17), periodontal disease, Rheumatoid arthritis.

INTRODUCTION

Rheumatoid arthritis (RA) is the most common type of re-inflammatory polyarthritis in clinical practice, it is an autoimmune disease that develops gradually, and this autoimmune disease with no known cause, characterized by antibodies against citrullinated antigens and immune-mediated destruction of the synovial joints [(1)].About 1% of people have RA, with a

female to male ratio of 2.5/1, the disease can strike anyone at any time, but its age-related increase in incidence ,those in their 40 to 70 at higher risk[2]. Although RA can affect any joint, it is typical to detect involvement of the metacarpophalangeal (MCP), proximal interphalangeal (PIP), interphalangeal, wrist, knee, and metatarsophalangeal (MTP) joints of the toes [3]. Joints that are impacted are swollen and painful, the cervical spine is the only part of the axial skeleton that is often spared, it's typical to feel lousy, stiff in the morning, and worn out[4]. The susceptibility to rheumatoid arthritis (RA) appears to be influenced by a complex interplay between a specific immune response to various environmental factors and a favorable genetic predisposition, infections are believed to play a significant role in triggering autoimmune diseases, often associated with specific microorganisms among the identified environmental factors[5]. RA is characterized by synovial inflammation, swelling (hyperplasia), the production of autoantibodies such as RF and aACPA, as well as the destruction of cartilage and bone (leading to deformity). It also presents with systemic features, including cardiovascular, pulmonary, psychological, and skeletal disorders[6]. Rheumatoid factor (RF) and antibodies against citrullinated proteins (ACPA) are well-recognized autoantibodies that serve as defining features of RA. In individuals with RA, testing positive for RF and/or ACPA (referred to as "seropositive") often indicates a distinct etiology and disease progression compared to those classified as "seronegative [7]. ACPAs are antibodies that recognize antigens containing the non-coding amino acid citrulline, IgG is commonly used in diagnostic tests to evaluate ACPA, and there are also other isotypes of ACPAs, including IgM, IgA, IgG1, IgG2, IgG3, and IgG4, second-generation assays are utilized to detect ACPA, with IgG1 subclass being predominantly involved and responsible for immunological activities through FcR-mediated cell activation. Immune complexes containing ACPA can stimulate the release of TNF by macrophages. Furthermore, ACPA has been shown to directly activate monocytes, leading to cytokine production and complement system activation [8,9] . Around 80% to 90% of RA patients with established disease exhibit ACPAs in their blood when using standard tests, these tests have a specificity close to 90% and are more accurate than RF in diagnosing RA [10]. Function of IL-17 encompasses a group of pro-inflammatory cytokines, IL-17A/F is responsible for inducing neutrophilia, promoting the mobilization of granulocytes through granulopoiesis, facilitating their migration via CXC chemokines, and prolonging their survival in target tissues. It also triggers the production of cyclo-oxygenase-2 (COX-2), nitric oxide (NO), and IL-6 in certain target cells[11,12].IL-17 Association with Diseases, IL-17 has been found to be elevated in various chronic inflammatory conditions including rheumatoid arthritis especially in cases resistant to anti-TNF therapy, psoriasis, cutaneous T lymphoma and multiple sclerosis,polymorphisms in the IL17RB gene which encodes a receptor for IL-17E now known as IL-25 have been linked to asthma [13] . A Role of IL-17 in RA Patients Complicated With Atherosclerosis[14] .

PATIENTS AND METHODS

This study was a case-control investigation conducted on a total of 140 participants were involved, with 70 of them diagnosed with RA, confirmed by rheumatologists using the ACR/EULAR 2010 Criteria and serological testing. The remaining 70 participants served as healthy controls.The data were collected from October 2022 to December 2022. Out of the 70 RA patients, 64 were female and 6 were male, and their ages ranged from 20 to 70. The healthy control group also consisted. A comprehensive questionnaire was used to collect this information.

Inclusion criteria (patients and healthy group)

***Patients group*:** Patients who will be enrolled in the research are thoroughly examined to ensure that they satisfy the precise diagnostic standards necessary for RA all patients between the ages of 20 and 70 who have a rheumatologist-diagnosed inflammatory arthritic condition and get a score of >or =6 on the 2010 ACR/EULAR Criteria and without Alzheimer`s disease or any other auto immmune disease.

Controls group: The number-age-gender was matched with patients apparently healthy individuals without joint discomfort or issues or Alzheimer`s disease or any auto immune disease and those without a family history of RA.

Exclusion criteria (patients and healthy group)

- Patients with other autoimmune diseases, systemic lupus erythematosus, Bachet disease, ankylosing spondylitis and multiple sclerosis
- Exclusion of Alzheimer's disease.
- patients over the age of 70 and those under the age of 20.

Samples Collection

Blood samples

In this study venipuncture was used to obtain 5 ml of blood from each patient and healthy control, 3 ml of this blood were then separated by centrifugation and a serum sample was divided into 2 aliquots in an Eppendorf tube after that isolated and stored at (-20°C) until it was needed (ELISA test) mean while 1.6 ml of blood was added to 0.4 sodium citrate to measure the erythrocyte sedimentation rate (ESR).

The diagnostic kits and their companies used in this study list in table No.1

Table No.1: The diagnostic kits and their companies

No.	Kits	Catalogue number	Company	Origin
1	Human anti-cyclic citrullinated peptide (ccp) ELISA kit	SL0154Hu	Sun long	China
2	Human interleukin 17 (IL -17) ELISA kit	SL 0978Hu	Sun long	China
3	Rheumatoid factor titer (ichroma II kit)		Spinreact	Spain

Ethical approval

The University of Kufa's College of Medicine's ethics committee gave its approval to this work. Additionally, approval from the Rheumatology Unit of Al-Sadr Medical City was received prior to the research project's start, as well as informed consent from each participant. All patients were informed about the study and gave their consent for researchers to collect a blood sample and complete a questionnaire for them.

Statistical analysis: Data was processed using Statistical Package for the Social Sciences (SPSS) version 26 for Windows (GraphPad Software, San Diego, California, USA) for statistical analysis.Used to compare the means between two groups, a T-test , while ANOVA was used for comparisons among multiple means. Statistical significance was defined as a p-value of <0.05, and high significance was considered if the p-value was <0.001. Chi-square (χ^2) test was utilized to compare two categorical variables.

RESULTS

In comparison of parameters between patients and controls, all inflammatory indicators were found to be higher in patients compared to the controls group these included heightened values for ESR (31.01), anti CCP (7.76) and IL-17(13.05) versus the ESR in control group was (12.13), Anti CCP was (5.57) and IL-17 was (6.25) these results demonstrate a statistically significant difference ($p < 0.05$).

Based on the disease activity score (DAS) 70 participants patients were divided into four groups remission (25 patients), mild (20 patients), moderate (20 patients) and severe (5 patients) the results of the correlation of parameters are shown in Table No.5. There are significant differences (p value 0. 001) of the concentration of ESR according to DAS-ERS the means of ESR are in remission (21.24 ± 2.92 mm/hr) in mild (29.90 ± 3.20), moderate (40.25 ± 5.70) and sever (47.40 ± 4.50), on the other hand RF titers, ACCP levels and IL-17 concentrations did not show any significant differences between the groups the p values of these parameters are 0.4, 0.6 and 0.1 respectively.

From other point shows patients who had gum problems were 43(61.4 %) while the control group was 9 (12.5%) had a gum problem Statistically, parameter had significant differences (p.value=0.0001), a total of 43 RA patients with gum problems and RA patients without gum problems were included in the study among the RA patients with gum problems 14 (20.0%) had experienced gum problems before the onset of RA 19 patients (27.1%) developed gum problems after the onset of RA and 10 patients (14.3%) had gum problems that were unknown either before or after the onset of RA.

In terms of completely tooth loss five RA patients experienced tooth loss with four patients in the age group less than45 years and one patient in the age group more than 45 years, the distribution of tooth loss indicated that 80.0% of the patients who lost their teeth were in the younger age group while the remaining 20.0% were in the older age group. Statistical analysis revealed a p-value of 0.09 suggesting a trend towards a higher occurrence of gum problems among RA patients, although the difference between RA patients with and without gum problems was not statistically significant.

Table No.2 The clinical parameters of patients and Healthy control

Parameters	Category	Patients		Controls		P.Value*
		No.	Percent %	No.	Percent %	
Hypertensive	Yes	29	41.4	7	9.7	0.000
	No	41	58.6	63	87.5	
Diabetics	Yes	13	18.6	2	2.8	0.000
	No	57	81.4	68	94.4	
Smoking	Yes	9	12.9	4	5.6	0.1
	No	61	87.1	66	91.7	
Gum problems & periodontitis	Yes	43	61.4	9	12.5	0.000
	No	27	38.6	61	84.7	

*Significant at p.value 0.05 or less

Table No.3 Patients' Clinical Parameters

Parameters	Category	No.	Percent %
Family history RA	Yes	25	35.7
	No	45	64.3
Diagnosis Disease duration	Early	21	30.0
	Established	49	70.0
DAS_ESR	Remission	25	35.7
	Mild	20	28.6
	Moderate	20	28.6
	Severe	5	7.1
Mean DAS_ESR ± SD	3.03 ± 1.18		

Table No.4 Parameters comparisons in patients and controls

Parameters	Groups		p. value*
	Patient (N = 70) Mean ± SE	Control (N = 70) Mean ± SE	
ESR mm/hr	31.01 ± 2.37	12.13 ± 0.88	0.0001
ACCP ng/ml	7.76 ± 0.65	5.57 ± 0.72	0.02
IL-17 Pg/ml	13.05 ± 1.25	6.25 ± 1.14	0.0001

Table No.5 parameters of RA patients according to DAS28-ESR

Parameters	DAS-ESR				p. value
	Remission(N=25) Mean ± SE	Mild (N=20) Mean ± SE	Moderate (N=20) Mean ± SE	Severe (N=5) Mean ± SE	
ESR mm/hr	21.24 ± 2.92	29.90 ± 3.20	40.25 ± 5.70	47.40 ± 4.50	0.001*
RF (Titer)	30.10 ± 5.28	42.27 ± 6.93	47.96 ± 10.76	52.65 ± 27.35	0.4
ACCP ng/ml	8.20 ± 1.25	6.80 ± 1.23	7.58 ±0.94	10.26 ± 2.98	0.6
IL-17 Pg/ml	12.09 ± 1.42	12.29 ± 1.94	16.93 ± 3.20	5.34 ± 4.36	0.1

Table No.6 Distribution of periodontal problems in patients with Rheumatoid arthritis

Variables	Category	RA patients with gum problems N=43 patients			RA patients without gum problems	P.value
		Patients ≤ 45 year N= 11	Patients >45 year N= 32	Total		
RA Patients with Gum Problems	**Before RA**	1	13	14(20.0%)	27 (38.6)	0.09
	After RA	7	12	19(27.1%)		
	Un known	3	7	10(14.3%)		
RA patients with completely tooth loss	No.	4	1	5	0	
	%	80.0	20.0	100%	0.0	

DISCUSSION

The gender distribution in this study revealed a significant difference in the incidence of RA between males and females, females showed a much higher prevalence of RA (91.4%) compared to males (8.6%) with a female to male ratio of 11.3:1, nearly findings was reported by Mohamed *et al.*[15] with ratios of 10.2:1. Increased prevalence of RA among women suggests that hormonal factors in women are involved in the onset and progression of the disease, the peak incidence of RA usually occurs during the fifth decade of life which coincides with the of menopause hormones such as estrogen for instance have been suggested to have a pro-inflammatory impact [16] . The statistical significance of the differences between the patient group and the control group for each measured parameter, in the case of the ESR (erythrocyte sedimentation rate) parameter, the p-value was determined to be 0.0001, the p-value for the ACCP (anti-cyclic citrullinated peptide) parameter was determined to be 0.02, indicating a statistically significant difference between the two groups, p-value for the IL-17 (interleukin-17) parameter was determined to be 0.0001.

Our results agree with Jafat [16] highlighted the significance of ACCP testing in predicting the prognosis of rheumatoid arthritis as it can detect ACCP production even before the onset of clinical symptoms, also our results align with the research conducted by Li *et al.* [17]. which observed a significant increase in serum IL-17 levels in patients diagnosed with rheumatoid arthritis (RA) compared to healthy controls.

IL-17 has emerged as a potential therapeutic target for RA due to its involvement in promoting the development of osteoclasts leading to bone destruction and

joint damage, IL-17-producing cells were initially identified within the synovial tissue of individuals with rheumatoid arthritis (RA). Several investigations have indicated elevated levels of both IL-17 and Th17 cells in the blood serum and synovial fluid of inflamed joints among RA patients, Furthermore, a large amount of IL-17 was synthesized in peripheral blood mononuclear cells (PBMC), with concentrations surpassing those found in the blood of healthy individuals[14]. the results indicate significant differences in ESR values among the four groups (p = 0.001*), the remission group had the lowest mean ESR value while progressively higher ESR values were observed in the mild, moderate and severe groups, this finding suggests a positive correlation between ESR levels and disease severity in RA patients.On the contrary the RF titer, ACCP level and IL-17 concentration did not exhibit statistically significant differences among the groups Regarding the assessment of DAS-ESR to RF this study found no significant difference with a p-value of (0.4)

The results of the study reveal that a majority of patients, around 61.4% of the sampled individuals with rheumatoid arthritis (RA), exhibited issues related to gum health and periodontitis, these results align closely with the studies conducted by Castellar-Mendoza *et al*,[18] which reported a prevalence of 70.5% for gum problems and periodontitis in RA patients, the increased occurrence of periodontal disease in RA patients may be attributed to the pro-inflammatory characteristics of bacteria which can act as a triggering factor in mucosal sites especially in individuals with genetic susceptibility or it may result from impaired periodontal healing in RA patients.

Conclusions:

the association between these biomarkers and disease severity in the study may not be clear, these results provide insights into the relationship between ESR and disease severity in RA patients. The rise in ESR levels as disease severity escalates underscores the potential practicality of using ESR as an indicator to evaluate disease activity in RA. Conversely, the absence of noteworthy correlations between RF titer, ACCP level, IL-17 concentration, and disease severity suggests that these biomarkers might hold greater utility for diagnosis rather than serving as dependable gauges of disease severity, The study findings demonstrate that a significant portion of patients, approximately 61.4% of those sampled who have rheumatoid arthritis (RA), experienced challenges concerning gum health and periodontitis, a noteworthy observation is that a higher proportion developed gum problems after the onset of RA compared to those who had pre-existing gum issues before the onset of RA.

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Prevalence Of Depressive Symptoms Among Women With Hysterectomy

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Abstract

Background: Depression is the most common psychological problem suffered by women after hysterectomy and is linked to postoperative complications, negative perceptions about body image, femininity, sexual desire, youth, level of energy, and activity, as well as the inability to have children.

Methods: A descriptive (Cross-Sectional) design is used in the present study to assess the level of depression among women's after hysterectomy. A Non-probability (purposive) sample consists of sixty women's. The current study was conducted at the Obstetrics and Gynecology Consultant Unit at Al-Zahra Teaching Hospital within Al-Najaf Al-Ashraf Health Directorate in Iraq.

Results: Most women after hysterectomy have mild levels of depression (47%).

Conclusion: The study found that most women after hysterectomy have depression.

Recommendations: Enhancing the psychological and emotional condition of women after hysterectomy by nursing professionals Additionally, coordination between the consultant in obstetrics and Gynecology and the hospital's Department of Psychiatry is needed to reduce depression. And providing an effective discharge plan for women with hysterectomy, including a follow-up visit schedule, the required examinations, and referral numbers for each type of expected complaint after hysterectomy, especially psychological complaints.

Keywords: Depression, Hysterectomy.

INTRODUCTION

Depression, a common mental illness, is characterized by a sense of sadness, worthlessness, and hopelessness; a loss of interest or pleasure; and difficulty concentrating(1). Depression is generally common in patients before or after different operations, and it might result from loss of an important and vital organs, immune system suppression, postoperative pain, pos-operative infection, and decreased social activities(2).

The uterus is a particularly important organ for many women because, in addition to serving reproductive purposes, it also has

associations with femininity, identity, and sexuality(3). Uterine removal has particular implications for women and has a significant impact on cultures, beliefs, and attitudes(4). Therefore,psychological issues that are associated with surgery in general can also arise after gynecologic surgeries. However, because gynecological surgery can directly impact female reproductive functions, it can also produce significant psychological issues. Gynecologic surgeries, including bilateral salpingo-oophorectomy (BSO), hysterectomy, vulvectomy, and pelvic exenteration, all have distinct psychological repercussions(5).

Hysterectomy is one of the most common gynecological operations for the treatment of uterine fibroids (such as leiomyomas), heavy or irregular menstrual bleeding, endometriosis, pelvic inflammatory disease, and uterine prolapse(6). Hysterectomies have been linked to depression and mental illnesses since the 1940s. In 1974, Richards coined the phrase "post-hysterectomy syndrome" to characterize the vast range of symptoms that women experienced after a hysterectomy, including depression(7).

Depression is a rising health concern nowadays. According to the World Health Organization (WHO), unipolar major depression was the fifth most important health issue in the world in 1990, and it is predicted that by 2020, it will overtake ischemic heart disease as the second most serious issue(8).

A 20%–78% increased incidence of depression was discovered following a hysterectomy for any benign disease among women who had undergone hysterectomy, which was linked to higher rates of identified mental health outcomes(9). The quality of life for these individuals might be improved by reducing and preventing the disabilities that result from their disabilities, which would be made possible by a greater understanding of the elements that contribute to depression and its reduction(10).

METHODS AND MATERIALS:

Study Design:

A descriptive (Cross-Sectional) design is used in the present study to assess the levels on women's depression after hysterectomy.

Ethical Considerations and Administrative Agreements:

The researcher obtains permission from the faculty of medicine at the University of Kufa to conduct the study. In addition, in order to implement the study questionnaire included in the current study, official permission must be obtained from the Ministry of Planning or the Central Statistical Organization. Another approval was received from the Al-Najaf Al-Ashraf Health Directorate, as well as a fourth from the Al-Zahra Teaching Hospital, consultat Obstetrics and Gynecology. Lastly, the subject agreement was also obtained from women with hysterectomy after the researcher explained the purpose of the study to them and the community, and the researcher offered to respect the confidentiality of the participants as well as make participation voluntary to answer the questionnaire items.

Sitting of the Study:

The current study was conducted at the Consultant Obstetrics and Gynecology Unit at Al-Zahra Teaching Hospital within Al-Najaf Al-Ashraf Health Directorate in Iraq. This department was selected due to the women's availability, in addition to women reviewing this department after hysterectomy.

Criteria for Including the Sample:

The women with hysterectomy were selected according to the following criteria:

- Women who are at least 18 years old; because hysterectomy most commonly occurs in adult women compared to young.

- Women who had hysterectomy at least two weeks after doing hysterectomy.

- Women with no psychiatric disorders, women with no past history of psychiatric illness.

- Women who are willing to engage, as their participation is voluntary.

Excluding Criteria of the Sample:

The study excluded the following:

- Women who have previously been provided with guiding advice to reduce or deal with symptoms of depression after a hysterectomy, whether in the hospital or their review to a psychiatrist's clinic.

- Women doing hysterectomy due to malignancy etiology as malignancy itself can precipitate psychiatric symptoms/disorders.

- Unwilling to participate, because women's participation is voluntary.

The Study Insrument: This tool consists of two parts:

Part 1: Socio-Demographic-Clinical Data:

A- Personal Information:

There are six items in a socio-demographic datasheet, which include: age, residency, occupational status, level of education, martial status, and number of children. In order to prepare for data analysis, these variables are coded.

B- Clinical Data:

This questionnaire consists of three items, which include the duration of the causes of hysterectomy, the reasons for performing hysterectomy, and the type of operation. In order to prepare for data analysis, these variables are coded.

Part 2: Beck Depression Inventory (BDI):

The Beck depression inventory (BDI) original scale is adopted from Beck et al. (1961) to assess the severity of depression in women after hysterectomy. It consists of 21 questions with a value of 0–3 for each answer that contain various features of depression such as mood, pessimism, sense of failure, lack of satisfaction, guilty feeling, sense of punishment, self-hatred, self-accusations, self-punitive wishes, crying spells, irritability, social withdrawal, indecisiveness, body image, work inhibition, sleep disturbance, fatigability, loss of appetite, weight loss, somatic preoccupation, and loss of libido, which were comprehensively scored as the level of depression ranging from (0–63).

Score Interpretation of Study Instruments:

Four scores are used for rating the levels of depression in women after hysterectomy in terms of no depression, mild depression, moderate depression, and severe depression. The maximum total scores of the women's answers are 63, and the depression levels are scored as (0–9) for no depression, (10–18) for mild depression, (19–29) for moderate depression, and (30–63) for severe depression, according to Beck et al. (1961).

Reliability of the Study Instrument:

Although the BDI scale used in the current study has a global validity and reliability scale, the researcher calculated the reliability due to the Arabic language being utilized to collect the data rather than English. By using the Cronbach's Alpha coefficient test in a pilot study, the reliability of the current questionnaire was assessed. With a Cronbach's alpha value of (0.79) for the Beck Depression Inventory (BDI) scale, the test's results showed that the reliability is satisfactory.

Data collection:

Self-report using a developed (Arabic version) questionnaire was used to collect data in the current study. Information about the participants was obtained through self-reports between January 11, 2022, and March 13, 2023. After obtaining permission from hospital officials, the researcher met with 60 women to discuss the aims of the study and obtain their verbal consent to participate in the study, with the right to refuse or withdraw from participation as well as retain the confidentiality of the information provided by the women. Each woman was given a copy of the questionnaire, and it was confirmed and recommended by the researcher to each woman to ensure that the questionnaire was filled out completely before handing it over to the researcher.

Statistical Data Analysis:

It has been emphasized that there is no lost data and then the data was transformed into calculated data and arranged in the Microsoft Office Excel 2010 program, and for statistical analysis transfer them to the Statistical Package of Social Sciences program (SPSS) version 26. Besides , to move the tables to the final results and presented for study, transforming the data to Microsoft Office Word 2010.

Descriptive Data Analysis Approach:

The statistician used Bar Chart as Statistical figures, statistical mean: a measurement of central tendency, Standard deviation: this statistic characterized how the values vary around the mean of the distribution.

Results:

Table (1): Distribution of Women According to their Socio-demographic Characteristics

Socio-Demographic Data	Rating And Interval	Women Participants	
		Freq.	%
Age/years	26 <= 34	7	11.6
	35 – 43	**21**	**35.0**
	44 – 52	19	31.7
	53 – 61	7	11.7
	62 – 70	6	10.0
	Mean		44.85
	SD		9.644
Residency Area	Rural	23	38.3
	Urban	**37**	**61.7**
Level of Education	Read and Write	12	20.0
	Primary School Graduated	11	18.3
	Intermediated School Graduated	9	15.0
	High School Graduated	12	20.0
	Institute/University Graduated	**13**	**21.7**
	Post-Graduated	3	5.0
Occupational status	**Housewife**	**25**	**41.7**
	Free works	17	28.3
	Employee	18	30.0

Marital Status	Single	2	3.3
	Married	**46**	**76.7**
	Divorced	6	10.0
	Widowed	4	6.7
	Separated	2	3.3
Number of children	<= 2	13	21.7
	3 – 4	**22**	**36.7**
	5 – 6	16	26.6
	7+	9	15.0

According to this table, the majority of women participants (35.0%) are between the ages of 35 and 43, urban residents (61.7%), those who are housewives (41.7%), (76.7%) are married women, number of children (36.7%) are within (3 – 4) and (21.7%) have graduated from an institute or college.

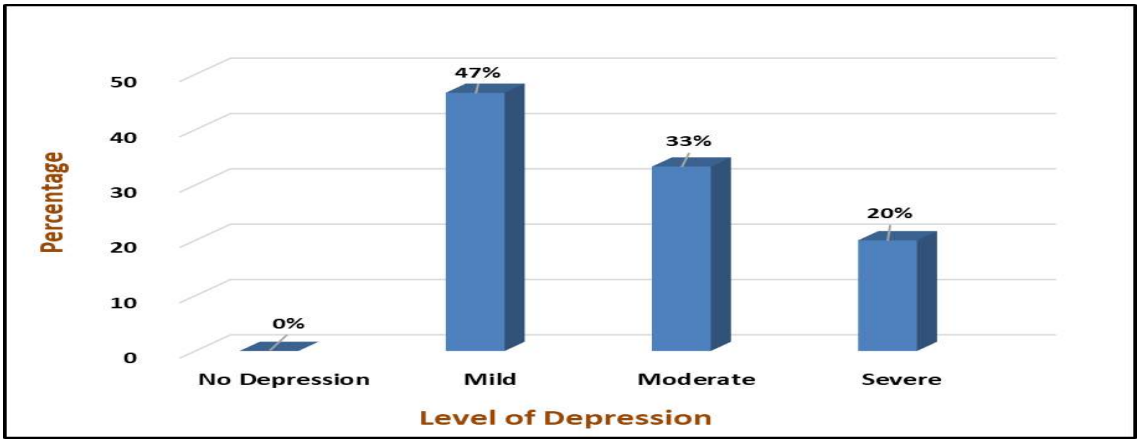

Figure (1) Levels of Depression among Women with Hysterectomy

Figure (1) shows levels of depression among women with hysterectomy. It reveals that (0%) of the participants have no depression; (47%) have mild depression; (33%) have moderate depression and only (20%) have severe depression.

Table (2): Descriptive Statistics and Assessment of Beck Depression Scale

Items	Resp.	Freq. No. = 60	%	MS	Assessment
Mood	I do not feel sad	7	11.9	1.24	Moderate
	I feel blue or sad	28	47.5		
	Iam blue or sad all the time and I can't snap out of it	20	33.9		
	Iam so sad or unhappy that I can't stand it	5	6.8		
Pessimism	Iam not particularly discouraged about	16	26.7	1.06	Moderate

	the future				
	I feel discouraged about the future	30	50.0		
	I feel I have nothing to look forward to	11	18.3		
	I feel I the future is hopeless and that things cannot improve	3	5.0		
Sense of Failure	I do not feel like a failure	24	40.0	1.24	Moderate
	I feel I have failed more than the average person	20	33.3		
	As I look back on my life, all I can see is a lot of failures	11	18.3		
	I feel Iam a complete failure as a person	5	8.3		
Lack of Satisfaction	I am not particularly dissatisfied	17	28.3	1.24	Moderate
	I don't enjoy things the way I used to	30	50.0		
	I don't get satisfaction out of anything anymore	12	20.0		
	I am dissatisfied with everything	1	1.7		
Guilty Feeling	I don't feel particularly guilty	19	32.2	1.47	Moderate
	I feel guilty a good part of the time	16	27.1		
	I feel quite guilty most of the time	14	23.7		
	I feel guilty all of the time	11	16.9		
Sense of Punishment	I don't feel I am being punished	39	65.0	0.65	Good
	I feel I may be punished	15	25.0		
	I expect to be punished	5	8.3		
	I feel I am being punished	1	1.7		
Self Hate	I don't feel disappointed in myself	16	26.7	1.12	Moderate
	I am disappointed in myself	35	58.3		
	I am disgusted with myself	8	13.3		
	I hate myself	1	1.7		

Self Accusations	I don't feel I am any worse than anybody else	23	38.3	1.24	Moderate
	I am critical of myself for my weaknesses or mistakes	19	31.7		
	I blame myself all the time for my faults	13	21.7		
	I blame myself for everything bad that happens	5	8.3		
Self-Punitive Wishes	I don't have any thoughts of killing myself	51	85.0	0.18	Good
	I have thoughts of killing myself, but I would not carry them out	9	15.0		
	I have definite plans about committing suicide	0	0.0		
	I would kill myself if I could	0	0.0		
Crying Seizures	I don't cry any more than usual	17	28.3	1.06	Moderate
	I cry more now than I used to	26	43.3		
	I cry all the time now	15	25.0		
	I used to be able to cry, but now I can't cry even though I want to	2	3.3		
Irritability	I am no more irritated now than I ever am	2	3.3	1.47	Moderate
	I get annoyed or irritated more easily than I used to	23	38.3		
	I feel irritated all the time	34	56.7		
	I don't get irritated at all at the things that used to irritate me	1	1.7		
Social Withdrawal	I have not lost interest in other people	15	25.0	1.35	Moderate
	I am less interested in other people than I used to be	26	43.3		

	I have lost most of my interest in other people	11	18.3		
	I have lost all of my interest in other people	8	13.3		
Indecisiveness	I make decisions about as well as I ever could	24	40.0	0.76	Good
	I put off making decisions more than I used to	29	48.3		
	I have greater difficulty in making decisions more than I used to	6	10.0		
	I can't make decisions at all anymore	1	1.7		
Body image	I don't feel that I look any worse than I used to	14	23.3	1.00	Moderate
	I am worried that I am looking old or unattractive	26	43.3		
	I feel there are permanent changes in my appearance that make me look unattractive	17	28.3		
	I believe that I look ugly	3	5.0		
Work Inhibition	I can work about as well as before	10	16.7	1.18	Moderate
	It takes an extra effort to get started at doing something	33	55.0		
	I have to push myself very hard to do anything	16	26.7		
	I can't do any work at all	1	1.7		
Sleep Disturbance	I can sleep as well as usual	9	15.0	1.29	Moderate
	I wake up more tired in the morning than I used to	24	40.0		
	I wake up 1-2 hours earlier than usual and find it hard to get back to sleep	24	40.0		
	I wake up early every day and can't get more than five hours sleep	3	5.0		

Fatigability	I don't get more tired than usual	10	16.7	0.82	Good
	I get tired more easily than I used to	34	56.7		
	I get tired from doing almost anything	14	23.3		
	I am too tired to do anything	2	3.3		
Loss of Appetite	My appetite is no worse than usual	12	20.0	1.06	Moderate
	My appetite is not as good as it used to be	33	55.0		
	My appetite is much worse now	15	25.0		
	I have no appetite at all anymore	0	0.0		
Weight loss	I haven't lost much weight , if any, lately	45	75.0	0.47	Good
	I have lost more than 5 pounds	9	15.0		
	I have lost more than 10 pounds	5	8.3		
	I have lost more than 15 pounds	1	1.7		
Somatic Preoccupation	I am no more concerned about my health than usual	8	13.3	1.06	Moderate
	I am concerned about physical problems like aches,pain, upset stomach, or constipation	30	50.0		
	I am very concerned about physical problems and it's hard to think of much else	21	35.0		
	I am so concerned about my physical problems that I cannot think of anything else	1	1.7		
Loss of Libido	I have not noticed any recent change in my interest in sex	27	45.0	0.59	Good
	I am less interested in sex than I used to be	31	51.7		
	I have almost no interest in sex	2	3.3		
	I have lost interest in sex completely	0	0.0		

MS : Mean of Scores ; Good : MS = 0-0.99; Moderate : MS=1-1.99 Fail : MS≥2

Table (2) reveals descriptive statistics and assessment of Beck depression scale, it explains that the assessment of most items is (moderate), except for the items numbered (6,9,13,17,19,21) in which the assessment is (Good).

This assessment is based on the statistical scoring system that indicated total mean of scores between (0-0.99) as (Good) , while those with scores between (1.0-1.99) as (moderate) and those with mean of scores equal or more than (2) as (poor).

Table (3) Assessment and mean of scores of depression among women with hysterectomy

Participants	Mean	Std. Deviation	**Assessment of the overall participants**
	0.98	0.43	Moderate

No Depression : MS= 0-0.49; Mild: MS=0.50.99; Moderate : MS=1.0-1.49; Severe : MS≥1.50

Table (3) reveals that the mean of score of depression among women with hysterectomy is (0.98±0.43) which indicates a (moderate) level of depression in the assessment of the overall women.

Discussion

The study's findings show that depression in women who have undergone hysterectomy was assessed using the Beck Depression Inventory (BDI) scale. The results show that 47% of the study's sample felt mild depression level, sadness, pessimism, loss of pleasure, and something changed in their bodies, which affected their sleep and appetite and may cause a significant disturbance in women's quality of life. This finding could be due to their negative perceptions of body image, energy, and femininity, as well as the loss of the ability to have children, are a major cause of depression in post-hysterectomy women. This result concordant with Helmy et al., 2008 their results showed that Symptoms of depression appeared in women (64.4%) after hysterectomy.

The findings of the current study showed that the majority of the participants (35.0%) were between 35 and 43 years old. This finding might be due to several studies reporting that prevalence of uterine fibrosis is higher in this age range. This result was congruent with an Egyptian study that was done by Abdelbaseer Mahmoud et al., 2022, who studied the "Effect of Psycho-educational Program on Depressive Symptoms, Post- traumatic Stress Response and Quality of Life among Women with Hysterectomy." Their results showed that 45 % of them are between the ages of 35 and 45, with an average age of 34.55±7.65 years.

Regarding residency, the results of the current study revealed that most of the participants live in urban areas (61.7%). This finding could be explained by the fact that more people live in urban than rural regions in Al-Najaf. Consequently, the researcher encounters more patients from urban residential areas rather than rural areas. In addition, an Egyptian study done by Eidfarrag et al., 2018, "Effect of an Educational Supportive Program on Self-Esteem and Marital Relation Among Women Undergoing Hysterectomy," found that nearly two -thirds (63.3%) of women that were studied come from urban areas, and urban is the dominant residential area for patients who were included in this study.

Regarding the level of education among participants, the researcher states that most of the participants are graduates of an institute (21.7%), followed by the those who graduated from high school (20.0%). This result is likely caused by the fact that the majority of the sample was drawn from urban regions, where a higher priority was placed on completing high education. This study consistent

with Gercek et al., 2016, who studied "The information requirements and self-perceptions of Turkish women undergoing hysterectomy." The results confirm that the majority of the study sample has a high level of education(29.7%).

Concerning occupational status, the findings of the current study showed that almost fifty percent of those participants (41.7%) are housewives. From the perspective of our culture, moms are responsible for the household and child care, while fathers spend the majority of their time working and serving as the provider. Therefore, mothers devote their entire day to caring for their children. This finding is supported by Eidfarrag et al. (2018), who found that more than half of samples were housewives.

In regards of marital status, the majority of the studied participants are married women. This result is probably due to social and religious norms or might be due to the fact that fewer than 50% of the women in this study were in the 35– 43 age range, which is the appropriate age for marriage. This finding is consistent with Abdelbaseer Mahmoud et al., 2022, who found that more than half of the participants are married women(76.7%).

In terms of the subjects' number of children. The findings indicate that the majority of the study sample has 3 – 4 children. In the point of view this result may be due to do not apply family plan or might be related to that hysterectomy multigravida parous women. This result comes along with Gercek et al., 2016, whose results confirm that the majority of the study sample has three or more children.

Conclusion

The study found that most women after hysterectomy have depression.

Recommendation

- Enhancing the psychological and emotional condition of women after hysterectomy by nursing professionals Additionally, coordination between the consultant in obstetrics and Gynecology and the hospital's Department of Psychiatry is needed to reduce depression.
- Providing an effective discharge plan for women with hysterectomy, including a follow-up visit schedule, the required examinations, and referral numbers for each type of expected complaint after hysterectomy, especially psychological complaints.
- Conducting identical research on a nationwide scale with the largest sample to evaluate depression of women after hysterectomy.

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Xanthogranulomatous Osteomyelitis: Two Rare Cases Report

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Abstract

Background: Xanthogranulomatous osteomyelitis (XO) is a rare chronic inflammatory lesion that is histologically characterized by the presence of foamy histiocytes and plasma cells. Radiologic and gross examinations can mimic malignancy (9), so carful workup and definitive diagnosis should be made by histopathologic evaluation.

Case Report: There are two rare cases being reported here; the first one is a 21-year-old male who presented with chronic pain and swelling of upper leg for one year. He has history of healed traumatic fracture of fibula 7 years ago. Radiological examination revealed radio opaque lesions of upper fibula. The second case is a 30 years old female, presented with pain and swelling of wrist for six months with clinical suspicion of Ewing sarcoma. Radiological examination revealed highly suspicious radio opaque, lytic lesions of lower radius. Biopsy of both lesions were done. Microscopic examination showed marked chronic inflammatory cells infiltration mainly foamy histiocytes and lymphoid cells with many foreign body giant cells. No evidence of tuberculosis or malignancy.

Conclusion: As these lesions were clinically highly suspicious of malignancy or associated with other diseases, so proper diagnostic roles in xanthogranulomatous osteomyelitis should include histopathological examination in order to rule out any malignant conditions of the bone.

Key words*:* Xanthogranulomatous Osteomyelitis, Chronic Inflammatory, Lesion.

INTRODUCTION

Xanthogranulomatous osteomyelitis is a rare form of chronic inflammatory disease confirmed microscopically with characteristic features of foamy histiocytes, neutrophils, lymphocytes, activated plasma cells and many multinucleated giant cells (1-8). It mimic malignancy both by radiological and gross examination (9). Fibroblastic cells proliferation may exist and forming considerable fibrosis in addition to occasional clefts of cholesterol (1,10,13,15).

Many bones are prone for development of xanthoma, particularly upper and lower extremities as humerus, femur, tibia, radius and ulna are frequently affected bones (16-20), while calcaneus and vertebral bodies and spines were less frequent (1,6). Interesting fibula is less likely to be affected by xanthoma

(17). Most xanthomas are lytic lesions, but intraosseous xanthomas are osteolytic expansile lesions and often associated with hyperlipidemia (20-22).

CASE REPORT

Case No.1. A 21-year-old male presented to orthopedic doctor with painful swelling of upper leg, he has history of trauma and fracture of fibula 7 years ago. No history of tuberculosis, diabetes, and other disease. Radiological examination revealed lytic expansile mass of upper fibula (Fig.1).

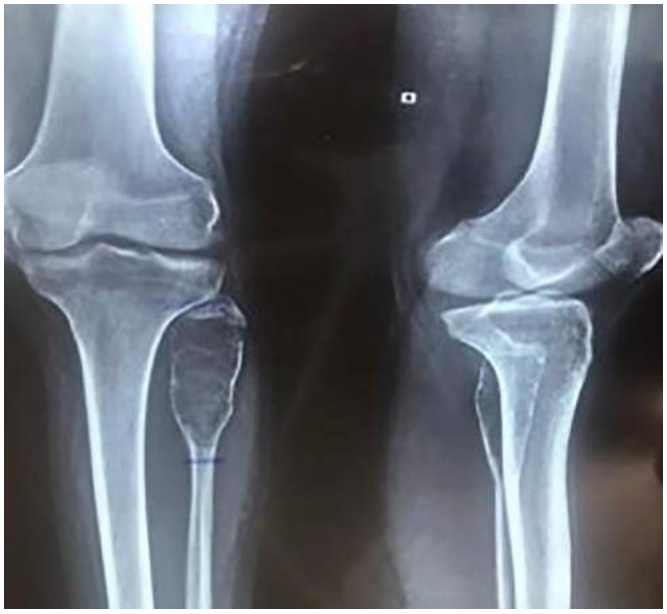

Fig.1: radiological image of left leg bones showed expansile lytic lesion of upper fibula.

Gross feature showed one piece of bone, covered by cartilage cup, measured 8x3 cm, several pieces were taken in three blocks. Microscopic features of bone lesion sections revealed abundant benign looking distorted osteoid tissue, showed marked chronic inflammatory cells infiltration mainly foamy histiocytes and lymphoid cells with many foreign body giant cells. No evidence of tuberculosis or malignancy (Fig.2).

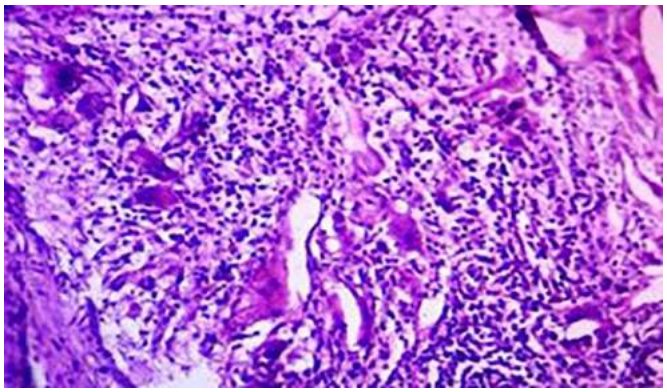

Fig.2: Histological section revealed marked chronic inflammatory cells infiltration mainly foamy histiocytes and lymphoid cells with many foreign body giant cells.

Case No.2. A 30 years old female presented to orthopedic doctor with painful swelling of left wrist for six months leg, without history of trauma or fracture. Radiological examination revealed lytic lesion of lower end of radius, with suspicion of Ewing sarcoma. No clinical evidence of any associated disease.

DISCUSSION

Xanthogranulomatous osteomyelitis is a rare disease firstly described and applied as a term in 1984 by C Cozzutto (22). Histologically, the lesion is composed from histiocytic and plasma cells infiltration in bone lesions (5). Till now little number of cases has been reported worldwide (Table.1). Only **20** cases have been recorded till writing this paper. Any age can be affected and most of them were ranging 5 years to 65 years (tabl.1). Both sexed were affected. Most of them were presented with painful swelling lesions preceded by traumatic fracture (18-20), while few were associated with other lesion as Crohn's disease (3), Xanthogranulomatous pyelonephritis (21) and genetic disorder (7). Some of cases mimic neoplastic lesions and give high suspicion of malignancy (10,13,15), while other was resembling tuberculosis (4). Most of reported cases were presented as unifocal lesions (1,5,15,18,22), while only 4 cases were multifocal (9,19,17,21). Long bones as tibia, femur and fibula were most frequently affected while rib and spine were rarely affected (1,12, 18).

In the presented two cases, both were presented with painful bone swelling. The first one was 21 years old with history of trauma accident 7 years ago, X ray revealed expansile mass of upper fibula, highly suspicious of bone tumor. So surgical resection was done with safe margin. Other case was 30 years female presented with painful swelling of the wrist, x ray revealed lytic lesion of radius, with high clinical suspicion of malignant tumor (Ewing tumor), curate biopsy was done. Both cases were not associated with any systemic disease. They were confirmed histologically as Xanthogranulomatous osteomyelitis. So the importance of this disease is enrolled in its clinical suspicion of malignancy that necessitates a special care and carful approach for diagnosis.

Conclusion

Owing to its rarity and clinical suspicion of malignancy, we present these two cases of Xanthogranulomatous osteomyelitis for documentation and making attention of surgical doctors and pathologists to take in consideration this disease entity for planning for proper management and to avoid misdiagnosis and unnecessary major surgical resection.

Table.1. The reported cases of Xanthogranulomatous osteomyelitis worldwide in sequence of dating.

Ref. N0.	D	S	N c s	A (	C f	E i	A d	L
21 .	1	1 d e	2	N	P	N b	, a f	N a
20	1	N	1	6	F p	T	T	S
19	2	F	1	5	P	U	-	S
18	2	N	1	1	P	T	-	S

					s			
16	2	M	1	1	P f	H a	-	N a
15.	2	M	1	5	P S	U	-	S
14	2	M	2	N	P	F	-	S
13	2	M	1	2	P	T	-	s
12	2	F	1	6	P	F	-	S
11	2	M	1	3	P	M ta c	-	N a
10	2	F	1	2	P	F a	-	N a
9	2	M	1	2	P	F	tr	S
8	2	F	1	3	P	T	-	S
7	2	F	1	5	P f	h	A s	N a
6	2	m	1	3	P	f	tr	S
5	2	M	1	1	P	T	T	
4	2	F	1	5	P	F	-	S
3	2	M	1	2	P	P	-	S
2	2	F	1	2	P	f b	-	S
1	2	F	1	6	S c c o	v	-	S

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Obesity Among Adult Patients Aged 18 Years Old And Above Attending Main Primary Health Care Centers In Babil Governorate, Iraq 2015: Prevalence And Some Possible Risk Factors

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Abstract

Background: A cross-sectional survey was conducted at the period from 1st of January to 31st of March 2015 in Babil Province-Iraq. A systematic random sampling technique was used to collect 420 patients from randomly chosen 8 main primary health care centers. They directly consented to an interview by the researcher by using questionnaire form. Of the 420 patients, 168 (40%) were obese. The body mass index classes had a statistical significant association with ; age, occupation, residence (P=0.000). Eating: sweet, chocolate (P=0.000); fruit (P= 0.001); skipping breakfast (P=0.027); TV watching time (P=0.004); moderate activity frequency and time consumed (P=0.000), sleep duration, family history of obesity (P=0.000). Logistic regression analysis predicted some factors that increased the odds of obesity; age (OR=1.159), no job or retired(OR=10), business (OR=12.6), skipping breakfast (OR=1.46), eating sweet and chocolate (OR=2.709), time of TV watching (OR=3.319), and family history (OR=3.746), whereas some factors decreased the odds like; farmer (OR=0.013), laborer (OR=0.042), rural residence (OR=0.136), eating fruit (OR=0.502), moderate physical activity (OR=0.26) .

Conclusions and recommendations: Obesity prevalence was 40%, and associated with socio-demographic features, eating habits, physical activity , sleep duration, and family history. The study recommended adoption of health education programs about obesity by Ministry of Health regarding healthy diet, decrease sedentary lifestyle, encouraging of physical activity at all ages for proper prevention of obesity.

Key words: Obesity, Lifestyle, Healthy diet.

INTRODUCTION

Obesity is a prevalent metabolic condition, which is in recent years has been increasing explosively becoming a major health challenge. Currently, the prevalence of obesity has been estimated to count 671 million individuals and, if trends continue, projection on models have estimated the global obesity prevalence to

reach 1.12 billion individuals by the year 2030 [1,2].

Obesity is defined as a state of accumulation of abnormal or excessive body fat that may impair individual`s health and well-being[3]. It is a major public health problem resulting in serious social , physical and psychological damage, with high rate of morbidity and mortality [4]. In 2014, World Health Organization (WHO) stated that more than 1.9 billion adults aged 18 years and older are overweight with 600 million adults are obese representing 39% overweight and 13% obese respectively [5] . It has been speculated that diet and lifestyle play a significant role in both the development and control of obesity [6] .

A strong association has been made between socioeconomic status (SES) and obesity with an inconsistent relationship that has been reported between these two factors, depending on the degree of the economic development of the country [7] . It is associated with the increased risk of serious health problems such as, cardiovascular disease, type 2 diabetes mellitus, and various types of cancer where, these 3 comorbid conditions are associated with great use of health care services among obese patients [8] .Obesity can be measured by various methods such as body mass index BMI, waist circumference, waist–hip ratio, skin-fold thickness, underwater weighing and bioelectrical impedance [9] .

In Eastern Mediterranean Region, it has been shown that there were certain possible factors determining obesity such as; nutrition transition, inactivity, skipping breakfast, high intake of sugary beverages, in addition to long period of time watching TV [10] .

In Iraq, especially in Babil governorate, there is no national figure available on obesity with anecdotal data about them and it is not representative. It has been stated, however, that obesity constituted 25% among Iraqi women attending 2 outpatients clinics in Baghdad with the significance of older age [11] .

Materials and Methods

A Cross-sectional survey conducted in Babil governorate in the middle of Iraq, due to the lack of research on adult obesity and its associated possible risk factors in this city. Male and female adult patients, aged 18 years and above attending main Primary Health Care centers in Babil governorate for any cause and meet the inclusion criteria of the study at the period from 1st of January to 31st of March 2015, would be included in the study. All the patients participated in the study gave informed consents of their participation before the enrollment in the study. Any currently pregnant women at the time of interview was excluded from the study.

An appropriate sample size was calculated according to the sample size determination equation. The following sample equation was applied [12] .

$$N = \frac{Z^2 \times p \times q}{d^2}$$

where : N is the sample size required for the study. $Z^2 = 1.96^2$ which is statistical for a level of confidence of 95%.

P: expected proportion (0.5) and according to the literature and related studies of the world, It is expected that prevalence (proportion) is around 50 %. q = 1-p = 0.5, d = absolute precision and it was set as 5% (0.05). According to the equation, the sample size required for this study is **384** patients. By adding about10% for non- response, the total sample at the end was **420** patients.

According to the data obtained from Ministry of Health (MOH) – Babylon Health Directorate/ Public Health Department, there are 42 main primary health care centers

distributed throughout the whole of Babil governorate, where 25% of the centers located in the northern part of the governorate (Al-Musayyeb and Al-Mahaweel provinces), 50% of them in the middle part (Al-Hilla province), whereas the rest 25% located in the southern part (Al-Hashimiyah province) with coverage of both urban and rural areas of the governorate.

Stratification was done on these centers and 8 centers being chosen by simple random sampling, 2 centers from the northern, 4 from the middle and 2 from the southern part. Then, the patients from each center were selected by systematic random sampling methods to choose every 5th patients who met the inclusion criteria; **50** patients were obtained from each center by estimating the daily attending patients to the selected centers and dividing this number on the sample needed by the researcher to find the interval between the selected patients.

Regular visits were conducted on these centers during the period of the study, 4 days per week with 2 days/ week for the middle centers and one day/week for each southern and northern centers respectively; 6-7 visits were conducted to each center throughout whole period of the survey. The time of attending in each center was 4 hours from 9 am o`clock to 1 pm o'clock including the time consumed for the interview with each patient, measurement of height and weight for each, explaining the benefit of the study. Number of patients included in the study was **420,** 100 from the northern, 220 from the middle and 100 from the southern part, where all of them agreed to participate in the study with 100% response rate.

Direct interview with patients according to the questionnaire which was written in English and designed after reviewing the literature. It was filled by the researcher through direct interview with the study participants which included the following parts:

1. First part, socio-demographic characteristics of the patients which includes; (name, age, gender, marital status, occupation, residence, and level of education).
2. Second part, eating habits of the patients which include; type of food eaten (carbohydrates, fatty foods, and drinks), skipping breakfast with their frequency per week (never, sometimes, often, and every day) in addition to the questions about fast foods with their frequency per week, and number of meals eaten per day.
3. Third part, physical activity: divided in to 3 categories with their frequency per week and the time of each activity ; passive entertainment activities (TV watching because this activity is very interested and common in all Iraqi people, and the time consumed of above activities (<2 hrs., 2-4 hrs., > 4hrs. /day) , moderate activity (walking, housework, cycling, gardening) with their frequency per week (never, < 5 times/week, ≥5 times/week), and the time consumed for them (<30 minutes, ≥30minutes), in addition to the vigorous activity (jogging, swimming, running, football) and it`s frequency per week (never, <3times, ≥3 times) and duration of each activity (<20 minutes, ≥20 minutes).
4. Fifth part, medical and surgical history including certain non-communicable diseases such as; hypertension, ischemic heart disease, type 2 DM, hyperlipidemia, asthma, and joint diseases. Also, sleeping hours per day with its duration (<5 hrs., 5-7hrs., 8 hrs. and more). Family history of obesity; father, mother , siblings, grandfather , and grandmother .

Anthropometric measures of weight and height of all patients included in the study were done by the researcher himself to obtain more accurate results :

- Height would be measured in centimeter in standing position by a plastic tape measure

fixed on the wall, with the patient was barefoot together, ensuring the nape, back, calves and ankles pressed against measuring tape with error accepted of 0.5 cm.

- Weight would be measured in kg by standard electronic scale (Seca type) for measuring the weight of the patient with barefoot and wearing of light clothes with an accepted error of 0.5 kg.

- Each questionnaire assigned a serial identification number. The data were reviewed, cleaned with double check entry into the computer using Statistical Package for Social Sciences (SPSS) version 20; then, it was coded by the researcher under supervision of the supervisor and a consultant statistician.

Results

The study included 420 patients. Body mass indexes were distributed among 3 groups, normal weight (BMI 18.5-24.9), overweight (BMI 25-29.9), and obese (BMI ≥ 30) .

Table 1. **The highest percentage among obese group 40.0% (168), the overweight group 37.6% (158), whereas, the lowest percentage among normal weight 22.4% (94).**

BMI classification (kg/m^2)	**F**	**%**
Normal weight (18.5-24.9)	9	2
Overweight (25-29.9)	1	3
Obese (≥ 30)	1	4
Total	4	1
Mean±SD (Range)		2

Table 2. Variables of age group distributed into 5 categories with lowest age of 18 years and highest one of 77 years with Mean ±SD (41.2±12.9), the highest percentage among the age category (40- < 50 years) with 26%, whereas, the lowest percentage in the age category (≥ 60 years) with 8.1%.

Residence: 70% of patients were living in urban residence, in comparison to 30% living in rural residence.

Occupation: was divided into six groups ; no job or retired 51 (12.1%), housewives 100 (23.8%), business 64 (15.2%), government officers 144 (34.3%),farmers 32 (7.6%), and 29 (6.9%) laborers.

Characters	**Frequency**	**%**
Age groups		
18 - <30 years	93	22.1%
30 - <40 years	98	23.3%
40 - < 50 years	109	26.0%

50 - < 60 years	86	20.5%
≥ 60 years	34	8.1%
Mean±SD (Range)	41.2 ± 12.9 (18 – 77)	
Residence	**Frequency**	**%**
Urban	294	70.0%
Rural	126	30.0%
Occupation	**Frequency**	**%**
No job or Retired	51	12.1%
Housewife	100	23.8%
Business	64	15.2%
Government officer	144	34.3%
Farmer	32	7.6%
Laborer	29	6.9%

Table 3: The Socio-demographic features in association with BMI categories.

Regarding age groups, the study has shown that the older age group of patients who were 60 years had the highest percentage of obesity 58.8%, with a highly statistically significant association between the age of patients with their BMI category (P= 0.000), as in Table (3).

Regarding occupation, patients with no job or retired had the highest percentage of obesity in regard to other groups of occupation 58.8%, whereas 0% in both farmers and laborers, with a highly statistically significant relation between occupation and BMI categories (P=0.000) as shown in the same table.

Urban residents had a higher percentage of obesity 46.3% than rural residence 25.4%, with a highly statistically significant association (P=0.000) as shown in table (3).

Variables	**B**			**T**	**X (**	**p**
	N (1 (1 N	C (2 (1 N	C (3 (1 N			
Age groups						
18 - < 30 years	5	2	1	9	8	0
30 - <40 years	2	4	3	9	(	

40 - < 50 years	1	4	5	1		
50 - < 60 years	7	3	4	8		
≥ 60 years	1	1	2	3		
Occupation						
No job or Retired	1	2	3	5		
Housewife	1	3	5	1		
Farmer	3	2	0	3	1	0
Laborer	2	5	0	2	(	
Business	1	3	3	6		
Government officer	2	6	5	1		
Residence						
Urban	3	1	1	2	4	0
Rural	5	3	3	1		
***Significant at alpha < 0.05.**						

Table 4 : The 3 Dietary and Eating Habits

Table (4) showed the 3 dietary and eating habits of the sample like eating carbohydrates like **sweet, chocolate** with *often* or *everyday* frequency had a higher percentage of obesity (50.6%, 53.8%) than never or *sometimes* frequency (21.1%, 29.1%) respectively with a statistically significant association (P=0.000).

Eating **fruit** showed a statistically significant association with BMI categories (P=0.001) as shown in the same table where patients with *never* or *sometimes* frequency had a higher percentage of obesity (57.8%) than those with *often* or *everyday* frequency (36.8%).

Skipping breakfast is another dietary habit which revealed a statistically significant association with BMI categories of the sample (P=0.027) where patients who skipped their breakfasts at *never* or *sometimes* frequency had a lower obesity rate 33.1% ,33.6% than those who skipped at *often* and *everyday* frequency 46.4%, 49.6% respectively.

Eating habits	**BMI classification (kg/m2)**			**Total (n=420); No. (%)**	**X^2 (df)**	**p-value**
	Normal (18.5-24.9); (n=94); No. (%)	**Overweight (25-29.9); (n=158); No. (%)**	**Obese (≥30); (n=168); No. (%)**			
Eating CHO like sweet, chocolate						
Never	38 (50)	22 (28.9)	16 (21.1)	76 (100)	71.57	0.000*
Sometimes	38 (30.9)	49 (39.8)	36 (29.3)	123 (100)		

Eating habits	BMI classification (kg/m2)			Total (n=420); No. (%)	X^2 (df)	p-value
	Normal (18.5-24.9); (n=94); No. (%)	Overweight (25-29.9); (n=158); No. (%)	Obese (≥30); (n=168); No. (%)			
Often	10 (11.2)	34 (38.2)	45 (50.6)	89 (100)	(6)	
Everyday	8 (6.1)	53 (40.1)	71 (53.8)	132 (100)		
Everyday	34 (21.9)	57 (36.8)	64 (41.3)	155 (100)		
Eating fruit						
Never or sometimes	5 (7.8)	22 (34.4)	37 (57.8)	64 (100)	13.36 (2)	0.001*
Often or everyday	89 (25)	136 (38.2)	131(36.8)	356 (100)		
Skipping breakfast						
Never	32 (27.8)	45 (39.1)	38 (33.1)	115 (100)	14.27 (6)	0.027*
Sometimes	31 (26.1)	48 (40.3)	40 (33.6)	119 (100)		
Often	16(23.2)	21 (30.4)	32 (46.4)	69 (100)		
Everyday	15(12.8)	44 (37.6)	58 (49.6)	117 (100)		
***Significant at alpha < 0.05.**						

Table 5. The two categories of physical activities of the sample to their BMI categories.

Table 5 showed two categories of physical activities of the included sample to their BMI categories; there was a statistically significant association between the time consumed by the patients during watching TV and their BMI categories (P=0.004) , where those who watched TV less than 2 hours had a lower percentage of obesity 30.6% than those who watched TV more than 4 hrs. 56.1% .

Regarding the moderate physical activity, the table showed that patients who never practiced this activity had the highest rate of obesity (63.7%) compared with those who practiced the same activity 5 times per week or more (13.5%) with a statistically significant association (P=0.000).

Parameters	BMI classification (kg/m2)			Total	X^2 (df)	p-value
	Normal (18.5-24.9) No. (%)	Overweight (25-29.9) No. (%)	Obese (≥ 30) No. (%)			
TV watching : time spent of watching (hour/day)						
< 2 hrs.	38 (31.4)	46 (38.0)	37 (30.6)	121 (100)	15.51 (4)	0.004*

2-4 hrs.	48 (20.6)	91 (39.1)	94 (40.3)	233 (100)		
> 4 hrs.	8 (12.1)	21 (31.8)	37 (56.1)	66 (100)		
Total	94 (22.4)	158 (37.6)	168 (40)	420 (100)		
Moderate physical activity : housework, walking, gardening, cycling (frequency/week)						
Never	3 (2.1)	50 (34.2)	93 (63.7)	146 (100)	146.21 (4)	0.000*
< 5 times/week	13 (10.3)	58 (46)	55 (43.7)	126 (100)		
≥ 5 times /week	78 (52.7)	50 (33.8)	20 (13.5)	148 (100)		
Total	94(22.4)	158 (37.6)	168 (40)	420 (100)		
*** Significant at alpha < 0.05**						

Table 6: Patients' Sleeping Hours and Obesity.

Table 6 showed that patients with sleeping hours less than 5 hours per day had the highest proportion of obesity 57% compared with those of sleeping more than 5 hours per day (5-7, 8 hrs. and more) 34.1%, 38.3% respectively with a statistically significant association (P=0.000).

Sleeping hours per day	**BMI classifications (kg/m^2)**			**Total No. (%)**
	Normal (18.5-24.9) No. (%)	**Overweight (25-29.9) No. (%)**	**Obese (≥ 30) No. (%)**	
< 5 hrs.	6 (7)	31 (36)	49 (57)	86(100)
5-7 hrs.	55 (25.7)	86 (40.2)	73(34.1)	214(100)
≥ 8 hrs.	33 (27.5)	41 (34.2)	46 (38.3)	120(100)
Total	94(22.4)	158 (37.6)	168 (40)	420(100)
X2 = 20.52 df=4 p-value= 0.000* (Significant at alpha <0.05)				

Table 7. Patients with Absence (No) Family History of Obesity

Table 7 : Showed that patients with absence (No) family history of obesity among their first degree relatives had a lower percentage of obesity 17.1% compared with those with positive (Yes) of family history of obesity 53% with a statistically significant association (P=0.000).

Family history of Obesity	BMI classifications (kg/m2)			Total No. (%)	X2 (df)	p-value
	Normal (18.5-24.9) No. (%)	Overweight (25-29.9); No. (%)	Obese (≥ 30) No.(%)			
No	57 (37.5)	69 (45.4)	26 (17.1)	152(100)	59.37 (2)	0.000 *
Yes	37 (13.8)	89 (33.2)	142 (53)	268(100)		
Total	94(22.4)	158 (37.6)	168 (40)	420(100)		
*Significant at alpha < 0.05.						

Table 8: A Binomial Logistic Regression Analysis of the Effect of Different Variables on Overweight and Obesity.

Variables	C	P	C	9
Age (years)	0	0	1	(
Occupation (Government officer is the comparative occupation)				
No job or Retired	2	0	1	(
Farmer	-	0	0	(
Laborer	-	0	0	(
Business	2	0	1	(
Residence (rural)	-	0	0	(
Eating fruit	-	0	0	(
Skipping breakfast	0	0	1	(
Eating CHO like sweet & chocolate	1	0	2	(
Family history of obesity	1	0	3	(
Time spent for TV viewing activity per day (<2 hours is the comparative time)				
2-4 hrs.	0	0	1	(
> 4 hrs.	1	0	3	(
Moderate activity per week	-	0	0	(
Constant	0	0	2	-
*Significant at 0.05 level				

Note :OR : odds ratio CI : confidence interva

Table 8: We used a binomial logistic regression analysis to predict the effect of different variables on overweight and obesity after using of Chi-square test which

compared between the dependent and independent variables.

The results showed that: **age** in years significantly affects overweight and obesity by 1.159 times when increased (OR=1.159; P=0.000; 95% CI for OR= 1.11-1.21); overweight and obesity in patients of **no job or retired** was significantly higher than state officials by 10 times (OR=10; P=0.026; 95% CI=1.317-75.943); **farmers** had less overweight and obesity than state officials by 0.013 time (OR=0.013; P=0.000; 95% CI=0.003-0.06). However, **laborers** had lower overweight and obesity than state officials by 0.042 time (OR=0.042; P=0.000; 95% CI=0.014-0.12) while **business persons** had higher overweight and obesity than state officials by 12.6 times (OR=12.6; P=0.014; 95% CI=1.666-95.315). **Rural residence** of patients had less effect on overweight and obesity than urban residence by 0.136 time (OR=0.136; P=0.000; 95% CI for OR=0.06-0.307). Yet, patients **eating fruit** frequently had less overweight and obesity than patients who did not eat fruit by 0.502 time (OR=0.502; P=0.04; 95% CI for OR 0.26-0.967), Overweight and obesity were 1.46 times higher in patients who **skipped breakfast** frequently compared with those of no skipping (OR=1.46; P=0.027; 95% CI for OR= 1.045-2.039); eating CHO like; **sweet and chocolate** had the highest effect on overweight and obesity by 2.709 times compared with patients with no such intake (OR=2.709; P=0.000; 95% CI for OR= 1.855-3.956). F**amily history** of obesity patients had overweight and obesity 3.746 times higher than those without history (OR=3.746; P=0.000; 95% CI=2.323-6.04). The **TV watching** activity had a great effect on overweight and obesity where watching for 2-4 hrs. per day were more overweight and or obese by 1.765 times than those with less than 2 hrs. per day watching (OR=1.765; P=0.025; 95% CI for OR=1.072-2.904). Finally, **moderate physical** activity had a significant effect on lowering overweight and obesity when practice for more than 5 days per week by 0.26 times is compared with patients of practice for less than 5 days per week or never (OR=0.26; P=0.003; 95% CI for OR= 0.108-0.624).

Discussion

This current research showed the prevalence of overweight and obesity among patients aged 18 years and above who attended main primary health care centers in Babil governorate of Iraq. The prevalence of overweight and obesity according to this present survey was 37.6%, and 40% respectively. This result was comparable to other results in Arabic-speaking countries neighbored to Iraq; where the prevalence of obesity ; in Kuwait (30% for male, 55% for female), in King Saudi Arabia (23% male, 36% female), in United Arab Emirates (25% for male, 43% for female) according to WHO estimate in 2010 [13].

Another cross-sectional study conducted in the South of Iraq (Basrah city) showed that the overall prevalence of obesity from 2003-2010 was 55.1% of the population (54.7% women, 45.3% men) [14] .

Age: According to the current study, the percentage of overweight and obesity had increased as the age increased; this result agreed with a study done in Pakistan to highlight that there was an increasing in the prevalence of overweight and obesity with increasing age (OR: 1.15, 95% CI: 1.12-1.18, P<0.05) [15]. When a patient gets aged, hormonal changes, less active lifestyle with low physical activity, and the amount of muscle mass tend to decrease with age which lead to decrease in metabolism.

Occupation: The current study showed highest percentage of obesity was among no job or retired, business, and housewife compared with both farmer and laborer. this result agreed with

a study conducted in the Kingdom of Saudi Arabia in 2004 which showed that the prevalence of obesity was higher among housewives (P=0.0001) [16]; it also agreed with another study conducted in Pakistan on 897 men their age 30 yrs. as the current study showed that occupation was a significant predictor of overweight/obesity among the study participants. Furthermore, the study showed that business persons were more prone to be obese than others by 2.29 times (OR=2.29, 95% CI=1.34-3.94, P<0.05) [15] .

Residence: The current study showed that urban residents had a higher proportion of overweight and obesity than rural residence; hence, it agreed with the studies in EMR which showed that the prevalence of overweight in urban areas of Egypt 45.3% in male, and 39.6% in females , whereas in rural areas 28% in male and 36.5% in female respectively. Similar findings had been seen in Morocco, Oman, Palestine, and Kingdom of Saudi Arabia. After adjusting some confounding factors, urban residence had a major determinacy of general obesity (OR=2.62, 95% CI= 3.32-3.92) [17] .

Obesity is more prevalent in urban than rural sectors because urbanization means decreased level of physical activity and increased availability of food, as well as exposure to fast food. In addition, another change in lifestyle between urban and rural areas leads to increase exposure to western media in urban areas, which influence the urban people to match with western ways of life [18] .

Eating Carbohydrates like; sweet, chocolate: The result here agreed with the association between sugar, sweets and some body weight adiposity because sweetened foods are often rich in fat with combined increase in fat and sweet intake can lead to weight gain and sweet elimination is one of the eating process associated with less body weight gain or loss [19]. Another study showed that carbohydrate quality is much more important in preventing more weight gain than quantity like; sugar, sugary drinks which had a high glycemic index and glycemic load that caused fast increase in blood sugar and insulin that in turn causing hunger to spike leading to overeating and subsequent weight gain [20] .

Eating fruit: The current study agreed with many studies indicating the benefit of frequent intake of fruit to lower or control weight; it had similar findings with a study held to show that the diet which is low in fat, sugar, and high in fruit and vegetables can decrease body weight or prevent weight gain over time, because fruit consumption can reduce the overall energy density of the diet, promote satiety, decrease the total energy intake, and increase diet quality with subsequent significant BMI decrease [19]. Another study, conducted in Iran on 486 women aged 40-60 years, showed that the dietary pattern characterized by high consumption of fruit, vegetables and legumes had lower risk of general and abdominal obesity by decreasing their odds (OR=0.34, 95% CI=0.17-0.63, P<0.05) [20] .

Skipping breakfast: Similar findings were obtained from a meta-analysis study in 2011, suggesting that a positive relationship between skipping breakfast and overweight and obesity is observed globally regardless of the cultural diversity among countries that encourage breakfast consumption in decreasing the risk of overweight and obesity (OR=1.17, 95% CI=1.08-1.28, P=0.003) [21] .

Skipping breakfast is common in both children and adults; breakfast is considered to be the first most important meal of the day; so, skipping it showed to have an inadequate intakes of key nutrients that could be made up later meals including; sugar and protein and vitamins [22] .

TV watching: TV is the most popular and commonly used media in all places of Iraq and among all age groups. The current result was in

agreement with the study done in USA which showed that there were two sedentary behaviors common in the U.S society who were TV watching and users of computer where both of them had a positive association with elevated insulin level, obesity, metabolic syndrome, and diabetes [23]. Watching TV can promote weight gain and obesity by promoting poor diet, displacing time for physical activity, giving more chances to unhealthy diet, and by interfering with sleep.

Moderate physical activity: Similar results were obtained from a cross-sectional study conducted in Morocco among 2891 adults; it has been found that the prevalence of obesity was lower in participants engaged in at least a 30-minute moderate physical activity per day compared to another group who were not engaged in such an activity (10.4% vs. 15.6%, P< 0.001) [24]. The current result coincided with that of the Canadian Health Measures Survey (CHMS) with a statistic collection of data from 2009-2011 from nationally representative sample of Canadian people aged 6-79 years; it showed that overweight and obese adults spend less time in a moderately vigorous physical activity compared to those who were normal weight: obese adults had 16 minutes /day, overweight had 21 minutes /day, whereas normal weight spent 27 minutes /day. In addition, physical activity is important in controlling weight by increasing metabolism, regular sleep, enhancing choices for healthy foods [25] .

This result was in line with a study conducted in Saudi Arabia, among Saudi students, which stated that the students who sleep for 7 hrs. or less significantly had increased the risk of obesity in both boys and girls, and those with intermittent sleep patterns also showed an increase prevalence of overweight and obesity [26]. Another meta-analysis based on experimental study highlighted that there was an association between reduced sleep amounts and obesity because sleep or sleep deprivation can cause a feeling of fatigue with reduction in physical activity, and due to neurohormonal effects that increase caloric intake [27] .

A similar finding was gained by a cross-sectional study conducted in Egypt from 2011 to 2012 among 500 males aged from 18-30 years; it showed that there was a significant association between obesity and the presence of family history of obesity as a logistic regression analysis revealed that positive family history of obesity increased odds of the young to be obese (OR=5.72,95% CI=1.05-32.43,P=0.012) which gave a similar result to that of the present study [28]. The reason behind the role of family history is that the genetic variations had an effect on metabolism, tolerance to physical activity and appetite which cause a strong argument for their role in current conductive environments of obesity which played a significant and consistent contribution to BMI at all ages [29] .

Conclusion

Socio-demographic characteristics like age, occupation, residence are significantly associated with obesity in the study group. Frequency of eating of different kinds of food or drinks were significantly associated with changes in BMI categories of the participants.

There was a statistically significant relationship between BMI classes and the moderate physical and vigorous activity frequency. Other variables like sleeping hours per day and family history of obesity showed a significant statistical relationship with BMI classes of the patients.

The following variables showed an effect on the odds of overweight and obesity: age, no job or retirement, farming, laboring, business, rural residency, eating fruit, skipping breakfast, eating carbohydrates like; sweet, chocolate, TV watching more than 4 hrs per day, moderate physical activities, and family history of obesity.

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Expression Of Cyclooxygenase-2 And Interlukin-6 Mrnas In Iraqi Patients With Breast Cancer

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Abstract

Background: Breast cancer is one of the most common malignant tumors that endanger women's health internationally, relatively uncommon in men, accounting for only 1% of all cancer cases. Location, way of life, age at marriage, and obesity are a few environmental variables that increase the risk of breast cancer.

Aim of study: the study aims to explain how the pro-inflammatory cytokines (IL-6) induce the inflammatory events in patients with breast cancer and to describe whether cyclooxygenase-2 promotes tumor growth in breast cancer or not.

Materials and methods: The current case-control cross-sectional study included 45 patients with a history of breast cancer, and it was done in multiple places in Hilla, Babylon Province, between November 2022 and March 2023.Interlukin-6 and Cyclooxygenase-2 by QPCR.

Results: The results have shown a significant increase of IL-6 ($P < 0.05$) in patients compared with control. Also, the results have shown a significant increase ($P < 0.05$) of COX2 in patients compared with control.

Conclusion: There is a significant increase in the means of Interlukin-6 and Cyclooxygenase-2 in the patients with breast cancer.

Keywords: Breast Cancer, Interlukin-6, Cyclooxygenase-2.

INTRODUCTION

Breast Cancer (BC) is one of the most common malignant tumors that endanger women's health worldwide(1). Men's cancer is exceedingly rare, accounting for about 1% of all cancer cases(2). It occurs when breast cells begin to proliferate uncontrollably as a result of an accumulation of essential gene changes(3). A multitude of genetic and environmental factors contribute to such alterations and tumor growth. The lump may be asymptomatic or detectable during a physical examination of the breasts(4). BC is a malignant tumor that starts in the breast tissue, usually in the lining of the breast lobules or milk ducts, and spreads to other parts of the body(5). The two most common types of BC are ductal and lobular carcinoma. Ductal cancer develops in the duct to the nipple, whereas lobular cancer begins in the gland that produces breast milk(6).

Geographic location, living circumstances, age at marriage, and obesity are all environmental factors that enhance the risk of BC. Gaining weight raises the risk of having BC considerably. Gender is another major factor in BC. Furthermore, women have substantially more breast cells than men, and therefore have a significantly higher incidence risk. Another risk factor for BC is age, which raises the probability of developing the disease in older people(7).

Early detection of BC is the most effective technique for saving lives and lowering healthcare expenditures over time. BC detection and diagnosis technologies continue to advance in order to give patients with less invasive options and more accurate diagnoses(8). Cyclooxygenase-2(COX-2) is a membrane-bound and rate-limiting enzyme(9) and has long been regarded as a therapeutic center for inflammation and pain(10). The COX-2 enzyme is also known as prostaglandin (PG)-endoperoxide synthase 2 because it creates prostanoids such as prostaglandin E2 (PGE2) and helps to manage many procarcinogenic effects(11). COX-2 overexpression does, in fact, play an important role in various stages of cancer(12). Furthermore, a number of studies examining the relationship between cancer and inflammation have proposed employing COX-2 for cancer therapy or chemoprevention(12). Furthermore, epidemiological studies and clinical trials have shown that long-term use of COX-2 inhibitors like celecoxib and rofecoxib may reduce the risk of breast, lung, prostate, esophageal, liver, pancreatic, gastric, and colon cancers, as well as the Interlukin-6 (IL6) is a pleiotropic cytokine that has both pro- and anti-inflammatory actions(13). IL-6 is produced by non-cancerous cells such as monocytes, macrophages, T cells, B cells, fibroblasts, endothelial cells, and adipocytes(14). When there is an infection, inflammation, or malignancy, many distinct cell types emit IL-6(15). Intravascular angiogenesis, a critical stage in tumor formation, is stimulated by IL-6 by boosting the production of vascular endothelial growth factor (VEGF)(16). IL-6 is of particular interest because to its higher levels in BC patients' sera compared to healthy patients' sera or tissue(17).

Materials and methods:

This is a case-control cross-sectional research including 45 patients previously diagnosed with BC illness was conducted between November 2022 and March 2023 at multiple locations in Hilla, Babylon Province. Patients with BC have already been identified at the Babylon Center for Oncology. The control group is a second, often healthy group of people. The age, length of illness, smoking history, medication dose, and medical history of each patient were all determined. There were two sets of samples made, one for healthy people and one for ill people.

In this study, a quantitative reverse transcription PCR (RT-qPCR) is utilized when RNA is used as the starting material. Reverse transcriptase turns total RNA or messenger RNA (mRNA) into complementary DNA (cDNA) in this method. The cDNA is then used as a template for the qPCR procedure. RT-qPCR has applications in gene expression analysis, RNAi validation, microarray validation, pathogen detection, genetic testing, and sickness research.

Results

The current study included 45 samples from BC patients and 45 samples from healthy participants.

Clinical and demographic characteristics

The clinical demographics of the patients group were summarized in [Tab: 1] illustrated the Cyclooxygenase-2 and in [Tab: 2] for Interlukin-6 of analyzed group which was 45 patients and 45 for healthy control group. The gender distribution was only women.

According to the findings of the study, there has been a statistically significant increase in cyclooxygenase-2 levels in BC patients compared to the control group. According to the data in [Tab: 1] and [Fig: 1] it was (P 0.0).

Table1: Statistical summary of concentration of cyclooxegenase-2 of patients compared with control.

Groups	Control	Patients
Number of tested samples	24	24
mean	0.6729	1.059
Std. Deviation	0.3986	0.3702
Range	1.377	1.375
P value	0.0011	

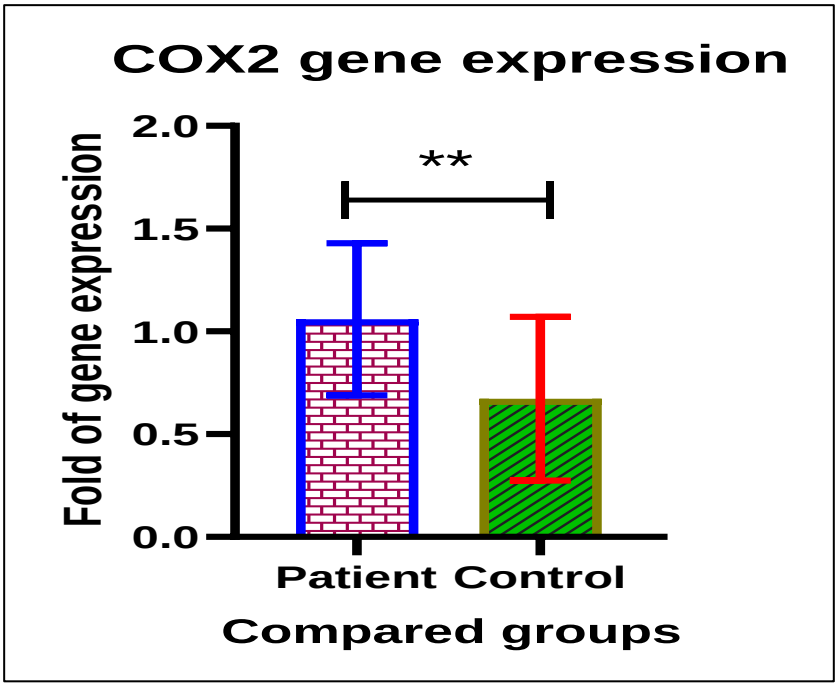


Figure:1: The change comparison between the groups expressed COX2 gene in patient and control.

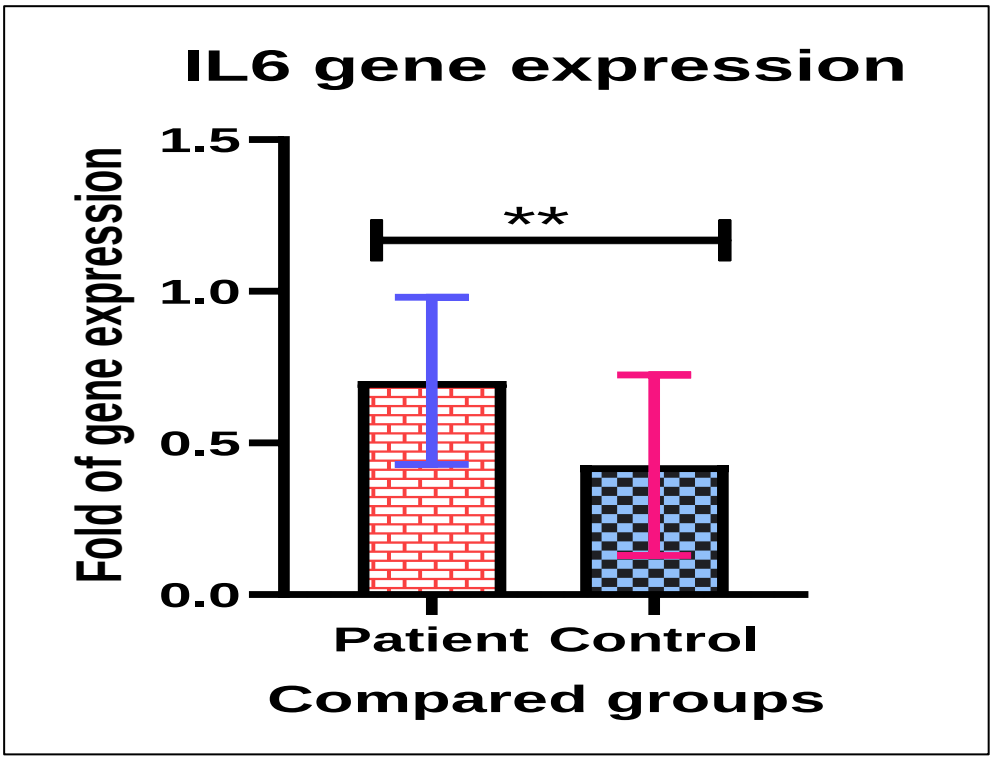
Cyclooxygenase 2 (COX-2) is an inducible form of the enzyme that catalyzes the first stage of prostanoid synthesis. Numerous studies have demonstrated that COX-2 plays an important role in the beginning and development of cancer via a number of processes, including cell proliferation, cell death, cell adhesion, and tumor neovascularization. COX-2 has also been linked to MDR via up-regulating efflux transporters (such as P-gp), which diminish intracellular drug concentration(18). Numerous studies have found that the presence of COX-2 is significantly related with large tumor size and advanced disease stage(19). The recent data reveal that COX2 levels in patients are significantly higher (P 0.01) than in controls, validating the idea that COX2 levels grow with tumor cell density. These findings are comparable to those of Basu et al. (2006), who discovered that high COX-2 levels are exclusively seen in highly invasive BC cells(20). This might explain the previously reported higher prostaglandin levels in breast tumors(21). In contrast, no COX-2 gene expression was found in normal breast tissue(22). It is unclear how COX-2 levels rise in BCs, but one possibility is that

cancer cells become intrinsically more active in COX-2 production than non-neoplastic cells(23).

Interlukin-6 was strongly associated with the group of BC patients, as shown by the fact that their levels of the protein were much greater than those of the control group, as illustrated by the [Tab: 2] and [Fig: 2]. (P 0.01), on the other hand.

Table 2: A statistical summary of concentration of Interlukin-6 of patients compared with control.

Groups	Control	Patients
Number of tested samples	24	24
mean	0.4266	0.7049
Std. Deviation	0.2974	0.2755
Range	1.142	1.019
P value	0.7175	



(Figure: 2): The change comparison between the groups expressed IL6 gene in patient and control.

Interleukin-6 (IL-6) is a cytokine that stimulates hematopoiesis and lymphocyte activation, but it is now being identified as a regulator of cancer formation, invasion, and metastasis. Inflammation and BC have long been associated. BC IL-6 expression increases with tumor grade, and increased blood IL-6 levels are associated with a poor prognosis for survival(24). High IL-6 levels have previously been associated with poor overall survival and tumor growth in a range of cancers(25). Interleukin (IL)-6 may influence how cancer cells grow and disseminate, how osteolysis and humoral hypercalcemia occur, and how estrogen levels in BC tissues are managed (26). However, its specific role remains uncertain and fluctuates. It suggests that the kind of tumor cell may influence how

IL-6 promotes tumor cell growth(27). A significant upregulation of IL-6 in patients compared to controls (P 0.01) has been detected. The unregulated inflammatory responses of IL-6 cause chronic inflammation and even malignancy. BC prognosis is connected to IL-6 expression(28).

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The Clinical Manifestations of Otolaryngology in COVID-19

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Abstract

Background: In late 2019, a new coronavirus known as SARS-CoV-2 emerged, causing an acute respiratory disease called COVID-19. The outbreak originated in China and quickly gained a global attention. COVID-19 can cause various upper respiratory tract symptoms such as sore throat, nasal obstruction, and loss of smell function

Patients and Methods: this is a cross-sectional descriptive study done during the COVID-19 pandemic from June 1st, 2020 to August 31st, 2020. The study was carried out in some isolation hospitals located in Baghdad and Najaf cities. The collected data are from laboratory-confirmed COVID-19 positive patients by using a pre-designed questionnaire which included demographic information such as age, gender, occupation, and place of residence. All participants were specifically asked about their symptoms related to the ear, nose, and throat (ENT) system.

Results: A Total number of 408 confirmed Covid-19 cases had been included in the current study. Age range of participants was from 12 to 86 years with average of 51.42 years. The study has revealed that sore throat is the predominant ENT symptom in COVID-19 cases, while ear symptoms are uncommon. The most common nasal manifestations observed in COVID-19 patients were anosmia/ hyposmia and nasal obstruction.

Discussion: This study demonstrated the different ENT manifestations occurred COVID-19 patients. These manifestations involved both lower and upper respiratory tract symptoms. Looking to these different manifestations with more interest can help in the early diagnosis and treatment of COVID-19 cases.

Keywords: SARS-CoV-2, ENT manifestations, COVID-19.

INTRODUCTION

In late 2019, a new coronavirus known as SARS-CoV-2 emerged, leading to an acute respiratory disease called COVID-19. The outbreak appeared first in China and quickly gained global attention. On January 30, 2020, the World Health Organization (WHO) announced COVID-19 as a pandemic and a public health emergency of international

concern. This marked the third occurrence of a highly pathogenic and widespread coronavirus epidemic, following the outbreaks of severe acute respiratory syndrome (SARS-CoV) in 2002 and Middle East respiratory syndrome (MERS-CoV) in 2012. The emergence of SARS-CoV-2 has resulted in significant public health crises worldwide [1] .

On February 24, 2020, the first case of COVID-19 was recorded in the city of Najaf in Iraq. The case involved an Iranian student of religion, and a sample from the individual was examined.

COVID-19 primarily manifests with lower respiratory tract symptoms, including cough and difficulty in breathing. In severe cases, it can progress rapidly to acute respiratory distress syndrome (ARDS) [2] . Additionally, COVID-19 can also cause various upper respiratory tract symptoms such as sore throat, nasal obstruction, and loss of smell function [3] .

Aim of the study:

The aim of the study is to determine and interpret the different ENT (ear, nose and throat) manifestations in patients who were reported as COVID-19 positive.

Patients and Methods

A cross-sectional descriptive study was conducted during the COVID-19 pandemic from June 1st, 2020 to August 31st, 2020. It was carried out in some of the isolation hospitals located in Baghdad and Najaf cities. The data were collected from laboratory-confirmed COVID-19 positive patients by using a pre-designed questionnaire which included demographic information such as age, gender, occupation, place of residence, number of rooms in the house, and number of family members residing in the house. Cases with mild to moderate conditions were included and those with severe to critical status were excluded.

All participants were specifically asked about their symptoms related to the ENT system. These symptoms included sore throat, changes in taste, difficulty swallowing (dysphagia), painful swallowing (odynophagia), hoarseness, nasal obstruction, nasal discharge, nosebleeds (epistaxis), facial pain, changes in smell, hearing loss, earaches, ear discharge, ringing in the ears (tinnitus), dizziness (vertigo), and facial paralysis (facial palsy).

Results

A Total number of 408 confirmed Covid-19 cases had been included in current study. Ages of participants ranged from 12 to 86 years with average of 51.42 years. There were 240 (58.8%) males and 168(41.2%) as shown in Figure (1) and Table (1) below.

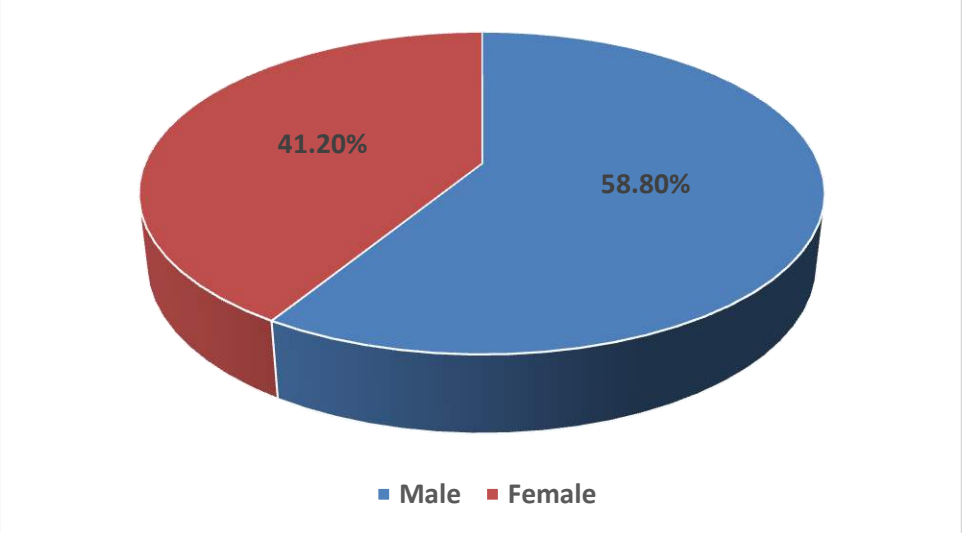

Figure (1) Gender Distribution of the Patients

Table (1) Distribution of Gender according to Age Groups.

	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90	Total
Male	2	22	35	56	51	42	30	2	240
Female	6	22	25	38	25	32	17	3	168
Total	8	44	60	94	76	74	47	5	408

Table (2) The Association between Symptoms and Gender

Symptoms	Male n=240(%)	Female n=168(%)	Total n=408(%)	P value
Nasal obstruction	81(33.7)	68(40.47)	149(36.51)	0.164
Nasal discharge	61(25.4)	40(23.8)	101(24.75)	0.711
Epistaxis	10(4.1)	3(1.78)	13(3.18)	0.177
Facial pain	16(6.6)	11(4.58)	27(6.61)	0.962
Anosmia/hyposmia	108(45)	98(58.3)	206(50.49)	0.008
Cacosmia	8(3.3)	10(4.16)	18(4.41)	0.204
Anosmia as only symptom	21(8.7)	20(11.9)	41(10.04)	0.296
Sorethroat	149(62.1)	101(60.1)	250(61.27)	0.688
Change of taste	90(37.5)	73(43.45)	163(39.95)	0.227
Dysphagia/odynophagia	96(40)	74(44.04)	170(41.66)	0.414
Hoarseness	41(17.1)	31(18.45)	72(17.64)	0.721
Otalgia	23(9.58)	19(11.3)	42(10.29)	0.572
Ear discharge	2(0.83)	3(1.25)	5(1.22)	0.389
Hearing loss	17(7.1)	17(10.1)	34(8.33)	0.274
Tinnitus	14(5.8)	17(10.1)	31(7.59)	0.107
Vertigo/dizziness	36(15)	39(23.2)	75(18.38)	0.035
Facial palsy	4(1.66)	0(0.0)	4(0.98)	0.804

Table (2) shows no significant association between gender and symptoms except for Anosmia/hyposmia and vertigo/dizziness which is higher in females than males

Table(3) Association between symptoms and age groups.

Symptoms	Age groups								total	P value
	11-20 n=8	21-30 n=44	31-40 n=60	41-50 n=94	51-60 n=76	61-70 n=74	71-80 n=47	81-90 n=5		
Nasal obstruction	5	23	22	43	28	18	8	2	149	0.00
Nasal discharge	4	14	13	28	18	14	8	2	101	0.23
Epistaxis	0	2	2	4	3	1	1	0	13	0.95
Facial pain	0	6	8	5	5	3	0	0	27	0.00
Anosmia/hyposmia	5	30	39	54	33	30	14	1	206	0.00
Cacosmia	1	3	5	5	3	0	1	0	18	0.29
Anosmia as only symptom	1	10	10	8	6	5	1	0	41	0.02
Sorethroat	5	25	35	62	46	44	31	2	250	0.88
Change of taste	4	19	22	46	27	26	18	1	163	0.51
Dysphagia/ odynophagia	5	12	14	49	29	33	26	2	170	0.00
Hoarseness	3	5	5	18	12	19	9	1	72	0.15
Otalgia	0	7	4	13	7	8	3	0	42	0.53
Ear discharge	0	2	1	2	0	0	0	0	5	0.39
Hearing loss	0	9	6	6	7	5	1	0	34	0.07
Tinnitus	0	4	6	9	6	4	1	1	31	0.60
Vertigo/dizziness	3	7	8	18	14	20	5	0	75	0.19
Facial palsy	0	0	0	0	1	0	2	1	4	0.00

Table (3) shows a significant association between nasal obstruction and age (higher percentage in 11-30 years age) as well as a significant with facial pain (higher percentage in 21-40). Anosmia was significantly higher in the age groups (21-50years); dysphagia/ odynophagia were significantly higher in (11-20years); the facial palsy was higher in percentage in the age group 81-90 years.

Discussion

In December 2019, a new epidemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) appeared in China, leading to the declaration of the disease as COVID-19 by the World Health Organization in February 2020. COVID-19 exhibits a wide range of clinical presentations,

varying from mild cases without specific symptoms to severe septic shock and multiple organ dysfunction [4],[5] . However, the clinical features of COVID-19 remain largely uncertain. While there is a significant focus on the lower respiratory tract manifestations and consequences of the virus, there is limited literature on the ENT manifestations of COVID-19, necessitating further study to define the epidemiological and clinical characteristics of non-respiratory symptoms.

This literature aims to provide an updated understanding of ENT clinical features in COVID-19 patients, based on published and peer-reviewed articles. The findings of this study align with previous reports, indicating that sore throat is the predominant ENT symptom in COVID-19 cases, while ear symptoms are uncommon [6] . These observations suggest differences in viral spread patterns compared to influenza, SARS, and MERS-CoV.

In the current study, the most common nasal manifestations observed in COVID-19 patients were anosmia/ hyposmia and nasal obstruction. However, nasal discharge was reported in a smaller proportion of patients.

Based on these findings, if an ENT manifestation were to be added to the definition of suspected COVID-19 cases or the COVID-19 checklist, sore throat would be a more suitable choice than nasal discharge. It is important to note that all ENT manifestations associated with COVID-19 are nonspecific, making them easily overlooked, and there are no emergency ENT symptoms such as epistaxis or stridor reported in COVID-19 patients. Post-viral anosmia, a condition characterized by a loss of smell following a viral infection, is a common cause of impaired sense of smell in adults, accounting for approximately 40% of cases of anosmia.

While it is assumed that coronaviruses, including the new COVID-19 virus, can cause loss of smell in infected patients, the occurrence of this symptom is not definitive [7] . The literature on smell and taste impairments in COVID-19 patients is limited, and there is a lack of peer-reviewed studies supporting a causal link between olfactory loss and COVID-19 [8].

Additionally, many olfactory studies in COVID-19 patients do not provide comprehensive descriptions of the patients' clinical features, which precluded their inclusion in the current study.

In an article published by Minnie et al, it was found that 59% of patients infected with the Covid-19 virus experienced a loss of sense of smell and taste, compared to 18% of those who tested negative for COVID-19. The authors suggested that a concomitant loss of smell and taste, fever, persistent cough, fatigue, and gastrointestinal symptoms could predict a positive COVID-19 test with a specificity of 0.86 and an average sensitivity of 0.54.

Lichen et al. [9] conducted the first multi-centre peer-reviewed study reporting olfactory disorders in 85.6% of cases. However, it should be noted that they used a questionnaire that focused on the psychosocial burden of olfactory disorders, which could lead to overestimation, especially considering the COVID-19 pandemic and the resulting restrictions on social life .

Kai et al. [10] , in a study involving 237 United State patients with COVID-19, found that 73% reported anosmia, with anosmia being the initial presentation in 26.6% of cases. Therefore, it is recommended to consider patients with anosmia, without nasal obstruction or a runny nose, as suspected cases of COVID-19 and advise them to undergo testing or self-isolation

Interestingly, a majority of COVID-19 patients (66%) reported a full recovery of the smell perception after treatment [11] .

It is worth-noting that auditory manifestations have not been widely reported in studies of COVID-19, and there is limited literature on auditory complications due to MERS-CoV. In a previous report on MERS-CoV infection [12] , brainstem involvement was noted, suggesting the possibility of neural hearing problems.

Mustafa et al. [13] also found that COVID-19 infection could have adverse effects on cochlear hair cell functions, leading to a decrease in high-frequency pure tone thresholds, even in asymptomatic individuals.

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The Association Of Adiponectin, Homocysteine, B 12 And Folic Acid In Iraqi Women With Preeclampsia And Its Severity

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Abstract

Background: preeclampsia is a common obstetric disorder that remains a leading cause of maternal and perinatal mortality and morbidity. Maternal serum concentrations of adiponectin, folate, homocysteine, and vitamin B12 have been found to be associated with pre-eclampsia. Nevertheless, reported studies involved still not clear with variable reliably. The aim of the present study is to examine the relationship between these biomarkers and pre-eclampsia and its severity in Iraqi population. **Aims:** The study aims to evaluate the association between maternal serum adiponectin, homocysteine, B12 and Folic acid and preeclampsia and its severity.

Study design and setting. A case control study carried out in Al-Zahraa Maternity and Pediatric Teaching Hospital in Najaf city/ Iraq from the 1st of December 2019 to the 1st of December 2020. **Patient and Methods:** The study included 50 pregnant women with preeclampsia and a comparative control group of 50 normotensive pregnant women. Preeclamptic women were further subdivided into 14 women with severe preeclampsia and 36 women with mild preeclampsia. Serum Adiponectin, Homocysteine, B 12, and Folic acid were measured by using special ELIZA (Enzyme linked immunosorbent assay) technique. **Results:** There was a significant increment in the level of Adiponectin and Homocysteine while vitamin B12 and Folic acid were significantly decreased in preeclamptic pregnant women in comparison to the control group. On the other hand, there was no significant relation between the severity of preeclampsia and the level of Adiponectin, Homocysteine, Vitamin B 12, and Folic acid.

Conclusion: Women with preeclampsia had significantly lower vitamin B12 and folic acid and significantly higher concentrations of adiponectin and homocysteine than normotensive pregnant women, but no relation with its severity.

Keywords: preeclampsia, Adiponectin, Homocysteine, Vitamin B 12, and Folic acid

INTRODUCTION

Preeclampsia (PE) is a common obstetric problem of about 3–10% of all pregnancies being diagnosed as having hypertension and proteinuria after the 20th week of pregnancy. PE is primarily managed by early screening and prevention[1] as it remains a leading cause of maternal and perinatal mortality and morbidity secondary to its complications such as; eclampsia, abruptio placentae, premature birth and fetal growth retardation and are associated with significant long-term detrimental effects on both maternal and offspring cardiovascular health [2,3].

The exact mechanism underlying etiology remains unknown. There are many theories about the etiology of PE including endothelial dysfunction, inflammation and angiogenesis[4,5]. Adiponectin, a specific adipocyte derived hormone, has been considered to improve insulin sensitivity, inhibits vascular inflammation and atherosclerosis. Thus, it has been hypothesized that adiponectin may be involved in the pathophysiology of PE[6] because of its regulatory roles in trophoblast proliferation, trophoblast differentiation, trophoblast invasion of the decidua, and decidual angiogenesis[6].

An increased concentration of total circulating homocysteine in serum is recognized as an independent risk factor for cardiovascular diseases (CVD) which might be the mechanism of endothelial injury and hence vasospasm [7]. Moreover, determinants of hyperhomocysteinemia, such as low concentrations of folic acid and vitamin B_{12} involved in homocysteine metabolism are also associated with increased risk of vascular damage[8–9]. Elevated plasma homocysteine, low concentrations of vitamin B_{12} and folic acid are atherogenic factors that trigger vascular changes compatible with atherosis and endothelial dysfunction similar to the vascular changes of the placenta in PE (10,11).

Despite extensive research, conclusive evidence on the cause and consequences of PE remains to be discovered and further studies are needed. The present study aimed to determine the levels of serum Adiponectin, Homocysteine, Folic acid and vitamin B_{12} and their correlationship in Iraqi women with PE.

Materials and Methods

Study designs and setting

This prospective case control study was performed in Al-Zahraa Maternity and Pediatrics Teaching Hospital from the 1st of December 2019 to the 1st of December 2020.

Study participants and sampling: a study group of 50 women having PE with comparative control group of 50 women who have an apparently well-run, non-preeclamptic pregnant women, have been included in the present study.

Data collection: For all cases, the following data and investigations were made: maternal age, parity, gestational age, blood pressure, BMI, urinary protein, complete blood count, renal function test , liver function test , serum albumin , weight of newborn and Apgar score.

PE is diagnosed when hypertension, systolic blood pressure ≥ 140 mmHg, or diastolic blood pressure ≥ 90 mmHg, and proteinuria (2-4 +) on dipstick test appeared after 24 weeks of gestations on two occasions in previously normotensive non proteinuria women.

Then, the women with PE were classified into mild, including 36 women, and severe, including 14 women, PE according to the following criteria:

Mild PE is defined as blood pressure equals to or more than 140/90 mmHg on two occasions at least 6 hours apart and proteinuria equals to or more than 300 mg/24 hour but less than 5 g /24 hour [12]

Severe PE is diagnosed when blood pressure equals to or more than 160 systolic or equals to or more than 110 diastolic with proteinuria +3

or more in 2 random urine samples collected 4 hours apart[12].

Furthermore, severe PE is associated with: headache, visual disturbances, oliguria (less than 500 ml/24 hr), convulsions, upper abdominal pain, pulmonary oedema, elevated serum creatinine ,uric acid ,liver enzymes and thrombocytopenia[12].

Inclusion criteria

Pregnant women diagnosed as PE who have a gestational age between 20- 40 weeks of pregnancy were to be included in PE group and women who are apparently well-run uneventful pregnancy were to be included in the control group.

Exclusion criteria

Patients with chronic renal disease and auto-immune disease, patients who had meals rich in protein, patients who had essential hypertension, obesity, polycystic ovarian syndrome, insulin resistance or diabetes mellitus were all excluded.

Biochemical analysis

For measuring a complete blood count, renal function test, liver function test, serum albumin, and urinary protein, a total of 5 ml peripheral venous blood from the ante cubital vein or from the dorsum of the hand is drawn from each woman in the study by using a standard venipuncture technique. Adiponectin, Homocysteine, Vitamin B12 and Folic acid levels were estimated from the sera of patients using ELISA (Enzyme linked immunosorbent assay).

Ethical consideration: An approval for the study was obtained from the Scientific Committee in the Department of Gynecology and Obstetrics, and from the Scientific and Ethic Committee in the Faculty of Medicine / University of Kufa. The procedures included in the study were clarified to all the women and take their agreement as a verbal consent for participation in the study, including taking information, investigation, and subsequent blood aspiration.

Statistical analysis

A statistical analysis was done by using SPSS (statistical package for social sciences) version 20 in which we use ANOVA test (analysis of variance) with LSD for comparison between groups. We set p value ≤ 0.05 as significant.

The Results

The case control study including 50 pregnant patients having PE :36 with mild PE and 14 women with severe PE, with comparative control group including 50 normotensive patients. The demographic and blood pressure with proteinuria are plotted in Table (1) below. Hematological, renal, and liver enzymes, and the outcome of pregnancy like the weight of the newborn, Apgar score in 1 minute and 5 minute in the groups of the study were all compared, as in Table (1).

Table (1) A Comparison of Different Parameters between the Groups

Parameter	Controls (n=50) (A)	Mild PE (n=36) (B)	Sever PE (n=14) (C)	P value		
	Mean±SD	Mean±SD	Mean±SD	A vs. B	A vs.C	B vs. C
Age/years	26.04±5.484	26.83±7.88	32.35± 10.27	0.615	0.005	0.017
GA/weeks	38.125±1.1036	37.00±1.603	36.07±1.141	<0.001	<0.001	0.027
Systolic BP	122±6.38	142.08±7.59	185±21.75	<0.001	<0.001	<0.001
Diastolic BP	78.4±4.67	99.16±8.98	111±7.11	<0.001	<0.001	<0.001
Proteinurea	0	1	2	<0.001	<0.001	<0.001
Platelet	193.52±42.254	192.75±50.10	159.07±45.56	0.939	0.014	0.021
WBC	10.50±2.836	12.56±3.52	16.56±3.54	0.004	<0.001	<0.001
Hb g/dl	11.88±1.623	11.91±1.158	12.73±0.519	0.922	0.042	0.059
RBC	4.643±1.07	3.98±0.469	4.41±0.183	0.001	0.364	0.118
RBS mg/dl	93.62±21.979	91.74±10.8	88.98±11.75			
SGOT U/L	11.77±4.546	8.48±1.423	15.09±7.067	0.001	0.011	<0.001
SGPT U/L	8.73±3.735	8.41±3.224	8.90±7.289	0.731	0.898	0.718
Cholesterol	225.25±10.88	187.33±23.64	196.00±35.60	0.003	0.041	0.514
S.Albumin	3.391±1.105	3.11±0.389	2.93±0.213	0.168	0.169	0.609
Urea mg/dl	19.168±4.413	24.00±6.65	20.42±3.43	<0.001	0.428	0.033
Creatinine mg/dl	0.825±0.198	0.87±0.166	0.73±0.108	0.203	0.1	0.014
BMI Kg/m^2	31.31±3.559	32.25±3.21	30.21±2.66	0.199	0.279	0.055
Newborn weight	3.344±0.373	2.82±0.725	2.69±0.449	<0.001	<0.001	0.428
Apgar score1	6.32±0.843	5.33±1.0	6.00±0	0.002	0.530	0.246
Apgarscore 5	8.24±0.656	7.91±0.87	7.57±0.85	0.057	0.005	0.157

Table (2) A Comparison of Adiponectin, Homocystine, Folic acid, and vitamin B12 in the Groups of Study.

Parameter	Control (n=50) (A)	Mild PE (n=36) (B)	Severe PE (C) (n=14)	P value		
	Mean±SD	Mean±SD	Mean±SD	A vs. B	A vs. C	B vs.C
Adiponectin µ/ml	11.02±0.917	14.72±1.10	14.77±0.97	<0.001	<0.001	0.865
Homocystine µmol/L	7.34±0.926	14.79±1.19	14.25±1.32	<0.001	<0.001	0.121
Folic acid ng/ml	11.22±0.598	9.71±0.509	9.67±0.449	<0.001	<0.001	0.851
Vitamin B12 Pg/ml	432.66±46.92	352.34±40.94	345.35±39.46	<0.001	<0.001	0.616

Table (2) shows the Adiponectin serum levels with the higher levels in PE group whether mild or severe 14.72±1.10 and 14.77±0.97 and lower in control group 11.02±0.917(p-value **<0.001)**. It shows a significant increment in the level of homocysteine between preeclamptic patients either mild 14.72±1.10 or severe 14.25±1.32 and normotensive control group 7.34±0.926 as p value <0.001 for both in comparison with the control group. There was a significant decline in the level of Folic acid and B12 in both mild and severe PE (9.71±0.509, 9.67±0.449) (352.34±40.94, 345.35±39.46) in comparison to the controlled non preeclamptic women (11.22±0.598) and (432.66±46.92, p-value **<0.001)**.

Discussion

PE is closely linked to various metabolic changes, altered inflammatory responses, endothelial dysfunction and, recently, to an anti-angiogenic state (13,14,15).

The findings of the present study have indicated that the mean plasma adiponectin concentration is higher in patients with PE than in normal pregnant women, but there is no difference between severe and mild PE. They are in agreement with some previous reports like that of Hayashi M. where a sample of 15 PE patient against 23 normal pregnant women. The mean adiponectin levels where the PE group had higher concentrations of adiponectin(16). This was true for other researchers in different sample sizes like Ramsay JE et al , Haugen F et al, Hendler I et al, Kajantie E et al, Lu D et al and Naruse K et al(17,18,19, 20, 21,22). Another study done by Khosrowbeygi found that the serum levels of adiponectin were significantly higher in the preeclamptic group than those in the normal control group and that this elevation of adiponectin levels might be a physiological feedback response to minimize endothelial dysfunction in PE patients(23). This, however, contrasted other observations in which serum adiponectin concentration is lower in patients with PE than in normal pregnant women (Cortelazzi D. et.al, when he compared serum adiponectin in 5 PE with 37 healthy pregnant women, D'Anna R and Suwaki N et al) (24,25,26). Differences in the study design and sample size may contribute to the discrepancies among studies.

As the homocysteine metabolism required Folate and vitamin B12, and their deficiency can result in increased homocysteine concentration, the present study has shown a significant increase in the level of homocysteine in preeclamptic women in comparison with normotensive pregnant women and vitamin B 12 and Folic acid which were significantly decreased in PE but they does not reflect the severity of the disease. Hyperhomocysteinaemia can result from genetic or nutrient related disturbances in the transsulfuration or remethylation pathway for homocysteine metabolism. Inadequate intake of vitamin B12, B6 or folate may underlie some cases of elevated homocyst(e)ine levels. It is furthermore known that renal function plays a significant role in homocysteine catabolism and it usually affected PE. Hyperhomocysteinemia may result in vasomotor dysfunction because the amended structure and biomechanics of blood vessels and enhanced thrombosis are considered to be independent risk factors for metabolic and cardiovascular disease. The mechanism of vascular damage by homocysteine has not been fully explained, but the importance of vascular smooth muscle cell proliferation and vascular remodeling leading to thrombosis and atherosclerosis should be considered. Wang et al. [27] had shown that maternal plasma homocysteine levels are significantly higher in pregnancy with pre-eclampsia and/or umbilical placental vascular disease.

Marzena Laskowska et al [28] compare the maternal serum levels of endothelial nitric oxide synthase, asymmetric dimethylarginine (ADMA). Homocysteine in normal and preeclamptic pregnancies shows that serum concentrations of homocysteine and ADMA were increased in both early onset and late onset PE. An additional study done by Shahid A. et al [29] also shows that there was significant hyperhomocysteinemia in patients with PE.

Another study done by Şanlıkan F.et al[30]shows that mean serum Homocysteine level was significantly higher in the preeclamptic group as compared to controls but there were no statistically significant differences in Homocysteine levels between mild and severe PE groups. In addition, Atis et al[31] also measured serum Homocysteine in women with mild and severe preeclamptic pregnant women and found that Homocysteine increases in PE, but the severity of PE is not correlated with homocysteine levels while a study done by Ingec et al[32] shows that plasma homocysteine significantly elevated in severe PE not in mild ones.

Stoĭkova et al[33] study finds a link between the serum homocysteine as an endothelial dysfunction marker and the development of PE and a relation between the severity of PE and the degree of the elevation of the serum homocysteine levels. Kharb study folate, vitamin B12 and homocysteine levels in cord blood and maternal blood in PE found elevated homocysteine and folate and vitamin B12 deficiency during pregnancy may be a risk factor for PE and future cardiovascular risk[34]. On the other hand, Nahid Shahbazian, Women with PE displayed higher maternal serum homocysteine and lower serum folate and vitamin B12 levels(35) while Acilmis YG et al concluded that maternal and fetal serum homocysteine levels were found to be significantly higher in severe pre-eclampsia group compared to mild pre-eclampsia and control groups suggesting that elevated serum levels of homocysteine might be associated with severity of pre-eclampsia but the elevated serum homocysteine levels were not associated with deficiency of folic acid and vitamin B12(36) and Makedos G[37] et al concluded that homocysteine levels are significantly elevated in patients with PE compared with control group, while no vitamin deficiencies were observed. Malahayati et al[38] found that

Low folic acid levels tend to increase homocysteine levels in severe PE, whereas high folic acid levels tend to lower homocysteine levels in normal pregnancy.

Conclusions

Serum Adiponectin and Homocysteine were significantly increased, and Vitamin B 12 and Folic acid were significantly decreased in PE but they do not reflect the severity of the disease.

Recommendations

1- Further studies are needed to confirm if the prescription of folic acid and vitamin B12 in women deficient in these vitamins could decrease the level of serum homocysteine, thereby reducing the risk of PE or (if it occurs) its severity.

2- Further studies should help define the role of genetic polymorphism in enzymes of homocysteine, folic acid, vitamin B_{12} metabolism and their role in PE.

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Competing interests

The authors declare that there is no conflict of interest.

Author Contributions

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The Effect Of Maternal Body Mass Index On Duration Of Induced Labor

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Abstract

Background: Induction is the stimulation of uterine contractions to aid childbirth. Meanwhile, the prevalence of obesity is predicted to grow by 33% worldwide by the year 2030. Genetic, environmental, behavioral, and social elements all have a role in the development of obesity. The prevalence of obesity is highly associated with both ancestry and ethnicity. Numerous illnesses and malignancies are only a few of the many that can be exacerbated by obesity. Menstrual irregularities, infertility, and premature birth are just a few of the ways that obesity negatively affects a woman's ability to have healthy, natural children. Longer labors and more cesarean sections are directly related to the rising prevalence of maternal obesity, which also correlates with an increase in the use of labor induction.

The present study aims to evaluate the effect of maternal body mass index on the duration of induction of labor. **Methods:** A prospective cohort study was conducted at Al-Zahraa Teaching Hospital from December 2022 to June 2023. It included 100 pregnant women divided into overweight/obese and non-obese groups. Prim and multi gravida term pregnant women with unfavorable cervix and not in labor were included. The collected data included demographical, menstrual, medical, and surgical history, and assessment of labor duration and success. Labor was induced by using PGE1 and oxytocin. Failed induction was defined as cervical dilatation >4 cm not achieved after 12 ± 3 h of labor or ending with a cesarean section. **Results:** The study examined 100 women undergoing labor induction, finding a success rate of 80% for vaginal delivery and 20% ending in caesarean sections. Notably, failed inductions were associated with larger gestational age and higher Body Mass Index (BMI). In fact, 90% of those who had a failed induction of labor were obese (BMI >30 kg/m²). Despite these findings, there were no significant variations in maternal age, gravidity, parity, and miscarriage rates between the successful and failed induction groups. **Conclusion:** Higher BMI increases the likelihood of failed labor induction but its impact on the duration of induction is not clearly established from the current data which may need further study with increasing sample size.

Key Word : Obesity, BMI, Induced Labor.

INTRODUCTION

Due to its link with obstetrical interventions and difficulties, the rising prevalence of overweight and obesity among pregnant women is a cause for a considerable concern (1, 2). Inducing labor (IOL) is a common necessity for morbidly obese mothers and is associated with an increased risk of post-term pregnancy and pregnancy problems(3, 4). However, there is a need to investigate the correlation between maternal MBI and the length of IOL because of the increased risk of cesarean section (CS) in obese first-time mothers' (BMI) (5).

Numerous health problems, including heart disease, diabetes, joint pain, and even some forms of cancer, have been linked to obesity(6). Sleep apnea, high blood pressure, cardiovascular illness, and psychological issues are all linked to being overweight(7). It also has negative effects on a woman's ability to have children, increasing the likelihood of infertility, miscarriage, and irregular menstrual cycles(8, 9). In addition, hypothalamic-pituitary-gonadal axis abnormalities, which are associated with obesity, can lead to anovulation and infertility(8, 10, 11). Obese women may need more time in labor before a diagnosis of labor arrest can be made, which has significant consequences for the length of induced labor(12).

Obese primiparous women, who may be considerably affected in future pregnancies and delivery, may benefit greatly from a better understanding of the correlation between maternal BMI and the length of induced labor.

Aims: The purpose of this article is to investigate the impact of maternal MBI on the length of induced labor, and thereby to illuminate the causes of labor delay in overweight women and informing clinical practice. It also aims to evaluate the effect of BMI on duration of IOL.

Patients and Methods:

This prospective cohort study was conducted at Al-Zahraa Teaching Hospital, Department of Obstetrics and Gynecology for a period extended from the beginning of December 2022 to the 1st of June 2023. The studied sample will include 100 pregnant women attending to the above-mentioned hospital for IOL.

The sample is divided into two groups; the first is the case group which included women with BMI equal or more than 25 kg/m^2 (overweight and obese women). The second group (the control group) included women with BMI less than 25 kg/m^2 (non-obese).

The inclusion criteria were prim and multi gravida term pregnant ladies (>37 weeks) with a vertex presentation, unfavorable cervix (defined as bishop score less than 6), and not in labor.

The exclusion criteria were previous cesarean delivery or rupture uterus, previous uterine or cervical surgery, suspected macrosomia (ultrasound suspected body weight >4500 gr), fetal congenital abnormality or fetal death, any contraindications to vaginal delivery, abnormal situated placenta, or breach or transvers lie.

All cases were interviewed with predesigned forma that included the demographical data: age, gravidity, parity, abortion, educational level, residency, and menstrual history including the age of menarche, regularity of the cycle, past medical history, and past surgical history. A clinical examination was offered with measuring patient weight and height with estimation of BMI. In addition, an assessment of bishop score and trans vaginal ultrasound examination followed to reach active phase >4cm or successful induction with recording of the duration of the labor and the mode of the delivery and finally report the success of the IOL.

Anthropometric Measurements

The pregnant were determined by using anthropometric measurements which were taken during the study like weight and height. Weight was measured, with the shoes and heavy clothes removed, to the nearest 0.05 kg. with the use of mechanical and electronic scales in kilograms and the height was measured, with shoes removed, to the nearest 0.1cm. by using a tape measure. The BMI calculation is done by dividing the adult weight in kilograms(kg) by their height in square meters (m).

Methods of IOL

When the Bishop score was less than 5, a vaginal tab of prostaglandin E1 (PGE1) - Misoprostol (Vagiprost 25 microgram, Adwia pharmaceuticals, Cairo, Egypt) was inserted into the posterior vaginal fornix to induce labor. After 6-8 hours, if sufficient cervical softening had not occurred, more dosages were administered. When the necessary level of cervical ripening has been reached, defined as a Bishop score >7, 4 pills have been used, or 24 hours have elapsed, the process is repeated.

An hour after PGE1 was administered, the fetal heart rate was monitored, and subsequent checks were made every three hours. In the event of uterine tachysystole, an unsettling fetal heart rate, effective cervical ripening, or after 24 hours of insertion, the vaginal PGE1 tab should be removed. Participants who showed positive responses to the IOL were taken to the delivery room, and oxytocin augmentation of labor was performed if necessary. The uterine contraction patterns informed the decision to inject oxytocin. An infusion of diluted oxytocin was injected intravenously. Starting at 5 mU/min, the infusion rate was doubled every 30 minutes all the way up to a peak of 30 mU/min at the time of delivery.

Failure of IOL was defined as the inability to achieve cervical dilatation >4 cm after 12 ± 3 h of IOL (with a goal 3 contractions/10 min), or those ended with caesarean section.

Ethical considerations

Faculty of Medicine's Scientific and Ethical Committees gave their complete blessing to the study's proposed methodology, and the scientific committee at Al-Zahraa Teaching Hospital also gave their approval. Each participant provided verbal agreement following a thorough explanation of the study's goals and the confidentiality of their data.

Statistical analysis

The information was entered into IBM - SPSS V26 and imported from Microsoft Excel worksheet 16. Data given as rates, frequencies, means, and standard deviations are analyzed using statistical tests such as the Chi-squared test and the Student's t-test, respectively, to determine any significant differences.

Results

The study includes 100 women underwent IOL. The mean maternal age at presentation was 26.92 ±6.87 years, with the mean gestational age being 38.88 ±2.74 weeks. The cause of IOL is shown in

Figure **1**; the most common indication was postdate (54%).

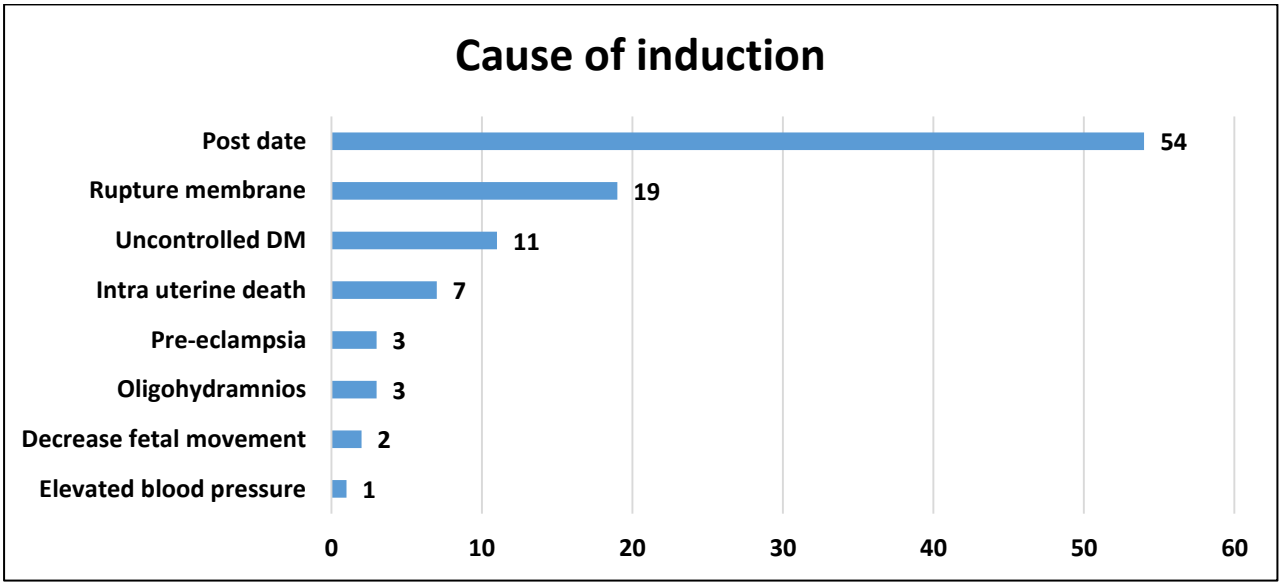

Figure 1: Causes of IOL.

The fate of the IOL was either successful, ending by vaginal delivery, in 80% or failure of IOL, ending by caesarean section, in 20%. According to the outcome of IOL, the data were divided into two groups, Group A with C/S delivery, and Group B with successful vaginal delivery.

The mean maternal age, gravidity, parity, and miscarriage were not different between the two groups while cases of failure of IOL had been associated with larger gestational age and BMI than those with successful vaginal delivery, as shown in Table 1. below:

Table 1: Distribution of Patient Characteristics according to the Groups of the Study.

Variables	Group A (n=20)	Group B (n=80)	P value
	Mean ±SD	Mean ±SD	
Maternal age	26.7 ±7.26	26.98 ±6.82	0.879
Gravidity	2.65 ±2.28	3.16 ±2.02	0.366
Parity	1.2 ±2.04	1.89 ±1.81	0.180
Miscarriage	0.45 ±0.89	0.23 ±0.57	0.292
Gestational age (weeks)	40.35 ±1.35	38.51 ±2.88	<0.0001
BMI	35.51 ±4.55	30.63 ±3.16	<0.0001

Regarding social and past medical histories, no difference was found in the outcome of the IOL; the BMI in was distributed as follow: 90% of those who had failure of IOL were obese (BMI >30 kg/m^2), as shown in Table 2. below.

Table 2: Distribution of Social and Past Medical Histories between the Two Groups

Variables		Group A	Group B	P value
		No. (%)	No. (%)	
Educational level	Illiterate	0 (0)	8 (10)	0.487

	Primary	8 (40)	33 (41.3)	
	Secondary	8 (40)	27 (33.8)	
	University	4 (20)	12 (15)	
Residency	Urban	10 (50)	36 (45)	0.688
	Rural	10 (50)	44 (55)	
DM	Yes	2 (10)	13 (16.3)	0.484
	No	18 (90)	67 (83.8)	
HT	Yes	8 (40)	16 (20)	0.061
	No	12 (60)	64 (80)	
Thyroid disease	Yes	1 (5)	3 (3.8)	0.799
	No	19 (95)	77 (96.3)	

The BMI in was distributed as follow: 90% of those who had failure of IOL were obese (BMI >30 kg/m^2), as shown in Table 1. below:

Table 2: Distribution of BMI according to the Study Groups.

BMI Group	Group A	Group B	P value
	No. (%)	No. (%)	
<25	0 (0)	3 (3.8)	<0.0001
25-30	2 (10)	16 (20)	
30-35	4 (20)	58 (72.5)	
35-40	8 (40)	1 (1.3)	
>40	6 (30)	2 (2.5)	

The cause for IOL and the method used was not different statistically in those who had successfully delivered than those who required C/S, as shown in Table 4. below:

Table 4: Distribution of the Cause and Method of Induction between the Two Groups.

Variables		Group A	Group B	P value
		No. (%)	No. (%)	
Cause of induction	Post date	16 (80)	38 (47.5)	0.231
	Decrease fetal movement	0 (0)	2 (2.5)	
	Elevated blood pressure	0 (0)	1 (1.3)	
	Intra uterine death	0 (0)	7 (8.8)	
	Oligohydramnios	1 (5)	2 (2.5)	
	Pre-eclampsia	0 (0)	3 (3.8)	
	Rupture membrane	1 (5)	18 (22.5)	
	Uncontrolled dm	2 (10)	9 (11.3)	
Type of induction	vageprost	19 (95)	62 (77.5)	0.074
	Pitocen	1 (5)	18 (22.5)	

The duration of labor was not different between the two groups, as shown in Figure 2. below:

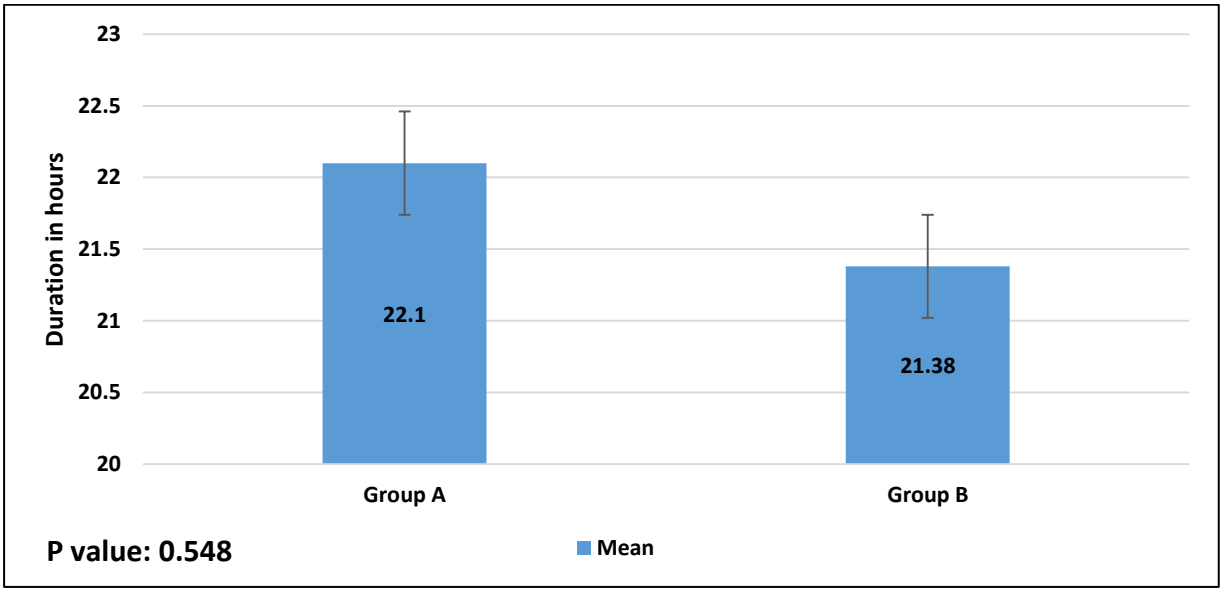

Figure 2: Duration of Labor according to the Study Group.

For the estimation of the predictors of duration of labor we applied regression analysis, which showed that BMI, is the independent variable that predict the duration of labor as shown in Table 3. below:

Table 4: Regression Analysis for Prediction of Duration of Labor.

Variables	Unstandardized Coefficients		Standardized Coefficients	t	P value
	B	Std. Error	Beta		
Maternal age	0.023	0.113	0.034	0.207	0.836
Gravidity	0.002	1.235	0.001	0.002	0.999
Parity	-1.428	1.174	-0.568	-1.217	0.227
Miscarriage	1.285	1.383	0.177	0.929	0.356
Gestational age	-0.306	0.251	-0.178	-1.221	0.226
BMI	0.322	0.144	0.272	2.235	0.028
Educational level	-0.629	0.612	-0.114	-1.028	0.307
Residency	0.438	0.996	0.047	0.44	0.661
Mode of delivery	-1.959	1.394	-0.168	-1.406	0.163
Cause of induction	-0.315	0.368	-0.194	-0.857	0.394
Diabetes	-2.107	2.112	-0.161	-0.998	0.321
Hypertension	-1.068	1.237	-0.098	-0.864	0.39
Thyroid disease	-2.86	2.35	-0.12	-1.217	0.227
Type of induction	0.034	1.967	0.003	0.017	0.986

Neonatal outcome was not different in the term of gender, requirement for NICU admission, and neonatal death, as shown in Table 5. below:

Table 6: Neonatal Outcome according to the Study Groups.

Variables		Group A	Group B	P value
		No. (%)	No. (%)	
Gender	Female	6 (30)	29 (36.3)	0.600

	Male	14 (70)	51 (63.7)	
requirement of NICU	Yes	4 (20)	16 (20)	1.000
	No	16 (80)	64 (80)	
Neonatal death	Yes	0 (0)	7 (8.8)	0.170
	No	20 (100)	73 (91.3)	

Discussion

Having a higher BMI can make it more challenging to induce labor, slow down the progress of labor, raise the risk of complications, and increase the possibility of a cesarean section; all of which can lengthen the overall time of labor(5). The present study's primary aim was to determine if maternal BMI was related to the outcome of IOL.

The study included 100 women with mean age of 26.92 ±6.87 years. The most common indication of IOL was postdate (54%), similarly found by Ramana et al(13). The rate of success of IOL in the current study was 80%, this result was consistent with the findings of previous studies (Tatić-Stupar et al(14) and Lueth et al(15)). The current study included women with a comparable maternal age to eliminate selection bias. Walker et al(16) found that maternal age did not affect the maternal and neonatal outcome in cases of IOL. Besides, the parity had no effect on the success rate of IOL, while Denona et al(17) found in their large cross-sectional study (n=2334) that nulliparous women had four time risk of C/S after IOL than multiparous women. This variability of the result could be attributed to the small sample size used in the current study,

The failure rate of IOL is significantly associated with the gestational age in the current study. Similarly found by Heffner et al(18), the larger gestational age is independent predictor of need of C/S in cases of IOL. As gestational age increases, the need for a C/S in induced labor tends to increase due to several factors. Larger gestational age often means a larger fetal size, which can make vaginal delivery more difficult. Additionally, post-term pregnancy and physiological changes in the mother's body may complicate labor, while induction could be less effective, leading to labor that fails to progress. Lastly, with advancing gestational age, the placenta may become less efficient, potentially causing fetal distress and necessitating a C/S for the safety of mother and baby.

Regarding BMI, the cases that required C/S had higher Mean BMI than those delivered vaginally. All of C/S cases were overweight or obese; furthermore, 40% of C/S cases were obese (BMI 35-40 kg/m^2). Abdo et al(19) found that higher BMI is associated with higher rate of postdate, failure of progression of labor, and failure of IOL. Myers et al(20) found that women with BMI >40 kg/m^2 had significantly increased risk of failure of IOL and requirement of C/S. Maternal BMI has been linked to increased C/S rates due to several factors. High BMI can slow labor progression, possibly due to differences in uterine muscle function as found by O'Brien et al(21) . Labor induction may be more challenging in obese women, while risks of complications such as gestational diabetes (Sugiyama et al(22)) and preeclampsia (Ahmad et al(23)) are higher, potentially necessitating a C/S. Furthermore, high BMI is often associated with larger babies (macrosomia), increasing the risk of delivery complications as stated by Song et al(24). Finally, administering regional anesthesia used in vaginal delivery can be more difficult in overweight and obese women, contributing to a greater likelihood of C/S.

The cause of IOL was not different statistically regarding success of IOL. The better patient selection and reviewing the indication of start

the trial of IOL is paramount to the success of the induction. Furthermore, monitoring maternal and fetal clinical state is essential to determine the possibility of continuation of the IOL. The type of medication used for the IOL did not influence the success rate of IOL and the duration of labor and neonatal outcome was not different between the two group.

Conclusion

A higher BMI increases the likelihood of failed labor induction that required CS, but its impact on the duration of induction is not clearly established from the current study data which may need further study with increasing sample size.

Recommendations

- Counsel High BMI Women: Inform them about the potential labor challenges they may face.
- Implement Weight Management: Include strategies during prenatal care to address risks of high BMI.
- Conduct More Research: Further studies with increasing sample size that focus on the impact of BMI on labor induction duration and how to improve outcomes.
- Provide Personalized Care: Plan care according to each patient's BMI, potentially considering different induction methods for high BMI patients.
- Educate Healthcare Providers: Train them in managing labor induction in high BMI patients.
- Promote Public Health Initiatives: Support efforts to reduce obesity, which can improve pregnancy outcomes.
- Implement Relevant Policies: Ensure BMI is considered in prenatal and perinatal care through effective healthcare system policies.

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