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Editorial

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Getting Your Work Published: Personal Reflections

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"Without publication, science is dead"

***Gerard Piel* [1]**

Good science will always make it to print but if there is no drive to publish then as Piel indicates our science will die [1]. I would go further to say if the work has been done, then attempting to publish is an obligation; never more so than if the work involved consented participants. In this editorial I will give some thoughts and reflections based on my experiences as an active researcher. Much of what I will cover will be in journal Instructions to Authors, I will use BJA as an exemplar [2]. ***Always follow the Instructions to Authors for the journal you will use.*** Instructions for Authors for Kufa Medical Journal are here [3].

What good science looks like is not an easy topic to address and assessment of this aspect is where reviewers, editors and publishers enter the mix; they are likely to disagree. The good science-paper continuum starts with a good idea; this is encompassed in the FINER (Feasible, Interesting, Novel, Ethical, Relevant) criteria for formulation of research questions [4]. When you have a good idea, assume others have had the same and do a thorough search before embarking on experimental work. This may save the 'lack of novelty' rejection letter!

Journal selection is a really important point to consider. This may be driven by impact factor, turnaround or publication model as well as a more general feel for standing in the field. Much of this information can be found on journal websites or using Clarivate [5]. As an extreme example there is little point in sending an anaesthetics paper to a dermatology journal but there is clearly more subtlety in selection. Most

journals will offer general advice as to suitability for submission (no guarantee of acceptance)[6] ***so choose your journal wisely taking advice from colleagues/co-authors and possibly the journal directly.***

Do not ever be tempted to plagiarise the work of others. All journals now run submissions through sophisticated detection software and will investigate where plagiarism is suspected. If proven this will usually result in a report being forwarded to your institution. Building a career and reputation takes time, skill and hard work; don't throw it away by plagiarising.

My next general point relates to writing; ***be direct, say what you mean and consider the reader***. Further general advice includes (i) get to the point, (ii) try to keep the writing simple and don't make readers and reviewers guess and (iii) be precise, especially in methods where others may try to replicate your work. It's not always possible but if you can, try not to overuse jargon, and if you must then explain it carefully. If the journal publishes in English and this is not your first language, then don't be afraid to ask for help.

Working with human subjects is tightly regulated and regardless of country of origin must follow the Declaration of Helsinki [7]. **What you can do is governed by your ethics approval**. You will need to state in your paper that you have ethics approval (including the location of the ethics committee and a reference number) and to indicate that consent has been obtained from participants along with the type of consent taken. Studies on human subjects usually require the clinical trial to be registered and for you to provide registration details. The reporting of clinical trials should follow Consolidated Standards of Reporting Trials or CONSORT guidelines, details can be found heren [8] along with two examples in this paper [9].

Working with animals is also tightly regulated [10,11]. You will need to state that your study has institutional approval; in UK there will also be a Home Office project number. In the case of BJA UK standards are the baseline. There is detailed guidance on the reporting of animal experimentation in 'Animal Research: Reporting of In Vivo Experiments' or ARRIVE guidelines [12]. You should follow these (that's at the study design stage) and say so in your paper.

I will make a few comments on sections of a typical paper noting where I have had issues when editing. The title is really important, this will be picked up by indexing and potential readers so use it to draw them into the substance of the paper. The abstract, is often the only part of a paper that is read; fill it with information. I usually write the abstract last and follow the flow of the main paper.

Your introduction should set the scene, covering essential background of what is known and what is not; why are you doing the work? As noted above this should be based on a thorough literature search and end with a hypothesis / aims. Introductions are often too long so; **make your case and get to the point**. With the above on clinical subjects and animal use in mind, the methods should give a clear description of how you performed the research; it is acceptable to reference methodology but if you do then give a brief summary. This is where you will describe data analysis, statistics and power; get help if you need it. There are some excellent resources on study design [13]. Some laboratory methodology is long and complex – consider putting some of this in an on-line supplement (most journals have this) along with any positive and negative methodological controls.

The results section is the part of the paper I enjoy writing the most and usually start here. Decide on your display items; tables and figures. Prepare to journal style and lay them out with your co-authors to work on the story you will tell. This will help with the sequence of your discussion. Display items are not always necessary for small data sets; use text. Journals have specifications on display item structure so **again follow instructions to authors**. Multi-panel figures can be very useful if well-constructed and impossible to understand if not. I try to tell a story in a multi-panel figure; building up from panel to panel. Don't forget titles, legends, units and statistical marking. Use colour where it helps. Above all, results should be factual, state significance and be in a logical order. **Please state negative findings. Knowing what hasn't worked can be as valuable as knowing what has**.

The final section of your paper will be to discuss the findings. **This is not a thesis**. When writing I usually use the following; summarize but not an extensive repetition of results, put the findings into context (with literature and work of others), explain anomalies and discrepancies with published literature if there is any, what does it all

mean? Conclude possibly with a suggestion for the future. There are alternatives [14]. In almost every paper there are errors in the references; this varies from simple format to wrong reference for material cited, to references in the text that are not in the list and vice versa. **Check this carefully**.

My final reflection is that publication is the final stage of a specific study, and a well-constructed paper is something to be proud of and shared. Based on good science your work will be cited and may spawn ideas for new studies, either alone or with new collaborators who have read your work. It may be just the start of a new experimental adventure. **Get researching, get writing and enjoy your research; Kufa Medical Journal looks forward to receiving papers from you**.

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Resting-state QEEG Neuro-Biomarkers for Diagnosis and Treatment Planning of Autism Spectrum Disorders

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Abstract

Background: Autism Spectrum Disorder (ASD) is a combination of complex neurodevelopment disabilities. Early resting-state EEG investigations of autism failed to identify consistent patterns of atypical neural activity. The evidence for the U-shaped profile of electrophysiological power alterations in ASD is primarily supportive, but a more hypothesis-driven effort is needed to confirm and validate it.

Aim of study: The primary objective of the present study was to investigate the resting-state QEEG neuro-biomarkers by amplitude analysis as a diagnostic tool for autistic children, compared with a normative group while recording qEEG during an eyes-open condition.

Patients and Methods: After excluding those with less than one-minute artifact-free EEG data or too many artifacts, the final participants were (N = 34) autistic children. The age range was 2-11 years (*mean* age 6.235 ± *SD* 2.7198 years), including 30 males (*mean* age 6.1667 ± *SD* 2.730 years) and four females (*mean* age 6.75 ± *SD* 2.986 years). For the qEEG recording, BrainMaster Discovery 20 module and BrainAvatar 4.0 Discovery (Acquisition software) were used.

Results: After calculating and analyzing all the QEEG data, the findings were categorized and confirmed the U-shaped power profile as an autism signature and as a diagnostic sign, characterized by excessive absolute power in low-frequencies (delta, theta) and high-frequencies bands (beta, hiBeta) and reduced absolute-power in a midrange frequency band (alpha).

Conclusions: Recent literature and our findings have shown that ASD individuals have disturbances of neural connectivity. Neurofeedback (NFB) treatment seems to be an excellent approach to regulating such disorders when using QEEG neuro-biomarkers as a part of treatment planning.

Keywords: Autism Spectrum Disorder (ASD), Resting-state QEEG, Neuro-Biomarkers, Autism Signature, Quantitative Electroencephalography, U-shaped power profile.

Introduction

Autism Spectrum Disorder (ASD) is a complicated neurodevelopmental disability that can clinically be characterized by impairments in language communication, various cognitive deficiencies, and lessened social interaction. Furthermore, it is characterized by repetitive, stereo-typed, and restricted patterns of behaviors, activities, and interests [1,2].

Symptoms of ASD usually appear in early childhood [3] and can be assessed and diagnosed in children as young as 1.5 years old [4]; the American Academy of Pediatrics (AAP) recommends developmental screening by the age of two years of all children. Nevertheless, many children – specifically those with only mild autism or limited speech delays may not be identified until they are of school-age [5].

Despite extensive research and investigations, and advancement in recognizing pathophysiological and etiological mechanisms, the exact causes of ASD remain unknown, limited, and poorly comprehended [2,6]. Nonetheless, it is a highly prevalent disorder impacting children and keeps increasing to be the most increased prevalence rate, indicating a much higher prevalence than previously thought[7-10]. As estimated by the Centers for Disease Control and Prevention (CDC)[11] and Autism and Developmental Disabilities Monitoring (ADDM) Network, the prevalence rate for ASD is 18.5 per 1,000, i.e., 1 in 54 children, and ASD was 4.3 times as prevalent among boys as among girls [11,12]. In 2021, the CDC changed the prevalence to 1 in 44 (2.3%) in children aged eight years [13]

Diagnosis and assessment of ASD: Improvements in the investigation of early diagnosis have resulted in the more initial diagnosis of autism [14]. A diagnosis accurately describes a child's difficulties [15]. Accordingly, reliable and valid diagnostic approaches are essential to help specialists make proper assessments and diagnoses of autism [16]. Moreover, a diagnosis can sometimes help make prognostic statements about the future of the child's health [15].

The diagnosis and assessment of autism can be made in various age groups. Even though some investigators and scientists from different locations worldwide also indicated that autism already exists at birthtime. Still, it is very demanding to form an earlier diagnosis [17]. Regardless, there are no consistent universal instrumenta-tions for evaluating and diagnosing autism, but the clinical diagnosis by The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [18], and even if there existed, not each and every country has the adequate resources to manage such procedures [19]. This can lead to consideration and explain the various rates of autism prevalence worldwide.

EEG and QEEG irregularities in autistic children: Electroencephalo-graphy (EEG) has been confirmed to be an exceptional instrument for studying complex neurotic and psychiatric disorders [20,21]. The EEG characteristics of frequency, amplit-ude and coherence during numerous tasks or conditions can be identified and analyzed quantitatively, i.e., the brain's activities can be recognized under different tasks and assessed from a more exhaustive viewpoint[22].

Quantitative EEG (QEEG, brain mapping, or mind mapping) is considered an assessment approach designed to identify abnormalities, and it can be applied to analyze dysregulation in brain functions and brainwaves [23-25]. Johnstone and Gunkelman [26] stated that QEEG assessment "refers to signal processing and extraction of features from the EEG signal" [22]. Until lately, no one could

pinpoint any “biomarkers” for ASD. QEEG can provide a newfound physiologyical means for assessing, studying, diagnosing, and a better understanding the autistic children’s brains [24].

QEEG and neurofeedback treatment

QEEG was one of the earliest methods that have been used for assessing autistic children, for evaluating underlying neurophysiolo-gical patterns associated with the symptoms and difficulties [27,28]. Numerous studies have demonstra-ted EEG's potential usefulness and advantages as a neuro-biomarker related to the efficacy of treatment [29,30]. QEEG is considered the first stage in neurofeedback therapy. As a valuable diagnostic tool, it can evaluate and identify learning disabilities, depression, ADHD, anxiety, OCD, seizure disorders, and other disorders [24].

Neurofeedback (NFB) (sometime-es referred to as EEG biofeedback) is a treatment approach designed to let the clients control their brainwaves' oscillation and improve their dysregulated brainwave patterns by utilizing a device that delivers information about brainwave activity. The main aim of the NFB technique is to enhance cognitive or behavioral processes related to brainwave activity. The NFB treatment approach, despite that available for a while, is swiftly earning attention and interest as a treatment and intervention approach for many disorders [31-34]. Present evidence displays that the approach may also be applied positively in the management of autism, as the QEEG investigations indicate under- and over-brain connectivity [3]. A wide variety of significant EEG differences associated with ASD have been reported [27,35-37], a significant improvement in autism behaviors and symptoms [3,37,38], and symptoms benefited include; seizures [39-41], hyperactivity [42,43], attention problems [44,45], anxiety (46), impulsivity, inattention, and response variability [47,48], and some executive test performance [49,50].

Resting-state QEEG discoveries in autism:

Resting-state QEEG investigations are usually utilized to monitor brainwave frequencies in the absence of sensory stimulation or overt task performance and to identify anomalies, which evoked potential research investigations, the most extensively used methods in QEEG studies with autism, are not well convenient [51]. Usually, resting-state methods do not include any response from the patients. This component is predominantly hopeful for investigating more severely impaired and younger subjects who may not be capable of accomplish-ing tasks correctly due to physical, developmental, or cognitive challenges. This approach is essential for investigating the irregular maturational path in autism through the early stages of childhood [2]. The investigations on resting-state QEEG in typically-developed subjects show increased alpha (α) power and coherence in individuals with autism [52], in addition to reduced power in low-frequency bands (delta Δ, theta θ) in adults relative to children [53]. No resting-state EEG research studies have investigated ASD associated with the co-occurring medical, developmental, psychiatric, and neurological disorders [54].

Resting-state QEEG investiga-tions have indicated that 20% of autistic subjects show epileptiform discharges at rest, generally without any apparent seizures [55,56]. Higher rates of epileptiform activity have also been noticed in sleep studies; e.g., Chez, Chang [57] said that 61% of autistic patients with no clinical history of seizures showed epileptiform anomalies. Heunis, Aldrich [54] stated that 30% of individuals with ASD have epilepsy. Moreover, resting-state QEEG

data has promise as an assessment and method for monitoring prognosis and treatment follow-up [2]. Furthermore, experimental studies recommend that increased resting-state power of gamma fluctuations is associated with autism [58].

Newborns at high risk for autism show unique EEG patterns before the onset of the complete disorder, highlighting its potential utility as a neuro-biomarker before behavioral exhibitions of autism emerge [59]. Even though investigations using qEEG biomarkers in autism clinical trials have mainly focused on theta and alpha activity, beta-band activity abnormalities (13–30 Hz) relevant to ASD have been reported [60-67].

Pineda, Brang [68] reported that autistic patients who undergo NFB sessions on management of the alpha-or mu-band showed reduced mu power and coherence, in addition to improved attention and reduced scores on some autism tests [69].

Early resting-state QEEG investigations of autism failed to recognize reliable shapes of atypical neural activity[70-74]. The documented prevalence of EEG anomalies in autistic subjects varied significantly among investigations, which may be due to the absence of standardized diagnostic methodologies at the time or to the limits in EEG data acquisition technology (e.g., number of electrodes) and analysis (e.g., different approaches to quantification, and qualitative conclusions).

Regardless of these unique benefits, few investigations have used resting-state QEEG to investigate the brain alterations in autistic individuals. As stated by Wang, Barstein [2], the available evidence for the model of a U-shaped pattern profile of electrophysiological power alterations in autistic subjects, i.e., increased the low power spectrum, while a decrease of the power in the midst frequencies, as mentioned above, is generally supportive. However, the additional hypothesis-driven effort is essential to validate and confirm it. Thus, the present research study aimed to investigate the resting-state QEEG neuro-biomarkers by amplit-ude analysis as a diagnostic tool for autistic children compar-ed to a normative group while recording EEG during an eyes-open condition.

Methods

The study design of the current research study is to provide opportunities for enhancing the understanding of ASD biomarkers in terms of biomarker data acquisition and clinical data collection.

A total of 45 autistic children were selected from the outpatient clinic of the Iraqi Association for Psychotherapy (IAP), Baghdad–Iraq, who were blindly clinically assessed and diagnosed by two specialists; a psychiatrist and a doctoral-level licensed clinical psychologist, free of drug treatment, based on the following inclusion criteria:

Inclusion Criteria: According to the "International Statistical Classification of Mental Disorders [ICD-10]" [75,76] and the "Diagnostic & Statistical Manual of Mental Disorders 5th edition [DSM-5])", the research sample had a documented diagnosis code of ASD; "Level 1: Requiring support.", "Level 2: Requiring substantial support." or "Level 3: Requiring very substantial support."[18], as stated in the records, patient database, and case folders.

According to the standards recommended by Thatcher [77], only data that had at least one minute of artifact-free EEG data were selected. After excluding those with less than one-minute artifact-free EEG data or too many artifacts, the final participants were (*N* = 34) autistic children. The age range was 2-11 years (*mean* age 6.235 ± *SD* 2.7198 years), including 30 males (*mean* age 6.1667 ±

SD 2.730 years) and four females (*mean* age 6.75 ± *SD* 2.986 years), gender ratio (male/female) was 7/1 (Table 1). The normative sample was recruited from the qEEG-Pro database [1].

All parents/guardians of the participants were asked to read, complete, sign, and dispatch the Consent Form to the principal investigator. Participants who had a previous history of mental retardation, epileptic symptoms, neurological problems, or abnormal developmental milestonees other than those conditions or symptoms directly related to autism were excluded from the study.

For the QEEG recording, BrainMaster Discovery 20 module and BrainAvatar 4.0 Discovery (Acquisition software) (BrainMaster Technologies, Inc.) were used (Figure 1). Additionally, *Autism Spectrum Rating Scales (ASRS)* (78-80) were used to assess and diagnose ASD.

Beginning on January 13th, 2020, and ending on March 15th, 2020, the investigator interviewed the parents of the ASD patients to select 45 children having autism to be the subjects of the current research study, where parents/guardians were asked to fill out the demographic data form, the child case history, along with the Informed consent.

Collecting an EEG record typically takes about 60–90 minutes. Since some children with autism have some sensitivity issues, it has been recommended that parents/ guardians bring their child to the examination office at a convenient time prior to the examination session to familiarize the child with the procedure settings and the clinicians. Moreover, instruction is delivered to the family to wash and clean the child's hair before the EEG data acquisition (the hair should be dry by the time of the recording). Moreover, any hair sprays, mousses, and gels are forbidden.

EEG recording was done in a laboratory that belongs to the Iraqi Association for Psychotherapy. Each child was tested individually in white-noise-free controlled rooms, with controlled temperatures from 24°-26°C. One family member and a trained specialist were present during the EEG recording sessions and the in-charge clinician. All subjects were seated in a comfortable chair. Before the EEG session, the child's parents were given a brief verbal explanation and a written description of the procedure. Informed consent was collected from the parents/guardians of all subjects. Before the EEG assessment, after the parents had indicated that they understood the process, an EEG cap with 20 electrodes, based on the International "10–20" system [81]: Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1, and O2. Referenced to linked-ears were positioned on the head of each child. Then we used a NuPrep gel to carefully clean and prepare the skin, scalps, and ears of the autistic child from any grease and dirt. Then we applied a conductive gel to each electrode hole in the EEG-Cap and connected it to the device's input of the digital EEG (BrainMaster Discovery Acquisition) device.

Usually, it is very challenging to perform EEG recording with autistic children, either in the eyes-open (EO) or eyes-closed (EC) resting condition, as autistic children are typically uncooperative during the investigational session [82]. It is challenging to do the EEG-recoding due to their restless hyperactivity, lower intellectual abilities, and refusal of sensory contact [83]. Accordingly, our EEG record-ings were conducted during the (EO) condition. During recordings, instructions were given to all the subjects to sit, as far as they could, in a state of calm, quiet, natural, eyes-

open rest (blinking allowed). To keep the participants engaged and conscious during the session, they were instructed to watch on a computer monitor, which displayed some swimming fishes in various colors or frogs. We recorded (8-10 min.) of uninterr-upted EEG signals in the (EO) condition.

Each raw EEG data file was uploaded to the qEEG-Pro website (QEEG Professionals, The Netherlands: https:// qeeg.pro/) and using the Standardized Artifact Rejection Algorithm (S.A.R.A.) [84].

This process eliminates segments from an EEG recording likely due to other sources, such as muscle tension, eye blinks, and other artifacts. Using such an automated process ensures that each file is handled in the same form and lessens the possibility of bias in the artifact elimination process. Raw data files were then visually inspected, and according to the standards proposed to yield a reliable measure [77], only recordings with at least one minute of artifact-free QEEG data were selected.

After the automatic processing of the digital data, it is compared statistically to an age and gender matched normative database banks of typically-developed subjects to produce a profile of irregularities. These database banks rely on individuals who have been regarded as typically-developed subjects based on standard screening and surveying tools for medical, behavioral, and psychological history [22]. Consequently, these QEEG reports become the basis for our further quantitative analysis.

Using Microsoft Excel (365) and Statistical Package for the Social Sciences (SPSS) v.23.0, all data were analyzed to determine whether the resear-ch would fulfill its aims. The researcher checked the data void of errors; then, the 'Brain Discovery' software for analyzing and extracting the results.

Normal distribution for absolute values was achieved through log-natural transformations and confirmed with the *ShapiroWilk's W* test. Descriptive statistics, a series of *t*-tests (two-sample assuming equal variances), and a series of *t*-tests (one-sample test) was conducted to analyze study data, the gender differences (male and female), and age levels (2-11 years old). *Cohen's d* (85) will also be used to measure the *Effect size* of our outcomes.

Results

Our study sample included (*N*=34) autistic children. The age range was 2-11 years (*mean* age 6.235 ± *SD* 2.7198 years), including 30 males (*mean* age 6.1667 ± *SD* 2.730 years) and four females (*mean* age 6.75 ± *SD* 2.986 years). Clinical evaluation, and the *Autism Spectrum Rating Scales (ASRS)* [78-80], confirmed ASD.

To characterize the resting state QEEG, the oscillatory patterns were broken down into bands of frequencies that share physiological properties. The following EEG measures were computed: relative power, total power, percent coherence, and amplitude asymmetry [85].

Descriptive statistics were calculated for each Z-score (Table 2). The absolute power of each frequency band for the participants was averaged. The topogra-phic maps representing the absolute powers of Z-Delta, Z-Theta, Z-Alpha, Z-Beta, and Z-hiBeta are presented in Fig. 2.

In the present research study, each frequency band's absolute and relative power among the 19 channels for ASD samples were averaged. The topographic maps demonstrate the mean absolute and relative powers of the delta, theta, alpha, beta, and hiBeta. After calculating and analyzing all the QEEG data, the findings of this research study were categorized under the U-shaped power profile, as

discovered by (2), characterized by excessive absolute power in low frequencies (delta, theta) and high-frequencies bands (beta, hiBeta) and reduced absolute-power in a midrange frequency band (alpha) comparing to the normative group. In the experimental ASD group, QEEG presented remarkably increased electrical potentials through all sensors. The irregularly low activity in the average alpha spectrum is outstanding. With regards to connectivity, the main findings showed occipital lobe hyperconnect-ivity as well as hypo-connectivity of the frontal region to other regions of the brain and diminished connectivity in language areas.

Figure 3 displayed the main general characteristics of qEEG brain mapping, along with Z-scores in two subjects of our sample. Absolute power for delta and theta increases. Moreover, the power of beta and hiBeta brainwaves, due to high nervousness, was also increased in our cases. It is essential to consider that, mostly, alpha brainwaves are positively correlated to cortical information processing, i.e. cognitive abilities. Children with neurological and developmental disorders such as autism showed significantly more delta and theta but less alpha power, corresponding to their cognitive impairment.

The amount of energy in μV^2 (absolute power) of each frequency band for all the ASD groups was calculated and averaged for all the Z-scores at each electrode site (Laplacian Montage), then we used only the Z-scores for each band (Z-Delta, Z-Theta, Z-Alpha, Z-Beta, and Z-hiBeta) for all the study sample (34 children). All measures showed a U-Shaped power profile (Table 3).

Then, a series of *t*-tests (one-sample tests) for all the Z-scores were calculated, and it was found that all the results were significant at ($p < 0.001$). The results showed a U-shape power profile in all the Z-Scores curves (Figure 4).

After calculating the total average for each band for Z-Scores for (Z-Delta, Z-Theta, Z-Alpha, Z-Beta, and Z-hiBeta) for all the study samples, a U-Shaped power profile, which represents a QEEG neuro-biomarkers in ASD, i.e., Autism Signature has been found (Figure 5).

Finally, *Cohen's d* [86] to measure the *Effect size* of the results was calculated (see Table 4). It has been found that Z-Delta (measured by Laplacian Montage) significantly differs from the delta brainwave of the Normative Group, *Effect Size (d)* = 0.92: large *effect size*), Z-Theta (measured by Laplacian Montage) significantly differs from the theta brainwave of the Normative Group, *Effect Size (d)* = 0.819: large *effect size*), Z-Alpha (measured by Laplacian Montage) significantly differ from the alpha brainwave of the Normative Group, *Effect Size (d)* = 0.713: medium-large *effect size*), Z-Beta (measured by Laplacian Montage) significantly differ from the beta brainwave of the Normative Group, *Effect Size (d)* = 0.782: medium-large *effect size*), and Z-hiBeta (measured by Laplacian Montage) significantly differ from the hiBeta brainwave of the Normative Group, *Effect Size (d)* = 0.881: large *effect size*).

Table 1: Descriptive statistics of (Ages) of all the study subjects of ASD children (females and males).

Descriptive statistics	*Total Sample*	*Female*	*Male*
Mean	6.235294118	6.75	6.166666667
Standard Error	0.466447918	1.493039406	0.498465077
Median	6	6	6
Mode	6	6	8
Standard Deviation	2.719835373	2.986078811	2.730205668
Sample Variance	7.397504456	8.916666667	7.454022989
Kurtosis	-0.94172445	2.602498035	-1.03949152
Skewness	0.178009534	1.380236621	0.106706849
Range	9	7	9
Minimum	2	4	2
Maximum	11	11	11
Sum	212	27	185
Count	34	4	30
Largest(1)	11	11	11
Smallest(1)	2	4	2
Confidence Level (95.0%)	0.948995425	4.75151774	1.019475551

Table 2 : Descriptive statistics of (Z-scores) of all the study subjects of ASD children (females and males).

Descriptive statistics	*Z-Delta*	*Z-Theta*	*Z-Alpha*	*Z-Beta*	*Z-hiBeta*
Mean	1.675232	0.8317337	0.6105263	0.8442724	1.4026315
Standard Error	0.123567	0.1016104	0.1045351	0.116998	0.1313472
Median	1.547368	0.7605263	0.6657894	0.8947368	1.3631578
Mode	2.021052	#N/A	#N/A	#N/A	0.5263157
Standard Deviation	0.720513	0.5924855	0.6095397	0.6822104	0.7658794
Sample Variance	0.519139	0.3510391	0.3715386	0.4654110	0.5865713
Kurtosis	1.664550	0.7969451	0.1781022	0.6401517	-0.2679363
Skewness	1.161626	0.4543409	-0.3939609	0.0318140	0.2643670
Range	3.310526	2.8	2.6736842	3.4052631	3.3368421
Minimum	0.521052	-0.363157	-0.8263157	-0.768421	-0.1684210
Maximum	3.831578	2.4368421	1.8473684	2.6368421	3.1684210
Sum	56.95789	28.278947	20.757894	28.705263	47.689473
Count	34	34	34	34	34
Largest(1)	3.831578	2.4368421	1.8473684	2.636842	3.1684210
Smallest(1)	0.521052	-0.363157	-0.8263157	-0.7684210	-0.1684210
Confidence Level (95.0%)	0.2513990	0.2067279	0.21267845	0.2380344	0.26722798

A Z-score is a value of the standard deviation from the mean of the normative group.

Table 3: The Z-scores for each band (Z-Delta, Z-Theta, Z-Alpha, Z-Beta, and Z-hiBeta) for each child for the whole study's sample according to their gender.

No.	Gender	Z-Delta	Z-Theta	Z-Alpha	Z-Beta	Z-hiBeta
1	Male	0.673684211	0.263157895	0.242105263	0.489473684	1.405263158
2	Male	1.031578947	0.736842105	0.5	0.731578947	1.168421053
3	Male	3.831578947	2.436842105	1.368421053	2.636842105	3.168421053
4	Male	1.194736842	0.978947368	0.936842105	0.963157895	1.189473684
5	Male	1.426315789	0.989473684	0.715789474	1.847368421	2.515789474
6	Male	3.121052632	1.184210526	0.7	0.363157895	0.784210526
7	Male	2.073684211	1.652631579	1.526315789	1.442105263	1.957894737
8	Female	1.942105263	0.873684211	1.1	1.657894737	2.157894737
9	Male	1.9	0.447368421	0.4	0.163157895	0.526315789
10	Male	3.194736842	1.542105263	1.847368421	1.615789474	2.884210526
11	Male	1.557894737	0.715789474	0.352631579	-0.06315789	0.310526316
12	Male	1.642105263	0.663157895	0.584210526	0.168421053	0.568421053
13	Male	1.536842105	0.747368421	0.768421053	0.773684211	1.321052632
14	Male	2.152631579	0.963157895	0.721052632	1.247368421	1.936842105
15	Male	1.357894737	0.589473684	0.394736842	1.357894737	2.389473684
16	Male	1.710526316	1.126315789	0.968421053	0.710526316	1.1
17	Male	1.457894737	1.2	1.273684211	1.268421053	1.731578947
18	Male	2.021052632	1.947368421	1.110526316	1.184210526	2.015789474
19	Male	1.021052632	0.221052632	0.289473684	1.047368421	0.852631579
20	Female	1.094736842	0.163157895	-0.25789473	0.852631579	1.952631579
21	Male	1.836842105	1.215789474	1.121052632	0.936842105	1.421052632
22	Male	1.615789474	0.905263158	0.484210526	1.173684211	1.805263158
23	Male	1.2	0.136842105	-0.10526315	0.231578947	0.568421053
24	Male	1.394736842	0.7	0.842105263	0.847368421	1.436842105
25	Male	2.710526316	0.715789474	-0.13157894	-0.10526315	0.689473684
26	Female	0.521052632	-0.36315789	-0.72631578	-0.27894736	0.526315789
27	Male	0.868421053	-0.23157894	-0.82631578	-0.76842105	-0.16842105
28	Male	2.221052632	1.731578947	1.436842105	1.610526316	2.078947368
29	Female	1.221052632	1.031578947	0.952631579	1.010526316	1.168421053
30	Male	2.021052632	0.310526316	-0.06842105	0.215789474	0.636842105
31	Male	1.063157895	0.205263158	0.168421053	0.457894737	1.052631579
32	Male	1.826315789	0.752631579	0.631578947	0.678947368	0.952631579
33	Male	1.121052632	0.768421053	0.394736842	1.026315789	1.726315789
34	Male	1.394736842	0.957894737	1.042105263	1.210526316	1.857894737

Table 4: *t*-test (one-sample test) results for all the Z-scores of all research study participants and the *Effect size* for each *t*-test.

	Z-Delta	Z-Theta	Z-Alpha	Z-Beta	Z-hiBeta
Mean	1.6752	0.8317	0.6105	0.8443	1.4026
Variance	0.7205	0.5925	0.6095	0.6822	0.7659
Stand. Dev.	0.8488	0.7697	0.7807	0.826	0.8752
N	34	34	34	34	34
T	13.5575	8.1853	5.8408	7.2162	10.6785
d.o.f	33	33	33	33	33
critical value	2.035	2.035	2.035	2.035	2.035
Cohen's d	4.72012	2.849755675	2.033505546	2.51236	3.717776498
Effect Size (r)	0.92076	0.818533536	0.712955982	0.78237	0.880656892

Figure 1: Brain Master Discovery 20 with Impedance Lid BrainAvatar 4.0 Discovery Acquisition system.

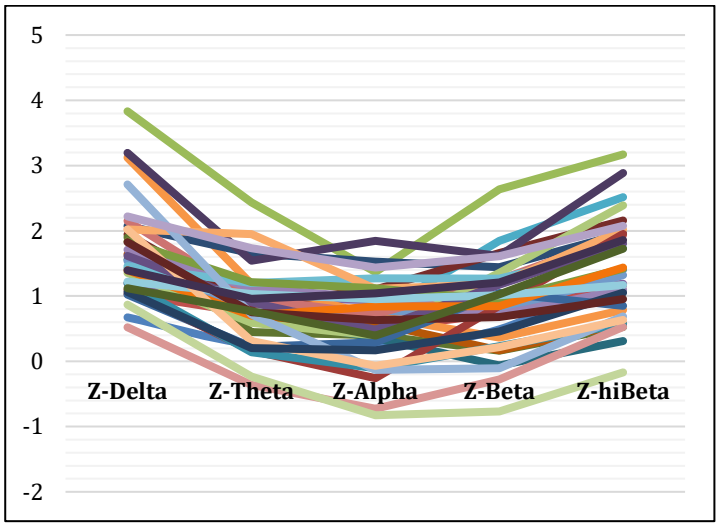

Figure 2: All the Absolute power of the frequency bands for the assessed ASD group.

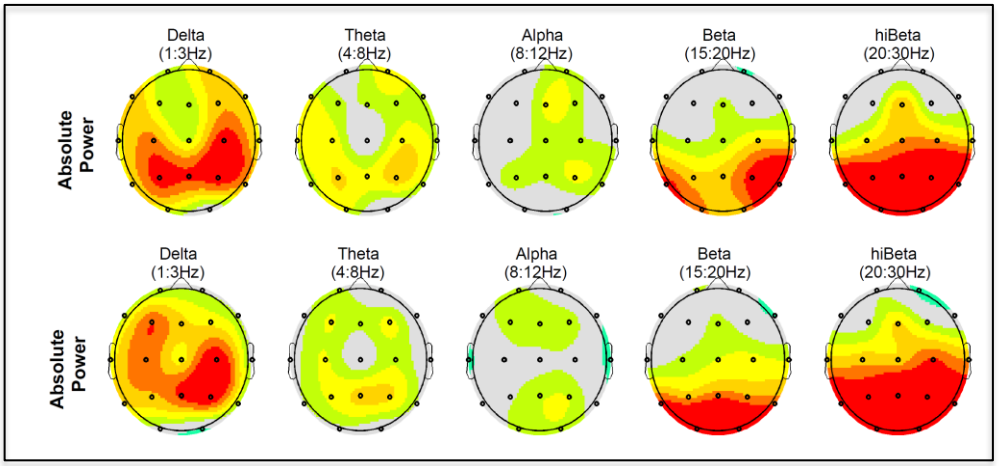

Figure 3: Summary information for absolute power for main brainwaves in two autistic children of our research.

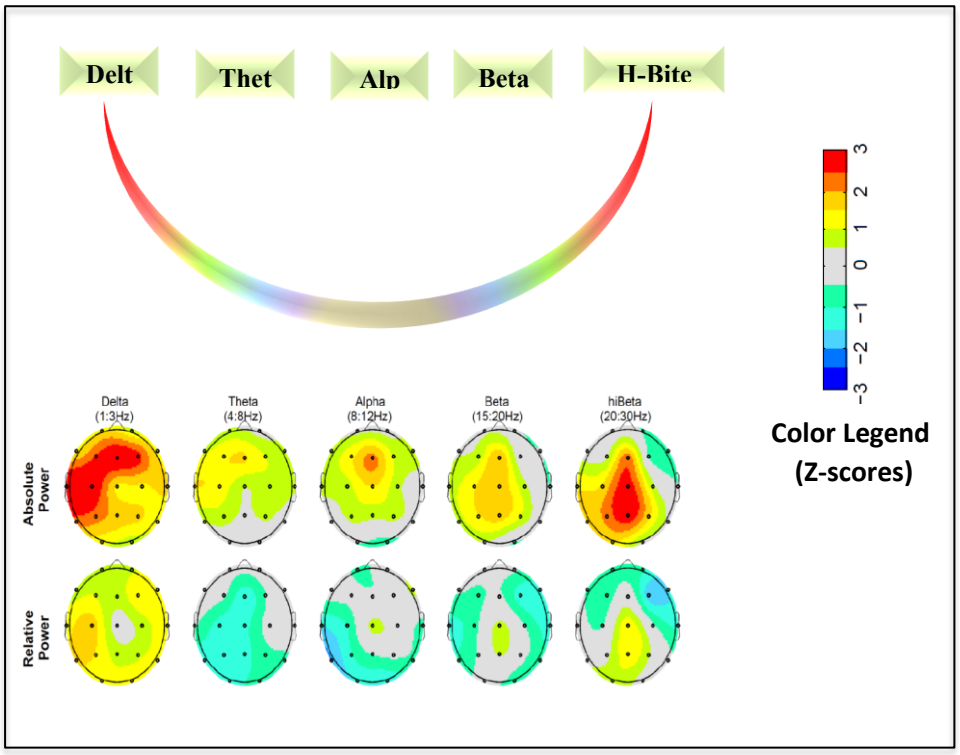

Figure 4: The U-Shape power profile as a final result of the resting-state QEEG neuro-biomarkers in autism spectrum disorders (Autism Signature).

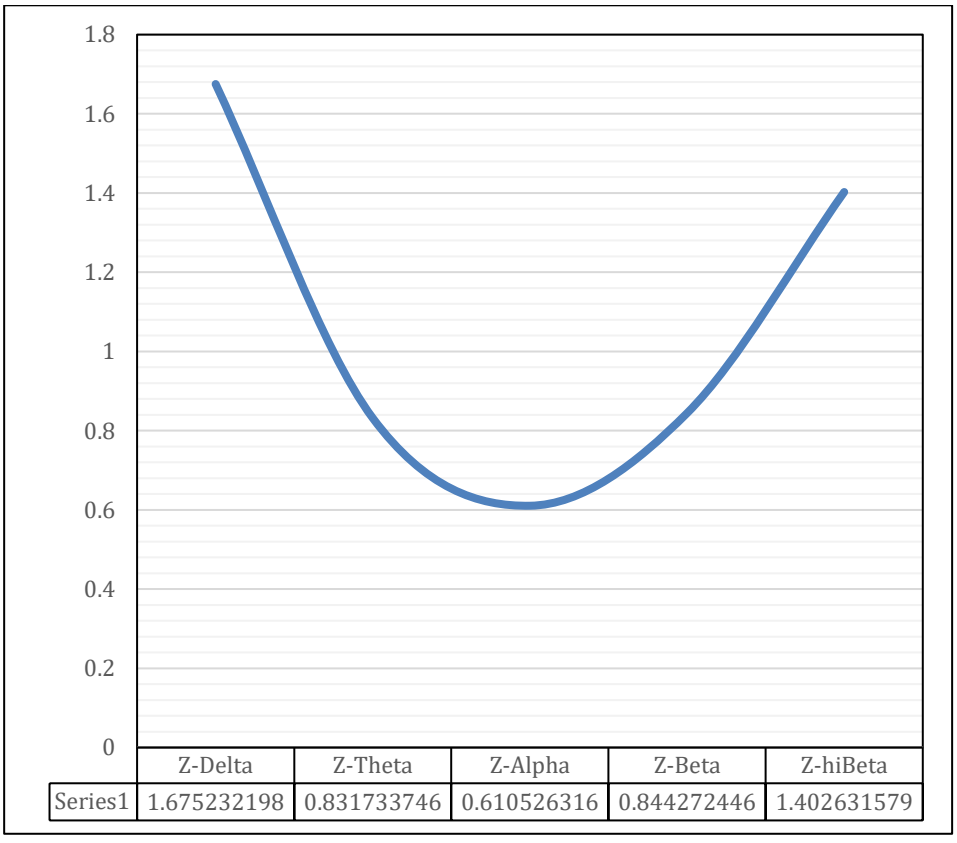

Figure 5: The U-shaped power profile as a final result of the resting-state QEEG neuro-biomarkers in autism spectrum disorders (Autism Signature).

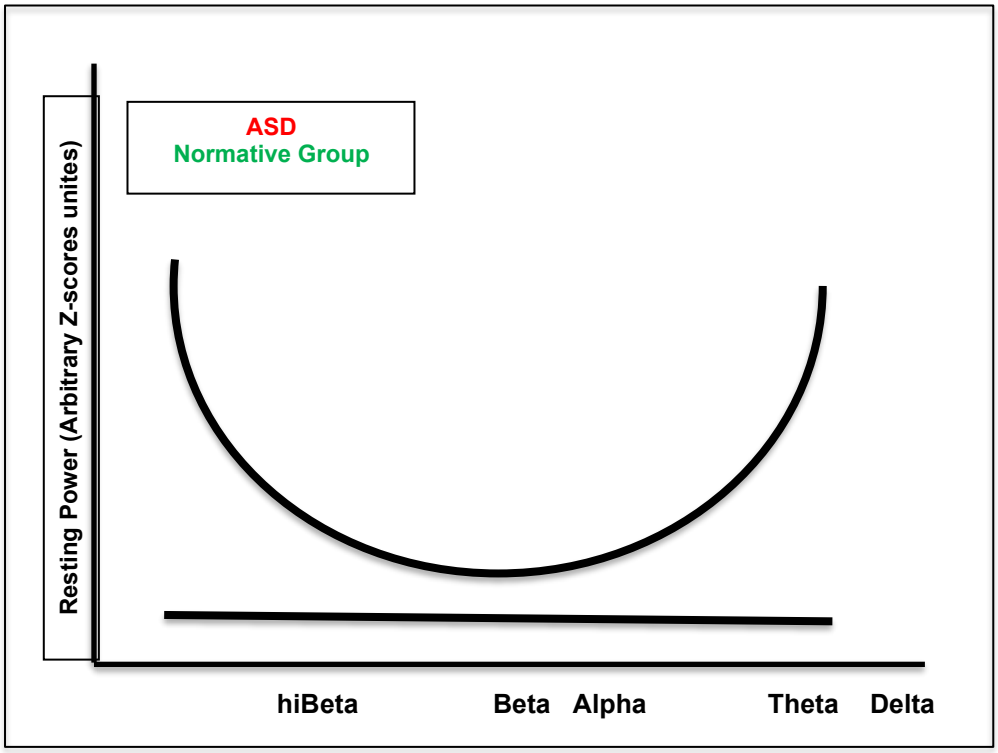

Figure 6: Illustration of the abnormal power pattern as a U-shaped profile in the ASD group compared to the normative group (Autism Signature).

Discussion

The findings of the present study have revealed that children with ASD demonstrated significantly excessive absolute power in low-frequencies (delta, theta) and high-frequencies bands (beta, hiBeta) and reduced absolute-power in a midrange frequency band (alpha) compared to the normative group, which may result from abnormal GABAergic tone in inhibitory circuits. This finding (U-shaped profile) is similar to results from Wang and his colleagues [2], but the current research disagrees with them regarding the differences between the ASD and the normative group profile, as the normative group in our study has a semi-straight line but not as an upside-down (U-shaped profile) (Figure 6). This pattern might indicate a unique QEEG endophenotype of the resting-state QEEG neuro-biomarkers in ASD. Additionally, these findings may explain some of the stereotypes, hyperactivity, and repetitive behaviors in autistic children.

These results also disagree with Linden and colleagues who have studied subtypes of autism over the past twenty years [3,28,87]. In (2004), Linden's paper identified four distinctive QEEG profiles of autism and two others for Asperger's syndrome [87]. Later, Coben, Linden [3], and recent studies extended the number of autism subtypes and have pinpointed six endophenotypes found in ASD. In addition to two more patterns specifically for Asperger's syndrome [22,24]. However, this study discovered one unique pattern profile, as stated above.

Here, EEG power spectra increased delta and theta power in central and frontal areas of the brain, which was previously documented in autistic patients [83,88,89]. These findings revealed a pattern of underconnectivity in autistic children, i.e., a decreased delta and theta coherence across the brain. Delta and theta

coherence were low across the frontal area, indicating the deficit in the executive functions in the frontal lobes of autistic children. Generally, delta and theta waves are presented at high levels during sleep stages; but in autistic children, they are abnormally high and constantly peak, even when awake [90]. The excess in delta power has also been found in relative power [88,91] and absolute power [83,88,92].

High levels of theta waves may be related to a lack of attention and some depressive disorders. At the same time, a healthy level of delta waves is good for emotional connection, creativity, and intuition. Moreover, increased delta and theta waves activity was reported in schizophrenic patients compared to healthy controls [93]. Accordingly, we can see some evidence of similarities in power spectra between schizophrenic and autistic patients. On the other hand, high delta and theta power activities in autistic children may be correlated with a lack of reading, deficiencies in other daily and educational activities, inaccuracy in reactions, and perceptual speed problems.

For this reason, these autistic children may have struggled to process all the incoming peripheral perceptual information adequately and fail in the tasks that require multiple cognitive processes [94]. While reduced alpha power was also noted as well as irregular beta and gamma power by Kouijzer, van Schie [95], the decrease in alpha correlates with reduced limbic system activation in subcortical structures such as the midbrain, brainstem, and hypothalamus. High beta and gamma power in the sample of the present study may indicate a deficit in verbal learning performance. Generally, spectral changes in subjects with autism were more evident than in control normative subjects [82].

The impact of anxiety on alpha wave activity, in general, can be complicated, as the present finding of decreased alpha in ASD is the opposite of what has been found by Cornew, L. et al. (2012) [96].

According to these results, QEEG can be used as a diagnostic and treatment planning tool for ASD. Nine previous studies reported the use of QEEG in ASD children; five used QEEG as a diagnostic neuro-biomarker, and four used QEEG in the course of ASD treatment [82,97-104]. Compared with other investigations, it is essential to consider that the resting-state QEEG was recorded in an eyes-open (EO) condition, which might clarify a decrease in the alpha activity. Additionally, autistic children showed significantly higher intrahemispheric long-range coherence in the left hemisphere than in the normative group. The ASD participants did not exhibit significant alterations comparing both hemispheres for the resting control condition.

Moreover, one of the limitations of our research study is the relatively small number of the research sample (N=34), although a detailed statistical power analysis processing showed that our research results were reliable and significant.

Conclusions

1. The outcomes are reassuring for developing a new essential and contributory technique for examining, assessing, and differential diagnosis of neurodevelopmental disorders such as autism.
2. No classical paper-based psychological tests and scales are required.
3. QEEG is more comfortable and not extended compared to some other techniques (for example, positron emission tomography (PET), computerized tomogramphy CT), and potential clinical evaluation of neuropsychiatric disorders [105] has been evaluated.
4. It is essential to perform further data analysis for a more extensive research sample to represent the results better.

5. Evaluating and developing treatment, therapeutic, and training plans, according to the founded neurobiomarkers (signature), help autistic children and allow them to lead a healthy life.
6. The current results emphasize the hypothesis that autism signature can be found as a U-Shape power profile.

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Autoimmune Hemolytic Anemia as Presentation of Celiac Disease

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Abstract

Celiac disease is a multisystem disorder in children and adults; it is considered as one of the most important malabsorption syndromes related to an auto-immune mediated response to gluten-containing food in a genetically predisposed patient. The most common involved system is the Gastrointestinal tract. Association with other autoimmune diseases such as thyroid disease and diabetes mellitus type 1 is well known but autoimmune mediated hemolytic anemia that responded to a gluten-free diet was interesting to be found.

A six years old male previously healthy child, presented with pallor and reduced activity, dark-colored urine, with clinical and laboratory features of hemolytic anemia, and multiple blood transfusions within a year of medical care-seeking to finally diagnosed with celiac disease and responded to a gluten-free diet of about 8 months now with no need of blood transfusion.

Key words: Autoimmune Hemolytic Anemia, Celiac Disease

Introduction

Celiac disease (CD) is an autoimmune multisystem disorder triggered by the gluten and other related prolamins substances present in wheat and other cereals, in those patients who are genetically predisposed.[1] Clinical features vary considerably; GI symptoms are more common in those diagnosed in the first 2 years of life,[2] as the patient grows the extraintestinal manifestation dominates, without accompanying gastro-intestinal (GI) symptoms. Short stature, delayed puberty, peripheral neuropathy, osteopenia and osteoporosis are the nonhematologic-al presentations reported in celiac patients. On the other hand, wide spectrum hematological manifestations are well established, mostly anemia (iron deficiency, folate deficiency, B12 and pyridoxine deficiency), thrombocytosis due to hypersplenism, hemorrhage due to vitamin K deficiency, or folate mediated thrombocytopenia. Although these nonimmune hematological problems are relatively common, autoimmune-mediated hematologic disorders have been reported infrequently.[3]

This paper reports a very rare association between CD and autoimmune hemolytic anemia, and the possibility of considering CD in the differential diagnosis of autoimmune hemolytic anemia (AIHA).

Case presentation

A six-year- old male child, known case of asthma and atopy with no chronic medication use (apart from occasional oral steroid use for asthmatic exacerbation) presented with sudden onset pallor, easy fatigability, exertional dyspnea, and repeated vomiting, with a low-grade fever over a week. The patient was initially examined to be found severely pale, ill-looking, having a soft abdomen with no organomegaly, no lymphadenopathy and with normal vital signs for his age apart from tachycardia 150 BPM. The patient was sent for laboratory tests that show WBC 10.4 $*10^9$/L, 47% granulocytosis, 43% lymphocytosis, Hb level was 6.3 g/dl, platelet count was $630*10^9$/µL. Bblood film at that time showed a severe iron deficiency anemia, hypochromic microcytic RBCs with anisopoikoilocytosis, normal-looking WBC and platelet with mild thrombocytosis.

The patient received a blood transfusion and started oral iron supplementation as S. iron was 57 mcg/dl (normal range 59-150), and serum ferritin was 70 mcg/dl (normal range 30-220). A week later on a follow-up visit, the patient was still symptomatic, Hb level was 7.1 g/dl, with no improvement in his general condition; further investigation had been done to show ESR of 90 mm/hr., positive CRP, normal liver function test, with negative Coombs test, and non-deficient level of G6PD enzyme, normal renal function test. Hence, another transfusion was done, and about 20 days later the patient had severe pallor, jaundice, and dark-colored urine. A new blood film showed a feature of hemolytic anemia with retic count of 7.1% and corrected retic 4%, which required an in-patient management for blood transfusion, intravenous fluid with frequent monitoring of PCV and renal function test. Besides, more advanced investigation was done with normal thyroid function test, deficient level of vitamin D, and positive Anti Ds DNA IgG and IgM level.

The patient was diagnosed with Autoimmune hemolytic anemia and started on oral prednisolone 2 mg/kg/day with a further search for the underlying cause. G6PD enzyme deficiency was excluded for the non-deficient enzyme level measured 2 weeks from the hemolytic attack; the patient had no respiratory symptoms or any features of mycoplasma or other infections that may cause hemolytic disease. In addition, there was no joint pain or skin changes, no neurological manifestations, and no features of serositis to collect criteria of SLE. Further, the patient had a negative latex test of Rheumatic disease; so, all these diagnoses had been excluded.

A month later, another attack of hemolysis occurred while on steroid with Hb level as low as 5.7 gm/dl, a trial of IVIG 1 gm/kg for two days. Meanwhile, a screening test for CD was done to show positive anti-tissue transglutaminase antibody IgG and the patient was tapered from steroid, and started on strict adherence to a gluten-free diet, with a gradual rise in Hb. After 8 months, the patient had been free of blood transfusion and the Hb level was kept in the range of 10-11 mg/dl.

Follow-up: the patient is free of symptoms with normal activity. A final diagnosis of celiac-associated hemolytic anemia was finally done.

Discussion

Patients with CD often have more autoimmune illnesses than healthy people. Many theories have been presented to explain why the CD or intestinal mucosal atrophy impairs antigen delivery underneath the intestinal mucosa, resulting in immune system activation or autoimmune. As a result, CD and autoimmunity are two distinct conditions. The most common

autoimmune illnesses is linked to celiac disease are type 1 diabetes and autoimmune thyroiditis. Nonetheless, AIHA is uncommon among CD individuals. [4]

Shah et al [5], have made a description of 21 cases with possible associations between CD positive serology and AIHA. However, they suggest a further exploration to prove this association.

In Ivanovski et al. [6] an 11-year-old girl with untreated CD who had hemolytic anemia was described and, accordingly, it was advised that patients with Coombs negative "immune" hemolytic anemia should be serologically checked for CD. The anemia improved after starting a gluten-free diet, as it did in this case.

Pallor and general weakness were the predominant symptoms in our case, and CD was diagnosed with a high anti-tTGAb titer. After eight months on a gluten-free diet, our patient's growth and complete blood count all returned to be normal. The failure of our patient to respond to corticosteroids and IVIG could be explained by the fact that the patient was fed, i.e., constantly confronted with gluten, and anti-tTGAb production was unrestricted until the gluten-free diet was introduced.

Conclusion

- Late presentation of CD mostly occurs as a non-GI complaint.
- CD should be kept in mind for differential diagnoses of Hemolytic anemia.
- Strong base scientific evidence needs to be present before initiating a specific therapy, to reach a clear non-cloudy diagnosis.

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Coating Orthodontic Miniscrew with Chlorhexidine Hexametaphosphate Nanoparticle (An in vitro-study)

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Abstract

Introduction: Inflammation associated with insertion of orthodontic miniscrews (OMS) may lead to their failure, therefore inhibition of microbial buildup is preferable. Chlorhexidine hexametaphosphate has offered persistent, slow release of active chlorhexidine over time, and hence a good anti-microbial agent.

Aims of study: To prepare and characterize CHX-HMP antimicrobial nanoparticle for coating and characterization of the stainless steel and titanium orthodontic miniscrews.

Materials and Methods: Suspension of 5 mM CHX-HMP nanoparticles were prepared. The formulated suspension was subjected to examination by AFM and FTIR. Sterilized miniscrews were immersed in the prepared suspension for half a minute, then inserted in deionized water for 10 seconds to eliminate any unbound material and then left to dry in air for at least 1 hour. The OMSs were examined by using SEM and FeSEM.

Results: The AFM micrographs displayed that the characterization of nanoparticles expressed a relative homogeneity in terms of particle size and in their topographical distribution with the regular shaped particles being well aligned vertically with mean particles size 45.2 nm. FTIR showed the presence of C=O bond in chlorhexidine digluconate and its absence in the mixed nanoparticles indicate the replacement of gluconate by hexametaphosphate. SEM and FeSEM showed that all coated OMS (stainless steel and titanium) revealed nanoparticles of spherical shape with perfect homogenous distribution with no agglomeration meaning that the coating of OMS with the prepared colloidal suspension have a good dispersion of nanoparticles.

Conclusion: OMS could be coated with antimicrobial CXH-HMP nanoparticles to assist reducing infection associated with the insertion of OMS.

Key words: orthodontic miniscrew, chlorhexidine, CHX-HMP nanoparticle.

Introduction

One of the most challenging phases during orthodontic treatment is controlling the loss of anchorage [1]. Orthodontic miniscrews (OMS) provide several advantages for both orthodontist and patient because of their simple insertion and removal, improved patient comfort, and advantageous cost-benefit ratio. Commercially offered OMSs

show a success rate of 60-75% [2,3]. Numerous things lead to the success percentage of OMS that may be associated with the shape, clinician factors and even patient. Another issue associated with the patient to reduce the miniscrews survival rate was poor dental hygiene [4,5,6].

Most available OMSs are titanium, but stainless steel OMSs are usually found. In spite of the distinct features of these two materials, they both justify the biomechanical requirements of devices used for orthodontic anchorage. Since it is difficult to maintain peri-implant hygiene, it is essential to screen the microbiological colonization in this area. Consequently, the authors directed to regulate the development and establishment of the microbial colonization activity in orthodontic miniscrews during their installation time. The understanding of the qualitative and quantitative features of these microorganisms must assist in reducing the inflammation, enhancing oral hygiene and subsequently rising the long-term success of orthodontic miniscrews [7,8,3].

Prevention of microbial accumulation is emphasized over treatment. The antibacterial activity of chlorhexidine (CHX) belongs to the biguanide pharmaceutical class, which is effective against gram-negative, gram-positive bacteria, and yeast. Numerous investigations were undertaken to create hexametaphosphate (HMP) nanoparticles as CHX-releasing materials [9-14]. CHX hexametaphosphate (CHX-HMP) is a soluble CHX salt that, upon contact with aqueous media, produces a slow release of soluble active CHX over an extended period; the duration of the release and the subsequent concentration of CHX in the surrounding environment are dependent on factors such as fluid flow [15].

At low doses, CHX exerts its effect by damaging membranes, especially phospholipid bilayers, while it causes cytoplasm to congeal at high doses. CHX does not enhance the development of bacterial resistance; therefore, CHX digluconate is frequently used in medicine in general and dentistry in particular [16].

CHX has a broad-spectrum antimicrobial activity as well as plaque removal by its cationic action. It has positive charges that react with the negative charge of microbial cell surface. This activity can increase the permeability of cell membrane by disrupting the osmotic barrier and impeding the membrane transport. It also has the capability to bind to the outer membrane of bacterial plaque and inhibit their attachment to epithelial cells. Due to its actions, it can prevent formation of new plaque rather than decreasing the deposits in pre-existing plaque [10,16].

The magnitude and rate of releasing CHX from CHX-HMP functionalized materials depend on several factors like the local conditions, the doping of CHX-HMP and the matrix where the CHX-HMP is embedded; the duration of release may be ranged from days to months or even years [10,17,18,14]. Therefore, this study aimed to investigate the ability of coating and characterization of the orthodontic stainless steel and titanium miniscrews with CHX-HMP antimicrobial nanoparticle.

Materials and methods

1. Nanoparticle synthesis

The nanoparticles (NPs) were prepared from sodium hexametaphosphate (Sodium HMP) nanoparticle in a crystalline powder form and CHX (CHX) 20% aqueous solution. The molecular weight of HMP is 611.77 gm/mm; so, 100 mL of 10 mM Sodium HMP was prepared by dissolving 0.61177 gm from the powder in 100 ml of double ionized distilled water (DDW). The molecular weight of CHX is 897.8 gm/mm; the CHX digluconate was provided as aqueous solution, so 100 mL of 10 mM aqueous CHX digluconate was prepared by diluting the 20% solution according to the dilution equation:

$$M1 \times V1 = M2 \times V2$$

$20/100 \times V1 = 0.8978/100 \times 100$

$V1 = 4.49$ mL

So, 4.49 mL from the 20% solution supplied by the company (Sigma Aldrich, Germany) was put in a glass container (sterilized by ultrasonic cleaner to exclude any contamination) and filled to 100 ml with DDW. This procedure was done under constant stirring and under ambient conditions. Mixture of the two reagents with rapid stirring lead to the immediate creation of a colloidal suspension of CHX–HMP NPs by a magnetic stirrer using to get a homogeneous suspension with a total concentration of 5 mM of both CHX and HMP. According to previous studies, the minimum inhibitory concentration was dose-related where by the specimens of CHX-HMP-5 displayed a further release of nanoparticles [10,19].

2. Characterization of Nanoparticles

After preparing nanoparticles, the particle size, shape and structure in the colloidal suspensions was characterized by using atomic force microscope (AFM) and Fourier-transformation infrared spectroscopy (FTIR).

A. Atomic Force Microscopy (AFM)

In order to obtain accurate AFM images for the nanoparticles in the colloidal suspension, one drop of the colloidal suspension was first applied to a flat surface of a special glass slides (Mica glass), spread evenly, and then blown dry by using pure nitrogen. The glass slide was then mounted on the AFM imaging Tab., and images were taken [19].

B. Fourier Transform Infrared Spectroscopy (FTIR)

Fourier Transform Infrared Spectroscopy (FTIR) was utilized for the chemical characterization of the created colloidal suspension to confirm the chemical reaction between the components of nanoparticle. This was done by comparing the FTIR charts of Sodium hexametaphosphate powder and CHX digluconate liquid nanoparticles with FTIR chart of the created colloidal suspension after being dried. The samples were prepared by using the classical KBr (Potassium bromide) pellet method FTIR measurement (the scan range was 400-4000 cm^{-1}).

3. Miniscrews preparation and coating

The orthodontic miniscrews (OMS) were divided into 4 groups: 2 control groups (one of stainless steel and one titanium). The other two experimental (coated) groups were stainless steel and titanium OMS coated with the CHX-HMP NP.

Each miniscrews was supplied from the manufacturer (Dentose, Korea) in a small pouch. According to the manufacturer instructions, the miniscrews were sterilized by autoclave steam sterilization at 121ºC for 20 minutes. To coat the sample with nanoparticles, each sterilized miniscrew was carefully removed from the package to prevent any contamination and inserted directly in a test tube containing 10ml of the previously prepared nanoparticle colloidal suspension for 30 seconds being stirred on a rapid stirrer device. Then, it was picked up with a sterilized pair of tweezers and inserted in deionized water for 10 seconds to eliminate any unattached material then leave to dry in a biosafety cabinate for at least 1 hour before further use to remove excess water. Finally, it was inserted in a sealed tube with a clear label till the day of test [9,12].

A. Scanning Electron microscope (SEM)

SEM was applied to study the morphological and topographical surface characteristics and the size of nanoparticles on the surface of the coated miniscrews [19,20]. Image J software program was used to measure the size of nanoparticles on miniscrews surface.

B. Field emission scanning electron microscopy (FeSEM):

To get a clearer image and nanoparticle size measurement, FeSEM scan was used for the coated OMS. FeSEM is an advanced technology used to capture the microstructure image of the material.

Results

Characterization of the prepared colloidal suspension

A. AFM findings

The AFM micrographs show that the nanoparticles characterized by relative homogeneity in terms of particle size and in their topographical distribution. They also show that the particles have regular shapes and well aligned vertically as seen in the 3D and 2D AFM micrographs (Fig. 1. A). From the histogram, the particles size range between 10-58nm with an average of 45.2 nm (Table. 1, Fig. 1.B). In general, the material had a nanoscale size, so it falls within the range of mesoporous materials because it has an average size of less than 50 nanometers.

The distribution of nanoparticles ranged in size in relation to the particles surface area in nm^2 (Fig. 2). It exhibited that the particles with 49 nm had the higher surface area which was about 0.06 nm^2 and the surface area of nanoparticles ranged between 0.01-0.05 nm^2.

Table 1: AFM grain statistics for the prepared colloidal suspension obtained from the AFM micrographs.

Number of Particles	**353**
Coverage	54.25 %
Density	3.502 e^{+10} particles/mm^2
Mean size of particles	45.2 nm
Total projected area	14.49 nm^2
Root mean square height (Sq)	7.886 nm
Maximum height (Sz)	64.71 nm
Arithmetic mean height (Sa)	6.199 nm
Developed Interfacial area ratio (Sdr)	13.53 %

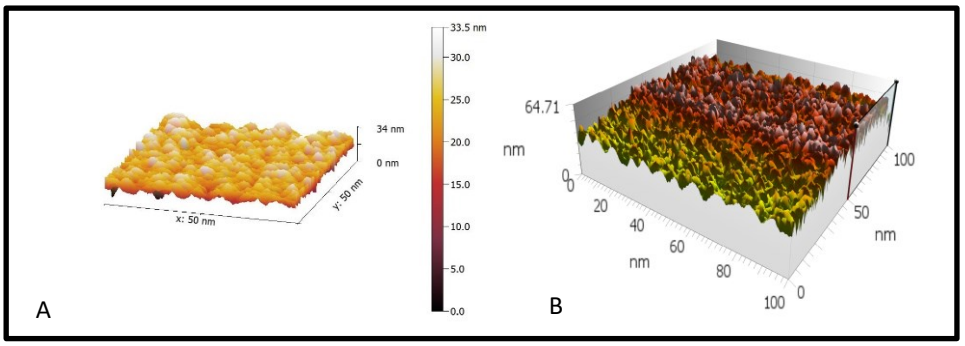

Figure 1: 3D AFM topographical micrograph for nanoparticles of prepared colloidal suspension at 100nm and 50nm respectively.

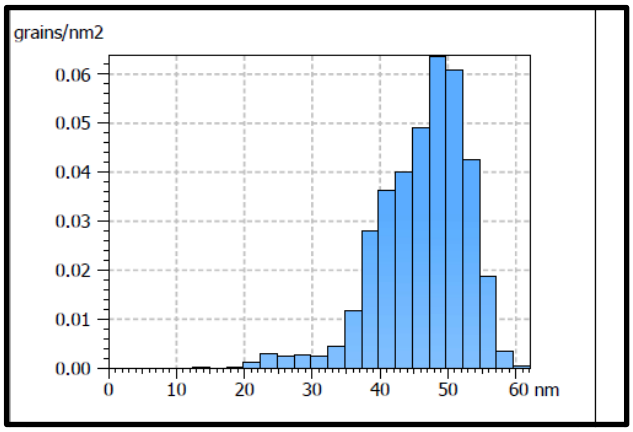

Figure 2: The distribution of nanoparticles sizes in relation to the particles surface area in nm^2 by AFM.

FTIR findings

The FTIR charts for the components of the prepared nanoparticles was studied to determine the chemical interaction between the CHX digluconate and sodium hexametaphosphate in the resultant colloidal suspension. Fig. (3.A) shows the FTIR spectra of CHX digluconate liquid of the nanoparticle before mixing, which shows the presence of characteristics transmittance bands at 3327 cm^{-1} for the O-H group, 2937 for CH_2 asymmetric group and 2860 cm^{-1} for C-H methanediyls group. More band were found at 1720 cm^{-1} for C=O, 1641cm^{-1} for C=O, 1604 for $(CH3)_2NC(=N–H)C(CH_3)_2$. For the aliphatic guanidine absorptions, 1533 (C=N), 1417 cm^{-1} (C=C aromatic), 1490 and 1373 cm^{-1} (C-H methanediyl), 823 cm^{-1} (C-H aromatic), and 717 cm^{-1} (C-Cl aromatic) were found. However, the FTIR spectra of sodium hexametaphosphate crystalline powder alone (Fig. 3.B) showed peaks at 1276 cm^{-1} for the P=O, 1095 cm^{-1} for the P-O, and 879 cm^{-1} for P-O-P.

Figure (4) shows the FTIR spectra of CHX hexametaphosphate colloidal suspension of the prepared nanoparticle in which the FTIR spectra were assessed at range between 400-4000 cm^{-1} in the transmittance mode. It shows broad peaks at 3392 and 3385 cm^{-1} mostly referring to OH bond and may cover the NH bond, 2933 cm^{-1} (CH_2 asymmetric bond) and 2860 cm^{-1} (C-H methanediyls). Yet, for the aromatic guanidine absorptions, peaks were found at 1614 cm^{-1} for the ArNHC(=NH)NHAr), 1531 cm^{-1} for C =N and 1417 cm^{-1} for the C=C aromatic, 1492 and 1375 cm^{-1} for the C-H methanediyl, 1257 cm^{-1} for the P=O, 1089 cm^{-1} for the P-O, 877 cm^{-1} for the P-O-P, and 721 cm^{-1} for the C-Cl aromatic groups.

In the FTIR charts, there are specific characteristic bands which indicate the chemical interaction between CHX digluconate and sodium hexametaphosphate. The presence of C=O in CHX digluconate and its absence in the mixed nanoparticles indicate the replacement of gluconate by hexametaphosphate. In addition, the presence of phosphate and Cl groups in the resultant colloidal suspension of the prepared nanoparticles may indicate the interaction between the sodium hexametaphosphate and CHX digluconate after mixing.

Characterization of OMS coated by nanoparticles

A. SEM findings

Scanning electron microscope images showed the surfaces of both Titanium and Stainless steel OMS before coating with CHX-HMP nanoparticle, and represented the original material of OMS without any interference to see the topography of the surface before coating with nanoparticles (Fig. 4 A-D). Figure (4 E-F) demonstrates SEM images for the stainless steel coated OMS revealing the nanoparticles with a

spherical shape and perfect homogenous distribution. The images showed no agglomeration and this means that the coating of OMS with the prepared colloidal suspension has a good dispersion of nanoparticles. Figure (5 A&B) showed that the particle size was around 32-65 nm and the average particle size was 49.77 nm.

SEM images for the titanium coated OMS revealed nanoparticles of spherical shape with perfect homogenous distribution. The images showed no agglomeration meaning that the coating of OMS with the prepared colloidal suspension have a good dispersion of nanoparticles (Fig. 4 G-H). The particle size was 30-65 nm and the average particles size was 49.08 nm according to Image J software (Fig. 5).

B. FeSEM findings

Figure 6 shows several FeSEM images at different magnification for the stainless steel and titanium OMS coated with the nanoparticle. It showed that the nanoparticle had spherical shape with normal and homogenous distribution of nanoparticles on the coated OMSs surfaces.

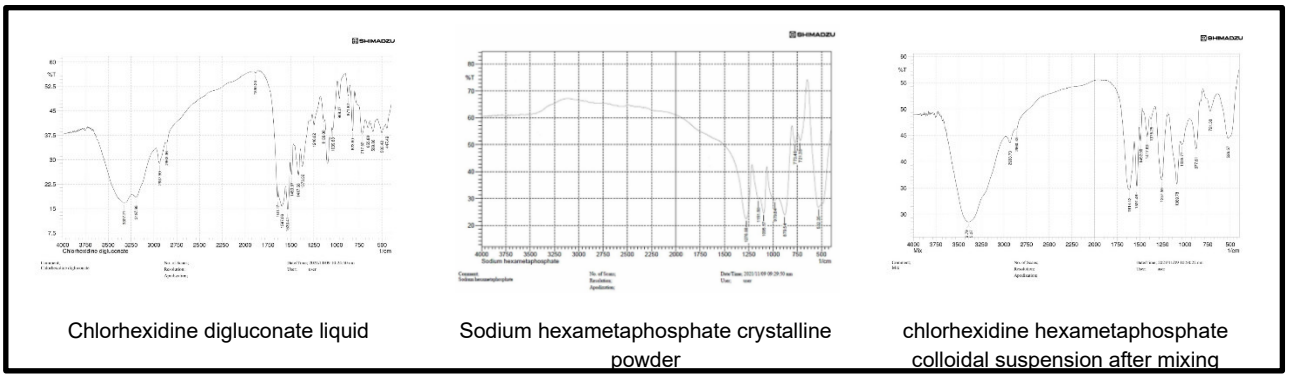

Figure 3: FTIR characterization chart for the nanoparticle with spectra measured at a range between 400-4000 cm^{-1}.

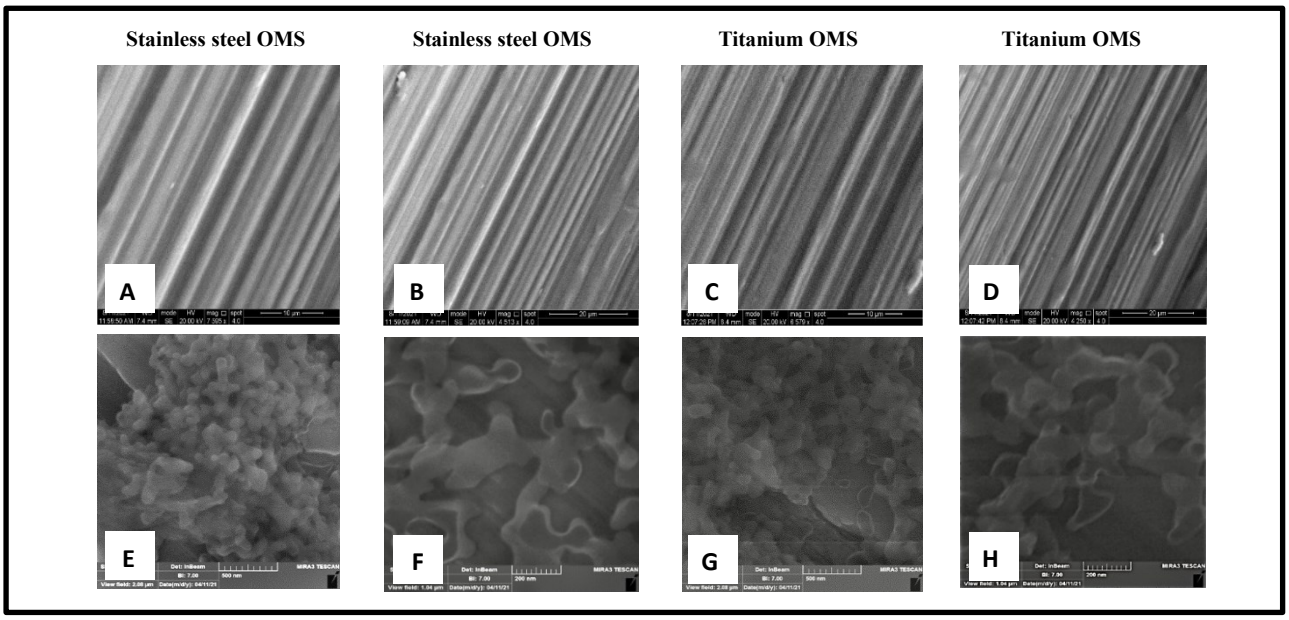

Figure 4: SEM graph for (A-B) uncoated stainless steel OMS, (C-D) uncoated titanium OMS; (E-F)coated stainless steel OMS, (G-H) coated titanium OMS.

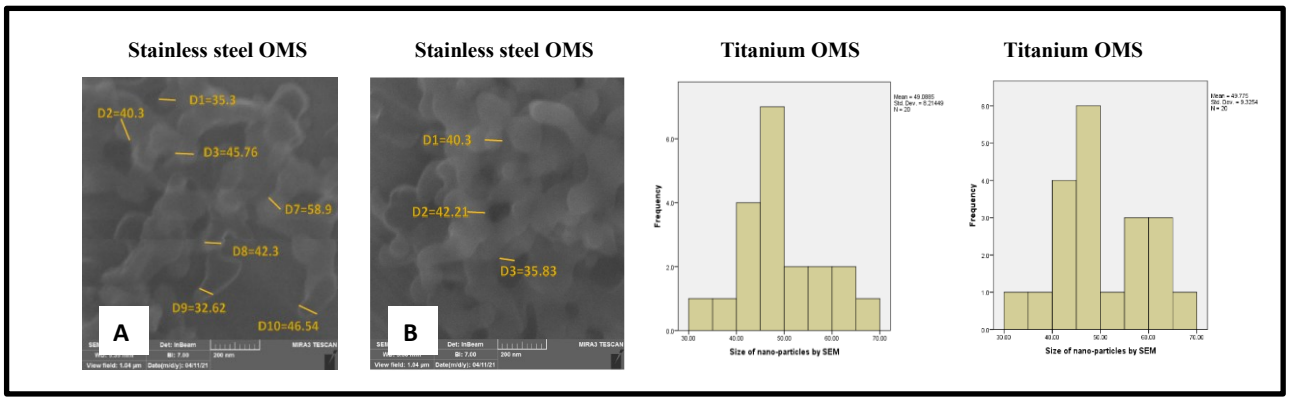

Figure 5: SEM measurement by Image J software to determine the size nanoparticles on the coated OMS for (A) stainless steel and (B) titanium OMS.

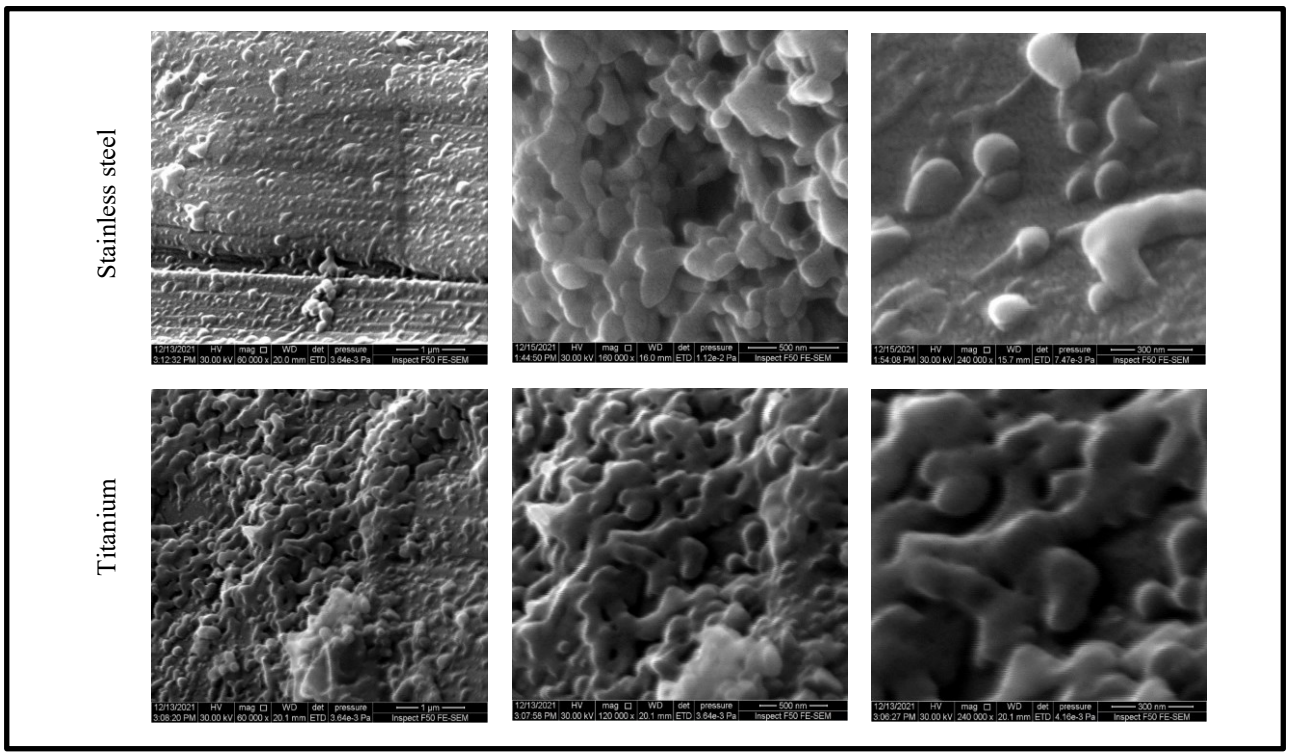

Figure 6: FeSEM images for coated OMS different magnification power.

Discussion

CHX is an effective antimicrobial means against gram-negative, gram-positive bacteria and yeast. The effectivity of CHX is due to damage to phospholipid bilayers in cell membrane at low concentration and at high doses it produces congelation of cytoplasm. As a broad-spectrum antimicrobial and antifungal agent, CHX is broadly used in medicine and dentistry in a CHX digluconate form, it does not stimulate the progress of bacterial resistance [13].

Barbour *et al.* and Wood *et al.* developed materials that release CHX by utilizing HMP nanoparticles in conducted studies [9,21]. Sodium HMP is a cyclic inorganic phosphate, because of its capability to prevent the establishment of extrinsic stains and inhibit the formation of dental calculus it is commonly used in the dental and food dentistry fields. According to a Wood *et al.* , CHX-HMP NP measuring ~49 nm in diameter were worked to coat dental implants [9].

In the present study, the colloidal suspension of nanoparticles was prepared according to the manufacturer's instructions that has also been used in previous studies [9,10,13,21]. The prepared colloidal suspension was characterized by using AFM to evaluate the particle morphology, distribution, and size because it is one of the most effective and proved methods to characterization especially for nanoparticles smaller than 50nm [22]. The mean size of CHX-HMP nanoparticles was found to be 45.2 nm; it was well distributed, homogenous, and had regular shapes. Unfortunately, no previous study used AFM to characterize these nanoparticles.

The prepared colloidal suspension was differentiated by FTIR spectroscopy to evaluate the chemical interaction between the CHX and hexametaphosphate nanoparticles, as one of the valuable method to identify such chemical reaction [23]. The presence of C=O in CHX digluconate and its absence in the mixed nanoparticles indicate the replacement of gluconate by hexametaphosphate. This was in agreement with Duckworth *et al.* whose FTIR results showed the lack of gluconate in the isolated CHX-HMP [11].

Scanning electron microscope (SEM) was used to test the nanoparticle coated OMSs because it is one of the best-approved tools for providing direct characteristic image of surface coated with nanoparticles. The size of nanoparticles ranged between 30-65 nm with an average of 49.08 nm for titanium coated OMSs and 49.7 nm for stainless steel coated OMS, which confirmed the FeSEM result. This was in agreement with previous studies which identified the size of prepared nanoparticles on the coated orthodontic power chain in which the size of nanoparticles ranged between 37-70 nm [13]. Another study by Wood *et al.* determined the size of nanoparticles on the CHX-HMP coated titanium dental implant with TEM which was about 49 nm [9].

In conclusion, stainless steel and titanium OMSs can be coated successfully by antimicrobial CXH-HMP nanoparticles that assist in reduction of the infection associated with the insertion of OMS.

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Prevalence of LBP among physicians in Erbil city

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Abstract

Background: Physicians are always exposed to work-related risk factors that may result in many diseases. Many studies showed the high prevalence of LBP (LBP) among physicians in comparison to other musculoskeletal diseases. The present study aims to estimate the prevalence of LBP among physicians in Erbil city and to detect its related risk factors.

Subjects and methods: a cross-sectional study was conducted among physicians from all specialties inside two tertiary hospitals from Feb 1st, 2021 to Aug 2021. A questionnaire prepared by the investigator was used for data collection. The severity of LBP was assessed by a visual analog scale: from 1-3 was considered mild pain, 4-6 was moderate, and 7-10 was severe pain.

Results: It has been found that the mean BMI difference between the two groups, with and without LBP, was (27.84 ± 1.18Vs 25.46 ± 1.28) with a significant p= 0.003. The proportion with irregular sleep was (83.07% Vs 22.53%) among both groups respectively with a statistically significant p=0.032. The overall prevalence rate of LBP among physicians was 78.6%; 71.4% were males and only 28.6% were females with a significant p=0.001. The result of logistic regression for the overweight, obese, regular sleeping, and lifting heavy objects, OR with 95% confidence intervals, were; 3.40 (0.37-30.6), 2.36(0.5-10.3), 1.57(0.99-2.48), and 2.63(1.63-4.25) respectively.

Conclusion: the prevalence of LBP among physicians appears to be high and constitutes a major health concern. The BMI, lifting heavy objects, and sleep patterns were good predictors of LBP among physicians.

Keywords: LBP, Physicians, Specialties, Risk factors.

Introduction:

Physicians are exposed to work related risk factors that may result in many diseases. Many studies showed the high prevalence of LBP (LBP) among physicians in comparison to other musculoskeletal diseases [1]. A study in Tunisia reported a 57% -lifetime prevalence of LBP and an annual prevalence of 50% among all

hospital staff [2]. The result of the meta-analysis reported prevalence rate ranged from 44%-67% [1]. The prevalence of LBP among physicians in China was 44% [3]. Many cross-sectional studies in different parts of the world examined the prevalence of LBP, In Australia,[4] prevalence was 44% while in Japan, a prevalence of 84% was reported [5].

This variation in the prevalence rate could be due to factors of the study such as age groups and the definition of LBP prevalence. Point prevalence is defined as the number of individuals in a specific population under study at a certain point in time. The number of individuals who have LBP during a specific time interval is called period prevalence. Individuals who had LBP at some point in their lives are called lifetime prevalence [6].

LBP is associated with many potential risk factors, like age, physical activity, lack of exercise, abnormal postures, smoking, gender, and high BMI. The LBP was three to four times higher in individuals aged over 50 years than in those between 18-30 years, as studies revealed [7]. Accordingly, multiple factors that contributed to LBP in the elderly, timely and appropriate management approaches could be framed.

Females with low education, smokers, and lower socioeconomic class, have a higher prevalence than males, educated and non-smokers. This gender variation is explained by biological factors such as menstrual fluctuation, or pain by females more than males, and weight gain during pregnancy [8]. Menopause women who had more severe narrowing of the discs with low sex hormonal levels, would have accelerate processes of degeneration, and increase the severity of pain [8]. A study that examined data from 34,525 United States adults had found a significant association between LBP and the number of cigarettes smoked [9].

The present study aims to estimate the prevalence of LBP among physicians in Erbil, to identify associated risk factors of LBP, to identify the characteristics of LBP episodes in terms of duration and intensity, and to compare the risk of developing LBP among the different specialties.

Subjects and Methods

A cross-sectional study was conducted among physicians including senior doctors and senior house officers from all specialties inside two main tertiary health care facilities in Erbil city from the public sector from Feb 1st, 2021 to Aug. 2021.

A questionnaire that includes information about demographic characteristics like age, gender, marital status, and BMI was prepared by the researcher and was used for data collection. It also included the work-related factors like hours of work per day, type of work, duration of work in the hospital, and work position. The severity of LBP was assessed by a visual analogue scale: a score from 1-3 was considered mild pain, 4-6 was moderate, and 7-10 was severe pain [10]. Other risk factors such as doing exercise, sleeping patterns, lifting heavy objects, and smoking were also explored. A factors like living in an apartment without using an elevator as some apartments don't have elevators which is a case that makes the subjects more prone to adopt bending positions and consequently to interfere for developing backache was also taken into consideration. A stratified random sampling method was used to include physicians from each department proportional to the total number in that department. The investigator divided the population of physicians into strata then from each stratum a random sample was selected until the sample size was completed. A frequency of LBP of 25.2% [11] from a previous study, was used in finding the sample size with a marginal

error of 5%, a design effect of 1, 95% confidence interval and the total number of physicians inside the two tertiary health facilities was 1000 physicians. The Epi-info was used to calculate the sample size and 225 physicians were to be included but the investigator recruited 500 physicians for convenience. The questionnaire was distributed by email to physicians and the response rate was 100%. The physicians included in the study were aged between 30 to 60 years with at least one year of work experience in that field. The physicians with a history of trauma, spinal surgery, pregnancy, fracture and musculoskeletal disorders were all excluded from the study before receiving forms.

The analysis was based on a comparison of the presence or absence of LBP among physicians, and the associated factor that they have. The data was recorded on a specially designed questionnaire, collected and entered into the computer via Microsoft Excel worksheet (Excel 2010) and then analyzed by using Statistical Package for Social Sciences (SPSS) version 25 and the results were compared between patients with different variables, with a statistical significance level of ≤ 0.05. The results were presented as rates, ratios, frequencies, and percentages in tables and figure and then analyzed by using an independent t-test and Chi-square test. The logistic regression was used to find factors predicting back pain and the odds ratio with a 95% confidence interval was calculated for each.

Ethical considerations: This research was submitted to the Ethics and Scientific committees of the Kurdistan Board of Medical Specialties for scientific and ethical approval. The purpose of this study is explained for each volunteer and a written consent is obtained from each one of them. Those volunteers disagree the consent were excluded from the study. Confidentiality and anonymity of data were ensured.

Results

As the study included 500 physicians from different specialties, their age were between 25 and 60, divided in to two groups, participants with LBP and those without LBP, it aimed to estimate the prevalence of LBP among physicians from all specialties during different periods of their work which was from 1 to 6 months, 6 to 12 months, and more than 12 months.

Table (1) shows the significant difference in mean age, BMI, weight and height between physicians with LBP and those without LBP; the mean age difference was (41.31±6.02 Vs 37.63±4.74, p<0.001). The mean BMI difference between the two groups was (27.84±1.18 Vs 25.46±1.28) with a significant p= 0.003. The mean weight and height were (81.63 ± 5.4 Vs 79.53±5.6) and (171.14±3.8 Vs 170±3.9) respectively.

In Table (2), the overall prevalence rate was 78.6%; 71.4% were males and only 28.6% were females with a significant p=0.002. The (95.77%) highest prevalence was reported between 45-54 years of age. Most of the physicians in the LBP group (94%) were overweight.

The highest rate of back pain was among Orthopedic and General Surgery with significant differences (p<0.001) (Table 3). There is no significant difference in relation to the working positions.

In Table (4) the back pain group showed a higher and significant mean difference in years of working, hours of working per a day, and hours of working inside the theatre room; (12.16±5.38 Vs 8.41 ± 4.22), (7.88±1.16 Vs 6.64±1.03) and (11.94±7.80 Vs 7.51±8.45) respectively.

In Table (5) no differences were reported between the two groups in living

in an apartment or using an elevator. A higher rate (86%) smoked in the first group in comparison to the (14.01%) second group with significant results (p=0.002). The proportion with irregular sleep was (83.07% vs. 22.53%) among both groups respectively with a statistically significant p=0.05. The history of lifting heavy objects was (87.26% Vs 12.73%) in both categories respectively and the p-value was less than 0.05.

Table (6) illustrated the assessment of the severity of back pain by a visual analogue scale. The pain is categorized into three stages according to its severity.

The persistent pain showed the highest rate 68.18% of participants with moderate LBP with p < 0.001. In 61.53% of mild cases, the duration was from 1-6 months.

Weakness in lower limbs was reported in 89% of moderate cases with p < 0.001 and 73.33% of moderate cases took sick leave.

Table (7) showed the result of logistic regression with odds ratio, the overweight, obese, regular sleeping, lifting heavy objects and smoking predicted back pain. OR with 95% confidence interval were; 3.40 (0.37-30.6), 5.32(0.5-10.3), 1.57(0.99-2.48), 2.63(1.63-4.25) and 1.152(073-1.79) respectively.

Figure (1) showed that more than half (57.25%) of physicians with back pain did not take any medication, (19.59%) of participants prescribed NSAIDs for relieving the pain. (5.59%, 4.58%, 4.32%) of Candidates took (Analgesics, Paracetamol, Paracetamol and muscle relaxants) respectively.

Table 1: Distribution of the studied sample by back pain with mean differences of age, BMI.

Variables	LBP N=393 Mean ± SD	No LBPs N=197 Mean ± SD	P-value
Age(years)	41.31 ± 6.02	37.63 ± 4.74	< 0.001
BMI (Kg/m2)	27.84 ± 1.18	25.46 ± 1.28	0.003
Weight	81.63 ± 5.4	79.53 ± 5.6	0.001
Height	171.14 ± 3.8	170 ± 3.9	0.015

Table 2: Distribution of the LBP by sociodemographic characteristics of the studied sample.

Variables	LBP 393 No (%)	No LBP 107 No (%)	Total 500 No (%)	P-value
Gender				
Male	294(82.35)	63(17.64)	357(100)	0.002
Female	99(69.23)	44(30.76)	143(100)	
Marital status				
Married	381(80.37)	93(86.91)	474(100)	< 0.001
Single	12(46.15)	14(53.84)	26(100)	
Age groups	Years			
≤ 34	111(68.94)	50(46.72)	161(100)	< 0.001
35-44	144(73.84)	51(26.15)	195(100)	
45-54	136(95.77)	6(4.2)	142(100)	
55-64	2(100)	0(0)	2(100)	
BMI (Kg/m^2)				
Normal	5(71.42)	2(28.57)	7(100)	< 0.001
Overweight	371(78.27)	103(21.72)	474(100)	
Obese	17(89.47)	2(10.52)	19(100)	

Table3: The prevalence of back pain according to specialty and working status

Variables	LBP N=393	No LBP N=107	Total N=500	P-value
Type of specialist	No (%)	No (%)	No (%)	
Internal Medicine	20(58.8)	14(41.17)	34(100)	< 0.001
General surgery	30(96.7)	1(3.2)	31(100)	
Orthopaedic	40(100)	0(0)	40(100)	
Ophthalmology	31(86.11)	5(13.88)	36(100)	
Radiology	33(86.84)	5(13.15)	38(100)	
Anaesthesia	25(96.15)	1(3.8)	26(100)	
ENT	37(74)	13(26)	50(100)	
Urology	31(70.45)	13(29.54)	44(100)	
Plastic surgery	30(85.71)	5(14.28)	35(100)	
Dermatology	21(46.66)	24(53.33)	45(100)	
Neurosurgery	22(84.16)	4(15.38)	26(100)	
Gynaecology & obstetrics	25(86.20)	4(13.79)	29(100)	
Maxillofacial	21(84)	4(16)	25(100)	
Endocrinology	6(0.6)	4(0.4)	10(100)	
Rheumatology	21(67.74)	10(32.25)	31(100)	
Working status				
Long-standing	4(100)	0(0)	4(100)	0.082
Sitting	148(74)	52(2.75)	200(100)	
Both	241(81.41)	55(18.58)	296(100)	

Table 4: Distribution of the studied sample by mean differences in years of working, hours of working, using mobile and exercising.

Variables	LBP Mean ± SD N=393	No LBPs Mean ± SD N=107	P-value
Years of working as a physician	12.16 ± 5.38	8.41 ± 4.22	< 0.001
Hours working per a day	7.88 ± 1.16	6.64 ± 1.03	0.049
Daily hours of using laptops, mobiles	3.64 ± 0.69	3.70 ± 0.71	0.433
Surgeons' working hours inside Theatre room per a week	11.94 ± 7.80	7.51 ± 8.45	< 0.001
Hours of back exercises per a week	0.92 ± 1.77	0.76 ± 1.82	0.427

Table 5: Distribution of the studied sample by back pain and lifestyle.

Variables	LBP N=393 No (%)	No-LBP N=107 No (%)	Total N=500 No (%)	P-value
Live in an apartment				
Yes	68(75.55)	22(24.44)	90(100)	0.437
No	325(79.26)	85(20.73)	410(100)	
Using elevator				
Yes	68(75.55)	22(24.44)	90(100)	0.437
No	325(79.26)	85(20.73)	410(100)	
Smoking				
Yes	92(85.98)	15(14.01)	107(100)	0.002
No	277(75.06)	92(24.93)	369(100)	
Ex-smoker	24(100)	0(0)	24(100)	
Sleeping				
Regular	231(75.73)	74(24.26)	305(100)	0.05
Not regular	162(83.07)	33(22.53)	195(100)	
Exercise regularly				
Yes	87(82.85)	18(17.14)	105(100)	0.143
No	306(77.46)	89(22.53)	395(100)	
Lifting heavy Objects				
Yes	185(87.26)	27(12.73)	212(100)	< 0.001
No	208(72.22)	80(27.77)	288(100)	

Table 6: Distribution of the studied sample by the severity of LBP.

Variables	Mild N=160 No (%)	Moderate N=219 No (%)	Severe N=14 No (%)	Total N=393 No (%)	p-value
Character					
Intermittent	159(42.85)	204(54.98)	8(2.1)	371(100)	< 0.001
Persistent	1(4.5)	15(68.18)	6(27.27)	22(100)	
Duration					
1-6 months	8(61.53)	5(38.46)	0	13(100)	0.378
6-12 months	107(41.31)	141(54.44)	11(4.2)	259(100)	
More than 1 year	45(37.19)	73(60.33)	3(2.4)	121(100)	
Weakness in lower limbs					
Present	5(3.03)	147(89.09)	13(7.8)	165(100)	< 0.001
Absent	155(67.98)	72(31.57)	1(0.43)	228(100)	
Sick leave					
Yes	2(3.3)	44(73.33)	14(23.33)	60(100)	< 0.001
No	158(47.44)	175(52.55)	0	333(100)	

Table 7: The results of the logistic regression analysis with predictors of LBP.

Variables	B	SE	Wald	df	P-value	Odds ratio (95% confidence interval)
Female	Reference					
Male	-0.73	0.22	10.21	1	0.001	0.48(0.30-0.75)
Age(years)	.314	.121	6.753	1	0.001	0.89(0.86-0.94)
Height	.252	.526	.230	1	0.002	0.93(0.88-0.98)
Weight	-.319	.565	.317	1	0.573	0.93 (0.89-0.97)
BMI(Kg/m2)			1.497	2	0.473	
Normal	Reference					
Overweight	1.224	1.122	1.190	1	0.027	3.40 (0.37-30.6)
Obese	.859	.756	1.291	1	0.025	5.32(0.5-10.3)
Years working as a physician	-.476	.135	12.494	1	0.001	0.86(0.82-0.90)
Working hours daily	-.135	.110	1.493	1	0.222	0.83(0.68-0.1)
Sleeping						
Regular	-.220	.301	.536	1	0.052	1.57(0.99-2.48)
Irregular	Reference					
Exercise						
Yes	-.247	.315	.613	1	0.233	0.78 (0.40-1.24)
No	Reference					
Lifting heavy objects	-.841	.271	9.626	1	0.001	2.63(1.63-4.25)
Smoking	0.14	0.227	0.387	1	0.534	1.15 (073-1.79)

B: Coefficient of Regression, SE: standard error, Wald: test named, it is a statistical test, df: degree of freedom

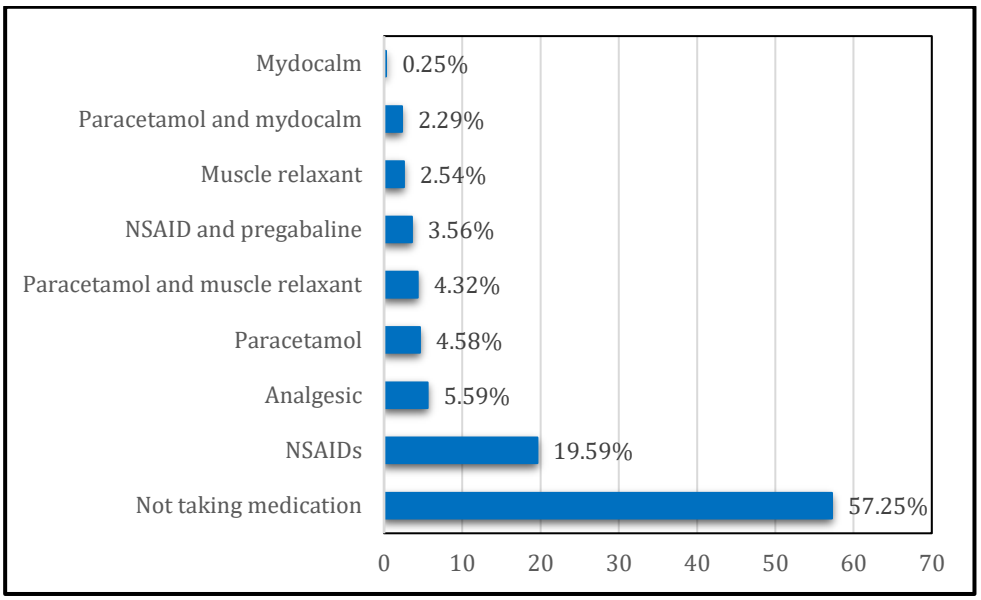

Figure 1: Types of medications taken by physicians with back pain. More than half (57.25%) of physicians with back pain did not take any medication. The NSAIDs were used by 19.59%.

Discussion:

In the current study, the evaluation of LBP was conducted among a sample of physicians including senior physicians and senior house officers working at two tertiary hospitals and to the best of our knowledge, this is the first study inside Erbil city. The prevalence of LBP reported in this study was 78.6%. This finding was consistent with other studies done earlier. This percent is near to estimates reported in other populations: 75.8% [12] in a study in Serbia and 65-80% [13] in the United States. Two previous studies reported lower percent in Iran than our study, 29.3% and 27% respectively [14,15].

The explanation for the differences in results could be due to different methodologies which yielded different rates. The definition of LBP varied in the current study from other previous studies in that evaluation of back pain was done based on the presence of pain in the past month or twelve months duration. The current study may be subjected to recall bias due to memory lapses. A higher rate of prevalence was reported among males in comparison with females: 74.80% vs. 25.19%. This finding was inconsistent with other studies. Females are more at risk of developing back pain due to factors such as pregnancy, contraceptives, estrogen, and menopause [16,17]. The high rate of LBP among male surgeon physicians might indicate that they are among the groups that stood for long hours in the theatre room and they will benefit from the involvement in prevention programs in future.

A significant difference of 27.84 ± 1.18 Vs. 25.46 ± 1.28, p=0.003 was reported in the mean BMI between the two groups. The higher rate (89%) of obese physicians indicated that loss of muscle mass and body fat distribution will aggravate the pain. The efforts should be directed to reduce BMI among physicians and may be considered a possible interference in reducing the prevalence of LBP among them [18].

A percentage of 83.07% of physicians who irregularly in this study have back pain

and the odds among those who sleep regularly is OR=1.57(0.99-2.48), p= 0.052. Earlier results confirmed that sleep is a protective factor and sleep disorders can lower pain threshold and worsen back pain. The high incidence of migraine and depression among patients with sleep disorders was reported in many studies [19]; this explains the bidirectional relationship between sleep and LBP.

The mean differences in hours of working reached a significant level of 7.88 ± 1.16 Vs 6.64 ± 1.03, p=0.05. A higher rate was reported among (100%) orthopedic surgeons, (96.7%) General surgeons and working inside theatre rooms also reached a significant level of 11.94 ± 7.80 Vs 7.51 ± 8.45 P< 0.001. The findings of the present study were in line with that of Mecca [20], Saudi Arabia cross-sectional study.

In this study, more than half (57.25%) of physicians with back pain did not take any medication. The best LBP reliever in 51.7% of physicians in Saudi Arabia's (20) study was rest and only 43.6% took medication.

The associations between LBP and the risk factors of living in an apartment, using the elevator and doing exercise did not reach a significant level. The LBP group had a positive history of lifting heavy objects in 87.26% (OR 2.63(1.63-4.25)). In Gaza study, 62% had a history of lifting heavy objects [21].

The descriptive statistics about LBP showed that most of them were mild and moderate cases: 40.71%, and 55.72% respectively. The intermittent character, weakness and no sick leave were 94.4%, 41% and 84%.

In this study, 56% had LBP in 6-12 months duration and, in 30.78% the duration of pain was more than 1 year. The point prevalence for the last six months (62.3%), and last year (71.7%) in the North Iran study was higher than these results [22]. The result of the logistic analysis confirmed some risk factors like BMI (OR 3.40 (0.37-30.6), p=0.027) as a significant predictor of LBP.

In this study, the prevalence of LBP among smokers was 86% and among non-smokers was 75% (p=0.002) and (OR =1.15 95%CI (073-1.79)). Back pain was valued to be present in 23.5% of never-smokers, 33.1% of former smokers, and 36.9% of current smokers in America study [9]. Another study in the US reported higher odds for back pain (OR=1.2) among smokers [23]. They explained the relation by the presence of a biological substance that aggravated back pain.

As this study is cross-sectional, inferences cannot be obtained about causation; this is one of the limitations. The second limitation is the representative-ness of the sample. The results cannot be generalized to other facilities inside Erbil city. The prevalence in the current study is within the range and this confirms the validity of the results. This point is considered one of its strengths.

Conclusion and Recommendation

The prevalence of LBP among physicians seems to be high and constitutes a major health concern. Most of the cases were mild and moderate. The BMI, lifting heavy objects and sleep patterns were good predictors of LBP among physicians. Further studies recommended with larger sample sizes and other health staff should be included. Physicians should be engaged in programs for muscle strengthening and reducing weight.

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Two Sisters were Diagnosed with Childhood Systemic Lupus Erythematous

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Abstract

We are herein reporting two female siblings with childhood-onset Systemic Lupus Erythematosus (SLE). The children were diagnosed as having SLE in reverse birth order at ages 2 and 6 years. Younger sister's initial symptoms were serositis, proteinuria, and hemolytic anemia with laboratory findings of hypocomplementemia and positive ANA/anti-dsDNA antibody. After 18 months, the older sister presented with high-grade fever, arthralgia proteinuria, oral mucous ulcer, butterfly rash, and positive ANA/anti-dsDNA antibody.

Key words: Childhood Systemic Lupus Erythematosus, SLE

Background

SLE is a chronic autoimmune illness characterized by inflammation and the production of autoantibodies. It can impact theer skin, joints, lungs, blood, kidneys, and nervous system due to inflammation. Furthermore, it has no established cause; however, research suggests that it is caused by a mix of genetic and environmental factors [(1)].

Relatives of patients with SLE appear to have a higher chance of developing SLE and other autoimmune disorders, but estimates of individual family risks are scarce or incorrect. In addition, the proportional contributions of genetic, shared, and non-shared environmental variables to SLE susceptibility are unknown [(2)].

This case report presents two sisters diagnosed with childhood-onset SLE and tries to explore the clinical and serological parameters of this disease.

Case Presentation

In October 2018, a 30-month-old female presented to the emergency department complaining of fever and shortness of breath for a week; she was treated with antibiotics and a bronchodilator but without any improvement. On examination, she is conscious, pale, dyspneic, tachypneic, with no cyanosis, periorbital swelling, no oral lesion, and no specific stigmata on the face. Chest auscultation shows a decreased air entry bilateral with muffled heart sound. The abdominal examination was unremarkable.

CXR has shown a huge cardiomegaly with pleural effusion and echocardiogram has revealed a lot of pericardial effusion that need pericardiocentesis.

Growth parameters: weight 13kg (above 10th percentile), height 86 cm (above 25th percentile). Vital signs: SpO_2 94% on room air, PR 140 bpm, RR 38 CPM, temp. 38.5° C.Investigations showed normal renal function, CBC (Hb 9.2 g/dl, WBC 18.7 × 109/L, platelets 678000 /mcL) and liver function tests were normal. However, serology has shown positive ANA/anti-dsDNA antibody.

According to the criteria of American College of Rheumatology, the diagnosis of SLE was made and started as a management in form of prednisolone, aspirin, and hydroxychloroquine.

Two years later, in February 2020, the patient presented to the emergency department with an abnormal body movement for more than half-hour refractory to three anticonvulsants. MRI revealed Hyperhintense on T2, hypointense on T1 involving right parietal lobe feature of focal infarction (fig 1). She was admitted to ICU until her fit stopped and discharged on levetiracetam, phenobarbital, and muscle relaxant. She is now having spastic diplegia and is still on prednisolone, aspirin, hydroxychloroquine, Levetiracetam and muscle relaxant with physiotherapy.

Unfortunately, on June 202; her older sister, 8- year old with a past medical history of spastic paraplegia came to the outpatient clinic complaining of fatigue, fever, facial rash, and inability to walk on an aid walker.

On examination, she is conscious, looks ill, feverish, not dyspneic, has periorbital edema, with erythematous raised skin across the nasal bridge and cheeks (Fig. 2), oral ulceration in the hard palate, pain and swelling of bilateral knee and ankle joints. Chest and abdominal examination unremarkable.

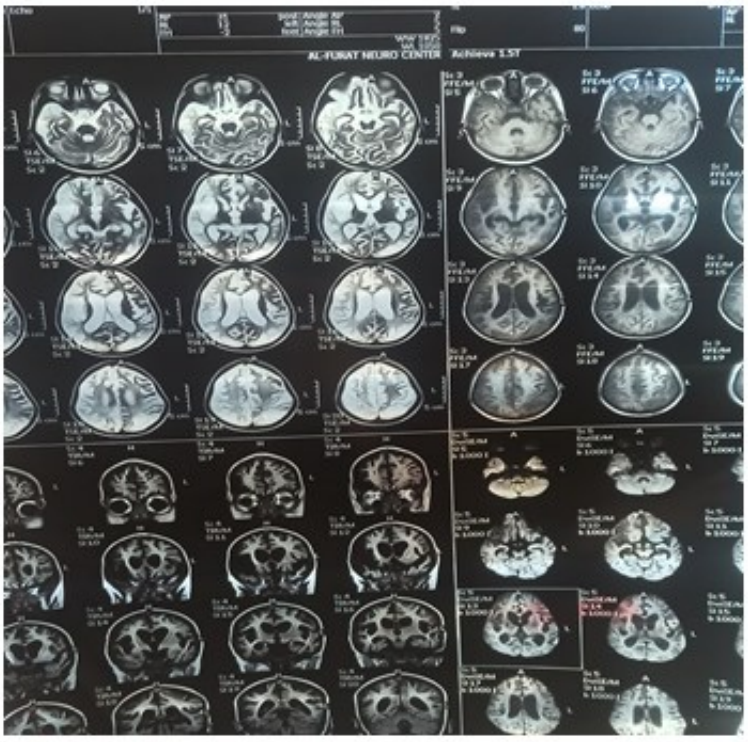

Figure 1: Bilateral diffuse atrophic changes with dilation of the ventricular secondary to atrophic changes. All features suggest atrophic changes secondary to old insult.

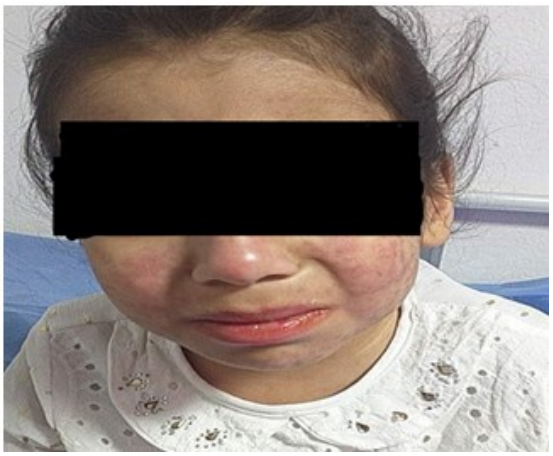

Figure 2: older sister presented with malar rash

Growth parameters: weight 22kg (on 25th percentile), height 115cm (on 10th percentile).

Vital signs: temperature 39º C, heart rate 110 bpm, respiratory rate 20 CPM, spO_2 on room air 96%.

Investigation: albumin in urine +, S. protein 4.9 mg/dl, S. albumin 2.8 mg/dl, blood urea 33 mg/dl, creatinine 0.4 mg/dl, S. cholesterol 225 mg/dl, ESR 65 mm/hr, WBC 16.9 × 10^9/L, Retic count 3, positive anti ds DNA 136 IU/ml (normal range < 20 IU/ml), positive ANA 4.7 IU/ml (negative <0.8), decrease complement 72 mg/dl (normal range 90_180), negative antiphospholipid antibody, equivocal anti smith antibody 17 IU/ml (negative <12, positive >18).

Treatment of older sister: in acute attack methylprednisolone 30 mg/kg/every other day then on prednisolone syrup 2 mg/kg/day for 4weaks then put on a 1mg/kg/day single daily morning dose that has one flare-up of the disease. In addition to hydroxychloroquine tab 40 mg bid.

Discussion

The etiology of SLE remains unknown, but genetic, hormonal, immunologic, and environmental factors are suspected to play a role. Individual risks of SLE and other autoimmune disorders were found to be higher in families with SLE patients. SLE has a heritability of 43.9 percent [(2)].

In 2008, Yokohama City University School of Medicine in Japan presented a case of two female siblings with childhood-onset SLE [(3)]. At the ages of 11 and 14, the children were diagnosed with SLE in reverse birth order. In 2008, Y Sano diagnosed two more sisters with childhood SLE. Antinuclear antibodies and LE cell preparations were negative in a 19-year old lady and her 15-year old sister who experienced a malar rash, arthralgia, and photosensitivity. During her childhood, the older sister suffered from recurrent bronchitis while the younger sister had no such problems[(4)].

Learning point

The significance of this case consists in the diagnosis of two female siblings with childhood SLE; this leads to putting a high index of suspension for the diagnosis of SLE in other siblings if present with non-specific symptoms.

Limitations

There was the inability to obtain HLA typing of two sisters due to the unavailability of genetic study. Renal biopsy especially for older sister was temporarily postponed until the agreement from her father.

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Sanjad-Sakati Syndrome in Al Najaf Governorate

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Abstract

Sanjad-Sakati syndrome is an inherited autosomal recessive disorder that presents primarily in the Arab countries, with its real prevalence not well established. It is a combination of specific facial dysmorphology, failure to thrive, hypoparathyroidism, and variable mental disability which is an unfortunately incurable disease with fatal outcomes .

Keywords: Sanjad-Sakati syndrome, case report, rare diseases.

Background:
Sanjad-Sakati syndrome (SSS), also known as Richardson-Kirk syndrome, has been classified as hypoparathyroidism-retardation-dysmorphism (HRD) syndrome in the Online Mendelian Inheritance of Men (OMIM) no. 241410 [1]. It is an autosomal recessive disorder that was initially described by Sanjad et al. in 1988 [2]. It affects both sexes equally and contains a gene on chromosome 1q42-q43. It has severe and often deadly consequences [4].

This disorder was found almost exclusively in people of Arab origin [5], with reported patients who were Saudi Arabian, Qatari, Palestinian, Kuwaiti, and Omani [6].

Although the exact prevalence is unknown, the estimated incidence in Saudi Arabia ranges from 1:40000 to 1:600000 live births [7]. The syndrome is characterized by dysmorphic features, short stature hypoparathyroidism, and mild to moderate mental retardation [6].

Case presentation

Case 1:
A four-and-a-half-year-old girl from a rural area presented with an attack of loss of bowel motion and vomiting lasting 2 days with refusal to feed. The family reported two previous attacks of acute gastroenteritis and a history of two attacks of seizures from early infancy; each attack lasted a few minutes with no change in the level of consciousness. She was delivered by vaginal delivery with a birth weight of 2 Kg .Regarding the family history, it has been found that the child had one dead sibling with the same clinical features, they reported the cause of death to be pneumonia. The child also has two alive siblings who were the product of consanguineous marriage (second-degree relatives). Besides, there were two nephews in the family with the same clinical features, one of them died at 4 with the cause of death unknown; furthermore, the family reported that she had a delay in walking time, speaking few words only and

she had some difficulties with obeying commands.

On examination, the child looks conscious and, with some dehydration, smaller for her age, with failure to thrive. She also had some odd facial features (small deep-seated eyes, long philtrum, poor dentition, and depressed nasal bridge), and small hands and feet.

Growth parameters: weight 9 kg (Z score -5.8), height 80 cm (Z score -5.7), and head circumference 46 cm (Z score -4). New investigations revealed a white blood cell count of 21100× 109/L (neutrophils 46.2%), hemoglobin 9.9 gm/dl, platelets 310000× 109/L, and C-reactive protein-positive while her previous investigations showed thyroid function test 4.7 µIU/ (0.25-5), T3= 1.19 nmol/l (0.92-233), T4= 96 nmol/l (60-120). Serum calcium is 7 mg/dl and the ionized fraction is 1.8, Parathyroid hormone level is less than 1 Pg/ml (8.7-79.6).

The echocardiogram report was normal and bone age was delayed (less than 1 year). She is on one alpha drop and calcium supplementation.

Due to the typical clinical and laboratory features, she is diagnosed with SSS although genetic testing was not done due to limited resources.

Figure 1: Phenotypes of Sanjad-Sakati syndrome (SSS) in case number one (small deep-seated eyes, long philtrum, poor dentition, and depressed nasal bridge).

Case 2

A nine-month-old male infant presented with repeated vomiting and diarrhea with some dehydration. According to case history, he had a previous attack of seizure in early neonatal life due to low calcium in the blood. His family history reveals that he is the younger brother of the aforementioned case 1. While according to developmental history, he cannot sit yet but he can roll from back to front and the reverse way.

On examination, he is conscious, alert, looks smaller than expected, and his vital signs are within normal for his age and sex. Growth parameter reads: weight 4Kg (Z score=-7), head circumference is 38 cm (Z score=-5.6) and height is 63cm (Z score=-4). He has a small head with deep-seated eyes, a depressed nasal bridge, large ears, and dentition didn't start yet. There are no visible skin lesions and his

chest and abdominal examination were unremarkable His investigations showed that the serum calcium is 7.1 mg/dl, phosphate is 5.5 mg/dl, alkaline phosphatase is of 143 U/l., serum parathyroid hormone level is 2.1 Pg/ml (8.7-79.6), and the echocardiogram was normal. He was put on calcium supplementation and one alpha drop.

Figure 2: Small head with deep-seated eyes, a depressed nasal bridge, and large ears in case number two.

Discussion

Sanjad-Sakati syndrome is a rare autosomal recessive disorder that is described in the Arab world. The mutation is in the tubulin-specific chaperone E (TBCE) gene in chromosomal area 1q42-q43 [5].

This syndrome may share the dysmorphic features with other syndromes namely DiGeorge syndrome and Kenny-Caffey Syndrome [6] although SSS and Kenny-Caffey syndrome have a mutation in the TBCE gene [8], the difference is that patients with Kenny-Caffey Syndrome have normal intelligence, exhibit macrocephaly, and the anterior fontanelle is large and closes late in KCS type 2 patients[9]. On the other hand, DiGeorge syndrome is characterized by hypoparathyroidism and has also T cell immunodeficiency and congenital cardiac anomalies, the two features that are not present in SSS [10].

The facial features of patients with SSS have been shown in many studies and observations of microcephaly, deep-seated eyes, and short stature[2,11] . Errors of refraction, retinal vascular tortuosity, strabismus, and corneal opacities are some of the ophthalmic symptom [2].

There is no cure for SSS but the treatment of its patients is to control the high serum phosphate levels, and the adverse effects of therapy including generalized calcifications. This is done usually by giving calcium supplementation intravenously in case of seizure or orally plus the active form of vitamin D.

Conclusion:

Sanjad-Sakati syndrome is an autosomal recessive disease that is not uncommon in the Arab population. Although there is no

cure for this syndrome, the family can be given genetic counseling and prevent comorbidities. Due to limited resources, genetic testing was not done for these siblings, hopefully, it can be arranged in the future for them.

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Prevalence of Complications in Laparoscopic Cholecystectomy in Extracting Gallbladder by Using Supra-Umbilical Port Versus Epigastric Port in Sulaimani Teaching Hospital: A Prospective Case Series Study

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Abstract

Background: Depending on the surgeon's preference, different locations for trocar incision can be used to extract the gallbladder. Some studies are claiming that epigastric port is better for retrieval due to easiness for the surgeon as there is no need to change the position of the telescope and readjustment of the surgeon's position. Other studies show the superiority of umbilical port in terms of pain.

Setting: Sulaimani Teaching Hospital.

Aims: The current work aims at evaluating the port site for gallbladder retrieval in LCin terms of time for extracting the specimen, frequency of port site pain, surgical site infection, and incisional hernia.

Patients and methods: This is a prospective randomized study including 108 patients who underwent laparoscopic cholecystectomy. It was conducted in Sulaimani Teaching Hospital from October 1st, 2020, to September 30th, 2021. Patients were divided into two groups matched in gender and age: Group A: Gallbladder was extracted from the epigastric port while in Group B: Gallbladder was extracted from the supra-umbilical port.

Results: A two comparable groups of patients matched in gender and age were recruited with a mean age of 41.2 + 11.04 years ranged 20-68 years. Overall, 52.78 % (n=57) were female and 47.22% (n=51) were male with F/M ratio of 1.11/1. The time of the LCfor [21±4 min] was more in group B [n= 42, 38.9%] patients in contra to group A[n=37, 34.3%] patients, while for [33±2 minutes] it was more in group A [n= 6, 5.6%] patients. Retrieval of the almost all the excised gall bladder (n=54, 98.18% patients) via supraumbilical port needs less time (≤5 minutes) in comparison to epigastric port (n=40, 75.47% patients).

Conclusion: Based on these findings the safety and ease of supra-umbilical port for extraction of gallbladder during LChas been better than that in using epigastric port. Furthermore, it has taken less operative time with less patients complained of pain or surgical site infection, abscess, and port site incisional hernia.

Keywords: complication, cholecystectomy, incision, laparoscopy, ports

Introduction

In 1985, Erich Muhe initially performed LC(LC); the procedure had gained clinical acceptance in France by efforts of Mouret in 1987, then after the practice of laparoscopic cholecystectomy (LC) spread worldwide in the 1990s.[1].

LC is a preferred method of gallbladder removal for symptomatic gallbladder stones and for other benign conditions; the use of LC in the management of gallbladder disease has shown several advantages over open cholecystectomies such as reduced postoperative pain, risk of surgical site infections, and incidence of incisional hernia, and quicker recovery[2].

However, the complications of port-site following laparoscopic surgery is around 21 per 100,000 cases, but is increasing with the size of the incision for the ports and number of the trocars[3]. Retrieval of the gallbladder is an important terminal event of LC and is reported as the factor inducing postoperative port site pain[6].

Both umbilical port and epigastric port have been recommended for retrieval of the gallbladder in LC; however, there is a huge debate on which one is superior[4]. Depending on the surgeon's preference, different locations for trocar incision can be used to extract the gallbladder[5], some studies are claiming that epigastric port is better for retrieval due to ease for the surgeon as there is no need to change the position of the telescope and readjustment of the position of the surgeon[4,5,7]. Other studies show the superiority of umbilical port in terms of pain[4,7].

To date, there is no evidence to support any one port being superior to the other for GB extraction while considering the postoperative-port site pain[7].

The current work aims to evaluate the port site for gallbladder retrieval in LC in terms of time for extracting the specimen, frequency of port site pain, surgical site infection, and incisional hernia.

Patients, materials, and methods:

This is a prospective randomized study including 108 patients underwent LC. It was conducted in Sulaimani Teaching Hospital from October 1st, 2020, to September 30th, 2021. An originally-designed questionnaire was reviewed and accepted by four professors in surgery from the College of Medicine-University of Sulaimani.

The informed consents were signed by both patients and the surgeons prior to their inclusion in the study. The work was also approved by the appropriate Ethics Committee of Arabic Board of Medical Specialties (No.1703 on 23 /09/ 2021), and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. The thesis was approved by qualified surgeons, board of surgery qualification, and did all the laparoscopic cholecystectomies with a four-port technique under general anesthesia (epigastric port and supra-umbilical port both as 10 mm while lateral ports both as 5 mm). No endobags was available for extraction of gallbladder. The fascia closed by aid of fascia closer in patients when the retrieval port was extended because of using Hasson's access technique and on extracting the large or rigid gallbladder specimens. A detailed questionnaire was used in the interview of the patients, regarding demographic, clinical, surgical, early postoperative course of the condition, and McGill Pain Questionnaire (MPQ) [8] included for evaluation of the postoperative port site pain.

Time of the cholecystectomies measured from skin to complete suturing of the incisions in minutes, and time of extraction of the gallbladder measured from separation to the complete delivery of the specimen out.

Exclusion criteria for patients and methods

1. Urgent LC.
2. Needs Exploration of common bile duct.
3. Operations by surgical trainees.
4. Covid-19 cases with gall stones.
5. Previous laparotomy or laparoscopy

A postoperative port site pain was assessed during the stay in the hospital. Other potential complications were observed clinically and ultrasonography when applicable, at first visit (one week after surgery), one month to 3, and 6 months. Patients were divided into two groups matched in gender and age; Group A: gall bladder was extracted from the epigastric port while Group B: gallbladder was extracted from the supra-umbilical port. The pain in all the incisions of the ports was estimated by analog pain scale. All the data were collected, organized, and analyzed by Statistical Package for the Social Sciences (SPSS) version 21.

The Results

A two comparable groups matched in gender and age were recruited with the mean age of patients was 41.2 + 11.04 years ranged 20-68 years. Overall, 52.78 %(n=57) were female and 47.22% (n=51) were male with F/M ratio of 1.11/1. Table1.

Gender was comparable in both groups A , B . However, male patients where slightly more [n =27, 25 %] in group B than [n=24, 22.2 %] in group A.

Overweight patients were larger in number in group B [n=12, 11.1%] patients than group A [n =9, 8.3%] patients. Obese patients were larger in number in group B [n=9, 8.3%] patients than group A [n=7, 6.5%] patients table 2.

The time of the LC for [21±4 min] was more in group B [n= 42, 38.9%] patients than in group A [n=37, 34.3%] patients, while [33±2 minutes] was more in group A [n= 6, 5.6%] patients, see Table 3

Retrieval of the almost all the excised gallbladder (n=54, 98.18% patients) via supraumbilical port needs less time (≤5 minutes) in comparison to epigastric port (n=40, 75.47% patients) as seen in Table 4. No perforation of gallbladder was recorded during or on extraction of gallbladder.

The LC was complicated in twelve patients of group A, and ten in group B, while one patient in each group was converted into open Table 5

The parkland grading scale [8] was comparable for all grades in patients in both groups A and B, as in Table 6

More patients in group B stayed only 6-10 hours in the hospital, while 3, 2 patients in group A, B stay in hospital for over 24 hours, see Table 7 and Figure 1 respectively.

The port site pain post operation was present in group A [n= 17, 15.7%] patients verses group B [n=11, 10.1%] patients, and the port site superficial surgical; site infection, port site hernia were present only in group A. There were neither sepsis nor mortality in the patients of the both groups A, B, as detailed in Table 8.

Table 1: Number and percent of male and female patients.

Male	Group A	Group B	Total
Female	29	28	57
Male	24	27	51

Table 2: Frequency of the body weight of the patients in both groups.

Body Wight	Group A	Group B	P value
Normal weight	32	31	0.56
Under weight	3	0	
Over weight	9	12	
Obese	7	9	
Morbidly obese	2	3	

Table 3: Time of the laparoscopic cholecystectomy from the skin to skin in both groups.

Groups	21±4 min	28±2 min	33±2 min	40±4 min	P value
Group A	37	8	6	2	0.39
Group B	42	7	5	1	

Table 4: Time needed for the gall bladder extraction from separation of the gall bladder from its bed to complete delivery of the gall bladder out of abdomen.

Groups	3min	3-5min	5-10min	Above11min	P value
Group A	23	17	9	4	0.032
Group B	29	25	1	0	

Table 5: History of open and laparoscopic surgery in patients of both both groups.

Groups	Laparoscopy	Laparotomy	P value
Group A	4	7	0.046
Group B	5	13	

Table 6: Consequences of the operations in both groups.

Groups	Straight forward	Complicated	Conversion to open	P value
Group A	40	12 22.64 %	1	0.79
Group B	44	10 18.18%	1	

Table7: Parkland grading scale for state of gall bladder in both groups.

Groups	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5	P value
Group A	43	5	4	0	1	0.98
Group B	44	6	4	0	1	

Table 8: Length of the Stay in hospital for patients of both groups.

Groups	6-10 hr.s	11-15 hr.s	16-20 hr.s	21-24 hr.s	> 24 hr.s	P value
Group A	39	4	6	1	3	0.81
Group B	45	4	2	2	2	

Table 9. Surgical post operations complications found during follow up in both groups .

Groups	Port site pain	SSSI	Port site abscess	Port site hernia	Sepsis	Mortality	P value
Group A	17	4	3	2	0	0	0.17
Group B	11	0	0	0	0	0	

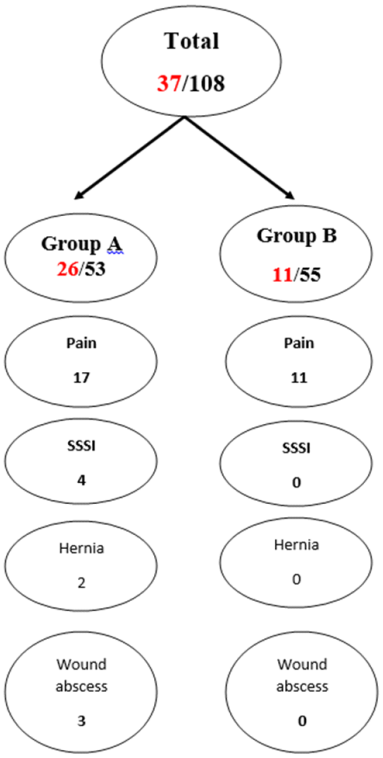

Figure 1: incoherence of post-operative complications in patients of both groups A, and B.

Discussion

The difference in body weight in patients of both group A, B had statistically non-significant correlation (P – value =0.56) with the ease of the operations and postoperative complications. More than half of the patients were with average weight in both group A, andB (n = 32, 29.6%) and (n = 31, 28.7%) in this order, meanwhile 3 patient were underweight in group A and larger number of patients were overweight in group B (n = 12, 11.1%).

Twenty-three patients in group B had an excess weight; others had comorbidity like diabetic mellitus and hypertension, in contrast to group A which contains nineteen patients with extra weight. Usually excess weight and obesity will make the LC difficult [9,10] and needs more time [11,12], but in the current work most of the operations in group B was straightforward and required shorter time. Meantime patients in group A were in need of longer operative time, and longer time for extraction of the gallbladder (Table 3 and 4) and it contains a smaller number of overweight and obesity. The time of the operations needed in both groups was less than that mentioned in the literature. Jacob, et al., [13] states in their study that the mean operation time was 50.92 ± 1.55 minutes, and prolonged surgery increases the risk of complications and prolongs the postoperative hospital stay [14].

More than three quarters of the operations were completed within 17 to 25 minutes (from skin to skin) in both group; group A (n =37, 34.3%) and in group B (n = 42, 38.9%).

Although the difference in time of the operation was statistically non-significant (P–value = 0.39) as seen in Table 3, the length of time of the laparoscopic cholecystectomies was greater in patients of group A.

The time for retrieval of almost all the excised gallbladder (n=54, 98.18%) was less than 5 minutes in supraumbilical port group versus two thirds of the patients in epigastric port group (n=40, 75.47%), table 4.

All patients with history of previous abdominal operations were excluded to avoid bias as it is well known that because prior abdominal surgery, raises the risk of abdominal wall adhesions, has been identified as one of the major risk factors", for complications during laparoscopy [14,15,16,17,18].

Albeit the patients in both group A and B were with comparable scales in Parkland grading (43, 44) in grade 1 (5, 6) in grade 2 (4, 40) in grade 3 respectively as seen inTable 6. These declare that the state of the gallbladder (P – value 0.98) was comparable and did not affect the time of the operation and sequel, period of the stay in the hospital, as seen in Table 7, whatever the method used for of the extraction of the gallbladder (tables 3, and 6), while other studies found the higher grades of parkland scale associated with more difficulty and complications [19,20,21,22].

Regarding the surgical complication of the port site incisions; there was pain at incision in eleven patients with supra-umbilical incision while seventeen patients in group A were with pain. Four patients developed (SSSI) three patients developed port site abscess, and two patient developed port site hernia. All these may mean that extraction of the gallbladder from supra umbilical port may be superior, easier and with less surgical complication in comparison to extraction from the epigastric port incision, as shown in Table 8, Figure 1. Meantime other studies considered other variables rather than port of extraction as a risk factor for complications, like male gender [23,24], advanced age, [25] ASA grade, [26] excess weight [27].

In supra-umbilical port incision there will be no fat to traverse [28], meanwhile in epigastric port incision, the trocar and contaminated gallbladder specimen will pass through the bulk of the adipose tissue of the falciform ligament, which will be traumatize, and infarcted partially, [29] and contaminated by the extraction[30]. It is well known that adipose tissue could perturbed by pathogens, with inbuilt ability to store pathogens, and get infection easily [31,32].

Conclusion

Based on these findings the safety and ease of supra-umbilical port for extraction of gallbladder during LC has been better than using epigastric port. Furthermore it needs less operative time and with less patients complained of pain or surgical site infection, abscess, and port site incisional hernia.

Conflict of interest:

The authors declare that there is no conflict of interest

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Prevalence and Determinants of Depression among Women with Breast Cancer in Middle Euphrates Cancer Center in Najaf Province -Iraq

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Abstract

Background: Breast cancer (BC) is the most prevalent cancer among women worldwide. The psychosocial consequences of illness among women with BC are so frequent that they result in depression and other psychological distress.

Objectives: The present study aims to estimate the prevalence of depression among BC patients and to identify the potential determinants.

Patients &Methods: An analytic cross-sectional study of patients with BC was carried out throughout the period from January 2016 to July 2016 at the Middle Euphrates Cancer Center in Najaf Province-Iraq. A purposive sample of 175 women with BC was selected from the outpatient clinic; patients were interviewed by a questionnaire which is specially prepared for this study and includes demographic data, clinical data, and Beck Depression Inventory (BDI_II).

Results: According to the results of BDI-II questionnaire, 65 patients (37.1%) were screened as having depression and 110 patients (62.9%) were considered normal. The mean score for depression ± SD is equal to 13.60 ±8.78. The data analysis has found that 12.0%, 21.7%, and 3.4% of respondents had borderline, moderate depression, and severe depression, respectively while the binary logistic regression analysis has shown that cases with inadequate income (P= 0.010, OR =2.52, 95% C.I = 1.28-5.08), and lower educational attainment (P= 0.031, OR = 2.34, 95% C.I = 1.07-4.90) were more likely to have depression.

Conclusion: it has been found that depression among women with BC is a considerable issue. Inadequate income and lower educational attainment can be independent risk factors for such a depression.

Keywords: Breast cancer, Beck Depression Inventory, Depression, Prevalence, Iraq.

Introduction

Breast cancer (BC) is the most prevalent cancer in women worldwide, estimated at nearly 2.3 million new cases in 2020. It accounts for about 11.7 % of all new cancer cases and 24.5 % of all cancers among women[1]. In Iraq, BC constitutes about 37.9% of the registered cancer cases, and it is the leading cause of death among 15.3% of women[2]. Often, women diagnosed with BC experience some psychological distress because of the burden of the disease, its treatment, and its consequences. As a result, this distress can negatively affect women's health, wellbeing, and social functioning[3]. Psychological distresses are common in women with BC, but they are often overlooked and undertreated, despite their effect on daily life functioning[4]. The main reason is that depression symptoms like pain, fatigue, and weight loss, are often considered normal and expected side-effects of treatment[5]. Many BC patients experience depression, fatigue, and/or anxiety months to years after their diagnosis; these psychological symptoms are often related to greater disability and a lower quality of life[6]. Patients with cancer are predisposed to psychological morbidity for different reasons, including metabolic or endocrine changes, debilitating chemotherapy regimens, immune response modifiers, and cancer-related chronic pain[7]. Furthermore, feelings of change in their family or work roles, and loss of control over life events have an impact on the patient's sexuality, femininity, and body image, in addition to maternal issues following mastectomy[8].

A wide variety of risk factors for depression or higher depressive symptoms in BC have been reported. These include age, educational status[9], cancer severity[10], type of treatment[9,11], pain[10], time since diagnosis, physical activity[12], diet, menopausal symptoms/status [11], physical functioning/symptoms[10,11], social functioning[10], self-esteem[9], and psychiatric history[10].

Earlier studies found a high prevalence of psychological distress among BC patients, and they are highly vulnerable to developing severe anxiety, depression, and potential mood disorders[13-15]. Among BC survivors, a systematic review of sixty studies has shown a high prevalence of depression that ranges from 30-50% [16]. Unfortunately, to the researcher's best knowledge, no sufficient published data on depression among BC patients in Najaf city or other Iraqi cities are available; therefore, this study was carried out to identify the frequency of depression and some possible sociodemographic risk factors for depression in women with BC.

Patients & Methods:

An analytic cross-sectional study of patients with BC was carried out throughout the period from 1st of January 2016 to 1st of July 2016 at Middle Euphrates Cancer Center in Najaf Province.

A purposive sample of 175 women selected from the outpatient clinic. During the period of data collection, all attended women with BC, and who accepted to participate in this study were included. A data collection process was conducted for 2 days per week during the period of the study; the time needed to fill the questionnaire was nearly 20 minutes. Eligibility criteria included all BC women aged 18 years and above, and were having the ability to understand and answer the interviewer's questions. Yet, the exclusion criteria include any patient who had a history of chronic disease (like diabetes mellitus and hypertension), or any previous history of psychiatric illness or substance abuse.

The sample size was measured according to the following formula: [Z2P(1–P)/d2], regarding the prevalence 21% from a previous study [19], 90% confidence interval, and 5% border of error (d).

The data was collected by interviewing the patients by using a questionnaire specially prepared for this study; it includes three parts: first; demographic data consisting of age, residence, income employment status, educational status, and marital status. Second, data on the clinical status of the patient such as time since diagnosis of BC, menopausal status, stage of disease, type of treatment, and surgery they received. The third part was the Arabic version of Beck Depression Scale (BDI-II questionnaire) [17], which consists of 21 multiple choice questions measuring the mood of the participants for the previous 2 weeks. The scores obtained from each question range from (0-3), the total score is calculated and it measures the presence and severity of cognitive and somatic symptoms of depression on a scale (from 0-63). A score of 0-16 is considered normal, 17-20 borderline clinical depression, 21-30 moderate depression, 31-40 severe depression, and over 40 is extreme depression [18].

A pilot study was carried out on a purposive sample selected from patients attending the outpatient clinic, but they were not included in the final sample of the study. The purposes of the pilot study were to have an idea about the time needed for the interview to collect the required data, and to find out if there are any difficulties and unclear questions in the Arabic version of the BDI-II.

An approval from the ethical committee of Faculty of the Medicine/University of Kufa was taken for performing this study. A verbal consent was obtained from all the participants after the explanation of the objectives of the study; they were informed that they could withdraw from this study at any time. Meanwhile, confidentiality and privacy of all collected data were preserved.

Statistical Package for Social Sciences (SPSS) version 20 was used for data analysis. To describe the demographic data, clinical data and depression status of the participants, standard deviation (SD), mean, percentage, and frequency were used. Sociodemographic and clinical features of patients were regarded as independent variables, whereas dependent variables are the presence or absence of depression. Univariate analyses between two groups were done by Chi-square test. A binary logistic regression was used for multivariable analysis to control for possible confounders. A P-value equal to or less than 0.05 was considered statistically significant.

Results

The sample included 175 women with BC; the majority of cases aged between 45 to 64 years represented (57.1%) followed by the age group 25 to 44 years representing (28%). Their mean age ± SD was 50.42 ± 12.38 years. The majority of responders were living in Najaf representing 71.4%, and the remaining were from other provinces. More than three-quarters of the women in this study were housewives (84.0%), and the rest were employers. About 50.9% of the studied samples had inadequate incomes. Women with an educational level less than or equal to six years constituted 65.7% of cases. About two-thirds of the participant women (65.7%) were married (Table1).

Table 2 below shows that menopausal women constituted most of the cases (73.3%). According to the clinical staging of BC, the frequencies were 27.4%, 41.7%, 17.1%, and 13.7% for stages I, II, III, and IV respectively. The time since diagnosis for most of the cases (63.4%)

was less than one year. The distribution of patients concerning the type of treatment showed that more than one-third (41.7%) of cases had surgery along with chemotherapy, 34.9% of cases underwent surgery with chemotherapy and radiotherapy. Regarding the type of surgery that was performed, more than two-thirds of cases 71.4% had modified radical mastectomy (MRM).

According to the results of the BDI-II questionnaire, 65(37.1%) were screened as having depression and 110(62.9%) were considered normal. The data analysis has found that 12.0% of the respondents had a borderline depression, 21.7% had a moderate depression, and only 3.4% of cases had a severe depression (see Table 3 below).

Tables 4 & 5 show that depression is significantly associated with inadequate income (P< 0.001), lower years of education (P= 0.001), menopausal state (P= 0.031), and type of treatment (P= 0.015). Further sociodemographic and clinical characteristics were not significantly associated with depression(P>0.05).

Discussion

The current study was carried out among 175 women diagnosed with BC; the prevalence of depression was 37.1%. This is consistent with findings of other studies which showed a prevalence of depression ranging from 21% to 50% [9,19-22]. A systematic review of observational studies from different countries showed that the global prevalence of depression in BC cases was 32.2%. Furthermore, depression was higher in the middle east region, and middle-income countries in comparison to developed countries[13]. However, this finding is lower than a descriptive cross-sectional study conducted in the north of Iraq which found a higher prevalence of depression equal to 60.4% by using Hospital Anxiety and Depression Scale (HADS) standardized questionnaires[23].

Currently, the mean(SD) of BDI- II score is 13.59(8.78), borderline, moderate, and severe depression are prevalent in 12.0%, 21.7%, and 3.4%, respectively. Consistently, Casavilca-Zambrano S et al. reported that mild, moderate, and severe depression are prevalent among 16.9%, 6.3%, and 2.4% of BC patients[24]. A higher result was reported by a study conducted in Kazakhstan in which the mean(SD) score of the BDI-II questionnaire was 22.34 (9.65%). Meanwhile, the prevalence of moderate, and severe depression among women with BC was 46% and 31%, respectively[25]. This incompatibility in results could be explained by the differences in the sociodemographic and clinical characteristics of the studied populations, in addition to differences in case definition, screening tools, and design of the study.

Concerning the sociodemographic factors, the results showed no significant association between depression in BC cases and residence, employment status, and marital status. However, Casavilca-Zambrano S and his coworkers found that being employed or married significantly decreased the likelihood of depression among Peruvian women with BC[24]. Another study reported that patients who were unemployed or retired had a significantly higher risk of developing depression symptoms than those who were employed[25], in contrast with a case-control study that found no significant differences in depression concerning employment status[26].

Table 1: Distribution frequency of the study sample by socio-demographic variables

Socio-demographic variables	N (175)	%
Age group (years)		
25-44	49	28.0
45-64	100	57.1
≥65	26	14.9
Mean=50.42, SD±12.38, Min= 25 years, Max=83 years		
Residence		
Al-Najaf	125	71.4
Other governorates	50	28.6
Employment status		
Employed	28	16.0
Housewife	147	84.0
Income		
Inadequate	89	50.9
Adequate	86	49.1
Years of education		
≤ 6 years	115	65.7
> 6 years	60	34.3
Marital status		
Married	115	65.7
Divorced	12	6.9
Widowed	32	18.3
Single	16	9.1
Number of children		
0	38	21.7
1-2	28	16.0
3-4	33	18.9
>5	76	43.4

Table2: Distribution frequency of the study sample by clinical variables

Clinical variables	N (175)	%
Menopausal state		
Menopause	129	73.7
Non-menopause	46	26.3
Stage of BC		
I	48	27.4
II	73	41.7
III	30	17.1
IV	24	13.7
Duration since diagnosis (years)		
< 1 year	111	63.4
≥ 1 year	64	36.6
Type of treatment		
Surgery	13	7.4
Surgery + chemotherapy	73	41.7
Surgery + chemotherapy + radiotherapy	61	34.9
Radiotherapy+ chemotherapy	9	5.1
Chemotherapy	19	10.9
Type of surgery		
Breast conservative surgery	42	28.6
Modified radical mastectomy	105	71.4

Table 3: Distribution of women with BC according to depression level as per Beck depression score

Level of depression	Score of depression	Frequency	Percentage
No depression	0-16	110	62.9
Borderline depression	17-20	21	12.0
Moderate depression	20-30	38	21.7
Severe depression	31-40	6	3.4
Mean score =13.60 (SD=8.78), minimum score =0, maximum score =36			

Table 4: Distribution of the study group by depression and selected socio-demographic variables

socio-demographic variables	Presence of Depression (N=110)		Absence of Depression (N=65)		Total (N=175)		X^2	P
	No	%	No	%	N0	%		
Age groups (years)								
25-44	15	30.6	34	69.4	49	100.0	4.058	0.131
45-64	36	36.0	64	64.0	100	100.0		
>65	14	53.8	12	46.2	26	100.0		
Residence								
Al-Najaf	45	36.0	80	64.0	125	100.0	0.245	0.621
Other governorates	20	40.0	30	60.0	50	100.0		
Employment								
Employed	8	28.6	20	71.4	28	100.0	1.049	0.306
Housewife	57	38.8	90	61.2	147	100.0		
Income								
Inadequate	45	50.6	44	49.4	89	100.0	13.968	0.000*
Adequate	20	23.3	66	76.7	86	100.0		
Years of education								
≤6 years	53	46.1	62	53.9	115	100.0	11.493	0.001*
>6 years	12	20.0	48	80.0	60	100.0		
Marital status								
Married	41	35.7	74	64.3	115	100.0	2.568	0.463
Divorced	6	50.0	6	50.0	12	100.0		
Widow	14	43.8	18	56.2	32	100.0		
Single	4	25.0	12	75.0	16	100.0		
Number of children								
0	12	31.6	26	68.4	38	100.0	1.535	0.674
1-2	10	35.7	18	64.3	28	100.0		
3-4	11	33.3	22	66.7	33	100.0		
≥5	32	42.1	44	57.9	76	100.0		

* significant of $p<0.01$

Table 5: Distribution of the study group by depression and certain clinical variable

Clinical variable	Presence of Depression (N=110)		Absence of Depression (N=65)		Total (N=175)		X^2	P
	No	%	No	%	No	%		
Menopausal state								
Menopause	54	41.9	75	58.1	129	100.0	4.678	0.031*
Non menopause	11	23.9	35	76.1	46	100.0		
Stage of BC								
1	16	33.3	32	66.7	48	100.0	7.559	0.056
2	21	28.8	52	71.2	73	100.0		
3	16	53.3	14	46.7	30	100.0		
4	12	50.0	12	50.0	24	100.0		
Duration since diagnosis(years)								
<1 year	39	35.1	72	64.9	111	100.0	0.524	0.469
≥1 year	26	40.6	38	59.4	64	100.0		
Treatment								
Surgery	2	18.2	11	84.6	13	100.0	12.295	0.015*
Surgery + chemo	32	43.8	41	56.2	73	100.0		
Surgery +chemo+radio	19	31.1	42	68.9	61	100.0		
Radio +chemo	7	77.8	2	22.2	9	100.0		
chemotherapy	5	26.3	14	73.7	19	100.0		
Type of surgery								
BCS	16	38.1	26	61.9	42	100.0	0.012	0.914
MRM	39	37.1	66	62.9	105	100.0		

* significant of p<0.05

Table 6: Binary logistic regression for factors associated with depression.

Variables	p-value	Odd ratio (OR)	95% Confidence interval	
			Lower	Upper
Constant	0.688	1.56		
Income	0.010*	2.52	1.25	5.08
Years of education	0.031*	2.34	1.07	4.90
Menopausal state	0.062	0.46	0.20	1.04
Type of treatment	0.397	0.91	0.73	1.14

* significant of p<0.05

Results of different studies found that the patient's marital status was significantly related to depression among women diagnosed with BC [25,27,28]. On the contrary, other studies reported a non-significant relationship between marital status with depression in BC patients[24,26]. This could be due to the sociodemographic features of the studied sample where most of them (84.0%, & 65.7%) were house-wives and married respectively; so, the presence of such association cannot be studied obviously.

The present study has demonstrated no significant relationship between having children and depression(P<0.05). However, earlier studies about having children as a risk factor for depression were contradictory with significant[14] as well as non-significant relationships had been reported[25,26].

Further statistical analysis using logistic regression revealed that those with inadequate income and lower educational years were independently significant predictors of depression. Numerous studies have found that a lower educational level was significantly associated with depression[26,28-30]; this agrees with the present result where patients with higher educational levels may have a greater chance of understanding their disease and its implications, in contrast to patients with lower educational attainment who have difficulty in getting enough information about the disease process, and its management. Hence, they have difficulty in understanding complex information and making decisions.

Regarding the income of the patients, financial status plays an influential role in the course of cancer treatments. Many studies showed that depression is associated with lower income/poor financial status[14,25-27], which is in line with the current finding. This could be attributed to the cost of transportation and the high cost of cancer management. Therefore, most of the patients felt burdened by treatment, and some required investigations, especially based on their economic status. If this feeling is not being treated, it could lead to psychiatric morbidity. Additionally, incomes and educational levels are found to be related to the quality of life and self-esteem among BC survivors[27], therefore both factors adversely affect the psychological status of BC patients.

Similar to earlier findings [28,26], this study has reported that menopausal status and the type of treatment are not significant predictors for depression, although a previous study reported that menopausal status and type of treatment were regarded as risk factors for depression [23].

Other clinical variables including cancer staging, duration since diagnosis, and type of surgery were found to be not significantly related to depression. Only a few researchers have suggested that cancer stage[14,25], time since diagnosis of cancer [14,31], and type of surgery[23] are risk factors for depression. However, the current findings are compatible with the majority of previous studies [26,32-34] that have failed to find such relationships.

There were two limitations to this study, firstly; since it is a cross-sectional study, casual relationships cannot be established. Secondly; the study is conducted in a single facility which is the outpatient clinic. Consequently, the depressive status of BC women elsewhere cannot be determined.

Conclusion

Depression among BC patients is a significant problem. Moderate depression is the commonest type among depressed patients. The identified independent risk factors for depression are inadequate income and lower educational attainment. So, it is highly recommended to enhance health care professionals to pay more attention to the psychosocial aspect of BC patients, with special attention to those with low income, and lower educational years. Monitoring psychological distress in patients with BC routinely can be made by using a quick, simple, and reliable self-administered questionnaire and ensure referring those screened positive for depression for further psychiatric support.

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Systemic Lupus Erythematosus with Initial Manifestation as Enlargement in Cervical, Axillary and Inguinal Lymphnodes: A Case Report

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Abstract

Systemic lupus erythematosus (SLE) is a chronic inflammatory disease that affects the nervous system, lungs, kidneys, joints, and other parts of the body. Changes in the distinctive characteristics and size of the lymph nodes help to identify lymphadenopathy. This is caused by a secondary reticuloendothelial proliferation in infection, malignancies, and inflammation. According to reports, 25–67% of SLE patients experience enlargement of the lymph node. Here, a thirty-three-year patient presented with lymph nodes enlargement in cervical, axillary, and inguinal regions, in addition to joint pain, renal involvement, and respiratory involvement is reported. The patient was diagnosed as Systemic lupus erythematosus according to ACR/ EULAR criteria , immunological and clinical domain SLICC (systemic lupus international collaborating clinics. In conclusion, lymphadenopathy was characterized as one of the manifestations of SLE. It might take years for the diagnosis of SLE to be made, as the instance given here demonstrates. It is possible that lymph node proliferative factors are also responsible for the development of autoantibodies.

Keywords: systemic lupus erythematous, lymphadenopathy.

Introduction

A chronic inflammatory condition called systemic lupus erythematosus (SLE) that affects the nervous system, lungs, kidneys, joints, and other parts of the body. Reports state that 25–67% of SLE patients had enlarged lymph nodes [1-3]. However, SLE rarely causes an enlargement in the mediastinal and hilar lymph nodes [4].

Rarely SLE presents with lymph nodes in the neck. The American Rheumatology Criteria do not list lymphadenopathy as a criterion; however, some case documents in the literature describe generalized or localized lymphadenopathy as the initial sign of the illness [5,6]. Modifications in the distinctive characteristics and size of the lymph nodes help to recognize lymphadenopathy. This is caused by

secondary reticuloendothelial proliferation in infection, malignancies, and inflammation. It is a benign sign that can appear at any stage of systemic lupus erythematosus illness [7-9].

A patient presented with lymph nodes enlargement in cervical ,axillary and inguinal regios, in addition to joint pain, renal involvement, and respiratory involvement is reported; she was diagnosed as an SLE according to ACR/EULAR criteria immunological and clinical domain SLICC (systemic lupus international collaborating clinics).

Case Report:

A 33 years old female patient from Kurdistan-Iraq presented in November 2020. The case started when she was pregnant on 24 weeks of gestation; she had joint pain in both hands, wrists, elbows, and knees with night pain, morning stiffness of more than 30 minutes with fever intermittent low grade. On 37 weeks of her pregnancy she developed recurrent episodes of lymphadenopathy, hepatomegaly, and fever; she delivered a a live baby on her 38 weeks by normal vaginal delivery at the hospital.

In February 2021, 2 days post-partum, the patient developed anasarca, a generalized body oedema, productive cough with dyspnea mostly on exertion. Since that time, she developed arthritis in small joints of the hand, wrist, elbow, and knee with painful movement; she had hair loss, painless oral ulceration, with photosensitivity; at that time, she was admitted to the hematology ward with a fever, lymphadenopathy, ascites, and generalized edema.

After a referral from internist suspicion of lymphoma, biopsy of lymph node were done which reveal activation of lymph node due to rheumatic disease. The hematologist refers the patient to rheumatology and she was really admitted in the rheumatology department, after assessing her vital signs checking: 130/85 mm Hg was her blood pressure, temperature was 38 °C, PR 100 bpm,SPO2 94% on room air, patient pale with bilateral leg oedema and ascites. There are enlarged lymphnodes in the inguinal, axillary, and cervical regions, their size ranging from one centimeter or more than one centimeters, investigations show hemoglobin was 9.1 g/dl, (11.5-16.5),WBC 9.7(4.5-10.0/L), PLT:48(130-400 per microliter). A rheumatoid factor was negative, CRP (C reactive protein):117.5 mg/l(5), ESR :118 mm/hr, albumin:2.14 low ,LDH 538 high, chest-ray show mild left lower lung plural effusion, ECHO : ejection fraction 70% , trace pericardial effusion size (0.5 cm).

Infection from other sites of the body were excluded by sending to blood investigations, general urine examination, and blood culture.

The ultrasound of abdomen shows hepatomegaly 20 cm with moderate to severe amount of ascites, her ANA 14.6 + (N: less than 0.8), Anti- double strand DNA positive 44.5 (less than 25), lupus anticoagulant 47 positive, anticardiolipin negative, C3; 52 low (90-180 mg/l),C4: 8 (10-40 mg/l). Two days later, she develop oliguria with urea : 161 mg/dl high (15-45), creatinine: 2.5 protein in urine +++ ,granular cast 2-4 in urine ,and 24 hour urine collection was 375, albumin creatinine ratio elevated, according to 2019 CR/EULAR criteria, diagnosed as an SLE with nephrotic lupus nephritis. Renal biopsy was not done for the paitient because when patient develop proteinuria and lupus nephritis, she was tired and her condition did not tolerate biopsy.

The patient received hydroxychloroquine tab 200 mg by 2, IV methylprednisolone 1g for 3 days, with IV cyclophosphamide 1g. Diagnostic and therapeutic

aspiration of ascites was done, the result of ascites fluid examinationwas exudative Sag ratio less than 1.1.

After a week of follow-up, her ESR became 24, CRP: 16 decreased, creatinine normalize, protein in urine become 1 plus. After 30 days of remaining in hospital, her ascites fluid starts to decrease and just small amount remains. Her edema subsides and weight at the first day of admission was 78 kg; now it became 60 kg after subsiding body edema, good urine output, stable vital sings.

Two days later, she develop ARDS (acute respiratory distress syndrome) admitted to RCU (Respiratory Care Unit). On examination, she was tired; hypoxic (SPO2 80 without Oxygen), chest was full of crepitation, her CRP reach to 117, PCR by nasopharyngeal swab for COVID-19 was negative, chest x ray show feature of chest infection and pulmonary hemorrhage and intubated for 10 days, she received treatment (covered with steroid IV, three antibiotic's IV with daily follow-up of vital signs later her chest start to improve (and follow up x ray became better and extubated).

After 48 days in the hosiptal, the patient improved and discharged home on treatment prednisone tab started by 40 mg with tapering, Vit D tablet, hydroxychloroquine tab 200 mg by 2 ,with iv cyclophosphamide 1g for 6 cycle every month.

Discussion:

Fever with cervical lymphadenopathy are the first presentation of various diseases. For example, common causes include tuberculous lymphadenitis, lymphoma, and even rheumatic diseases, for instance SLE and sarcoidosis. A comprehensive physical examination and collection of a full medical history should allow for a more accurate assessment of each patient. Evidence of infection or immunological disorder can be found by laboratory testing. The gold standard investigation is an excisional biopsy to distinguish malignant from benign association with inflammatory disease [10].

Multiple organs are affected by SLE, an autoimmune condition. Women are affected more than men. Four or more of the eleven American College of Rheumatology (ACR) criteria must exist to diagnose SLE [11]. The ACR criteria are not involved and do not include Lymphadenopathy. According to an investigation by Shapira et al. [12], out of 90 patients with SLE only 23 had lymphadenopathy; it was also observed that those patients had more systemic symptoms.

The estimated prevalence for lupus lymphadenopathy (LL) ranges from 5-7% at the illness beginning to 12-15% at the disease stage [13]. LL mainly affects the axillary and cervical areas. The lymph nodes are mobile, soft, tender, and not attached to deep planes [2]. Lymph node biopsy is advised to rule out lymphoproliferative or infectious diseases if there is severe lymphadenopathy [1-3]. There are two different categories of LL: focal: involving two chains of lymph nodes, and general, three or more [14].

Generalized lymphadenopathy was a frequent early symptom of SLE in children, according to research by Kitsanou et al [15]. Regional or systemic lymphadenopathy is included as a symptom in much older English literature on SLE [16,17].

In conclusion, lymphadenopathy was characterized as one of the manifestations of SLE. It might take years for the diagnosis of SLE to be made, as the instance given here demonstrates; It is possible that lymph node proliferative factors are also responsible for the development of autoantibodies.

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The patient has given her consent for information to be reported in the journal.

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The Relationship between Knowledge and Practice in Clinical Breast Examination among Women in Baghdad, Iraq

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Abstract

Background: Breast cancer is the most commonly worldwide diagnosed cancer in women. Regular screening can help in early detection and hence reduction in the mortality of breast cancer.

Aim: This study aims to determine both the level of knowledge, attitude, and practice in clinical breast examination in women and the relationship between knowledge and practice.

Subjects and Method: A cross-sectional analytical study included 657 non-randomly selected women visiting primary health care centers in Baghdad city with an average of age between (20-59) years old. Data collection was performed within a three-month period starting from February 2019 on. A designed questionnaire was adopted and filled out through direct face-to-face interviews.

Results: Only 51.8% ever heard of clinical breast examination. The mean knowledge score for clinical breast examination was (51.2±44). Only 5.5% of women performed regular clinical breast examinations. Participants who adequately practice clinical breast examination had a statistically significance higher mean score of knowledge than those without adequate clinical breast examination (100 vs 44.2), (P<0.001).

Conclusion: The study has concluded that practices of clinical breast examination were inadequate in the majority of participants and need to be improved by educational programs.

Keywords: Breast cancer, Clinical Breast Examination, Knowledge, Practice, Iraq.

Introduction

Breast cancer (BC) is the most common cancer in women in both developed and developing areas [1]. It represents 30% of all incident cancer cases among women over the world [2] .

A total of 1,783 BC deaths were reported in Iraq, accounting for 1.22% of all deaths. The age-adjusted death rate is 15.07 per 100,000 populations, ranking Iraq number 115 in the world, according to the latest data published by World Health Organization (WHO) in 2020 [3]. In developing countries, high death rates are due to the lack of early detection programs, resulting in many women presenting with late stages of BC, in addition to a scarcity of adequate diagnosis and treatment services [4]. The chance of survival increases by early detection and early treatment of BC. Early detection of BC includes Breast Self-examination (BSE), Clinical Breast Examination (CBE), and mammography. For early detection of BC, the American Cancer Society (ACS) recommends CBE and mammography. Although CBE is a relatively simple and inexpensive method, the effectiveness of CBE in reducing BC mortality has not been directly tested in randomized trials [5]. To reduce the risk of BC, it is important to be aware of the symptoms and to undergo early detection [6]. Over the past few decades, BC survival rates in the 'Western' world have increased significantly due to improved health-seeking behavior by women, access to diagnostic facilities, and well-organized population-based screening programs, in addition to the stage-appropriate treatment of cancer [7].

Previous studies were performed in different places of the world including Iraq to assess the level of knowledge and the practice of women in early detection procedures, especially for BSE [8-10]. One of these studies was conducted among women in Mosul in Iraq which found that only 9.6% of them practiced CBE [8]. To the researchers best knowledge, few or no published articles in Iraq study the knowledge, attitudes, and practice regarding CBE. So, indirect evidence suggested by eleven systematic reviews published in the last three decades clarified that a well-performed CBE is as effective as mammography regarding mortality despite CBE's apparent lower sensitivity (40–69% vs 77–95%). Greater sensitivity was found among Asian and younger women. Furthermore, CBE contributed to the shift of diagnosis from advanced to early-stage cancer in about 17 to 47% of cases [11]. Hence, this study is expected to enable healthcare professionals and planners to modify, emphasize, strengthen, and select the best and most effective health education programs and breast awareness campaigns.

Subjects and Methods

Study Design and Setting: A cross-sectional analytical study was performed in six primary health care centers (PHCCs) in Baghdad city. These PHCCs were providing early detection programs to all attendant women, including physical breast examinations, in addition to increasing awareness about breast self-examination. To be engage in this program, all doctors and nursing staff were involved and taught properly. Data collection was completed over three months starting in February 2019 .

Study Population: A purposive sample included women between 20 to 60 years old and visiting PHCCs in Baghdad city for different reasons other than breast problems and those presenting with any acute problem during the period of the study. Women with a family history of BC (first-degree relatives) and those with past

or present breast problems requiring medical care were excluded from the study.

Sample Size and Sampling Method: The sample size was calculated according to the cross-sectional survey formula [12]; the final sample size was 667 after being multiplied by 2 and adding (15%) non-response rate. The prevalence of BC screening practices used in this formula was 28% according to a recent study conducted in the Kingdom of Saudi Arabia (KSA) [13].

Participants were selected by using a non-probability purposive sampling procedure in each PHCC. The study aim was explained to all women attending the center consecutively with inclusion criteria, and their verbal consent to participate was obtained. Participants were directly interviewed either while waiting for a doctor to see them or afterward.

Data Collection Tool: An interview was done by using a structured questionnaire developed from a previous similar study [14,15] and designed for the purpose of the current study and adapted to best suit the Iraqi community. It was translated from English to Arabic, tested for validity by two expert professionals, and then its reliability was tested by a pilot study. It was divided into two major parts: the first includes socio-demographic characteristics like age, educational level, and employment while the second includes knowledge, practice, and attitudes towards CBE .

Variables: knowledge of CBE was evaluated by three items; each measures knowledge and correctly identifies 1 score; any incorrect answer was scored zero. The scores of knowledge items were summed and then multiplied by 100 divided by the total count of items to yield a knowledge score. Attitude regarding CBE was measured on an ordinal scale using “Likert Type” scale of 5 grades from 1 (strongly disagree) to 5 (strongly agree). The practice was either adequate or not according to National Comprehensive Cancer Network guidelines for average-risk, asymptomatic women [16]. The criteria of adequate practices for CBE, are for every 3 years for women of 20-39 years, while annual CBE starts from age of 40. Women who adequately practiced CBE scored 100 whereas those who were inadequately practiced CBE scored zero.

Ethical Consideration: Before the study, official approval from the University of Kufa and the Faculty of Medicine was obtained. Participants verbally consented to participate in the study after an explanation of the rationale for the study and their freedom to refuse to answer any question and leave at any time.

Statistical Analysis: A computer-aided data analysis was performed by using SPSS version 26. frequencies and percentages were used to represent nominal and ordinal variables, while means and standard deviations were used to represent quantitative variables. Chi-square tests were used to assess associations between categorical variables. Statistical significance of the difference in mean for quantitative variables was assessed using independent samples t-tests. P values less than or equal to 0.05 were considered statistically significant.

Results:

Out of those 667 eligible women, only 10 (1.5%) were not responding, with a response rate of (98.5%). The mean age was of (37.6±11.3) years. Regarding educational attainment, (22.8%) of the participants were illiterate while (20.2%) of them were with university and higher educational attainment. All other educational levels were below the above two levels in percent. The majority of respondents (71.1%) never worked outside

home (housewives), and none of them were part-time workers or students.

Table 1 shows that nearly half of the sample was ever heard of CBE. Ever heard of CBE was significantly associated with selected socio-demographic variables except for age which had no significant association. Higher education and higher social class were mostly associated with ever heard of CBE.

Table 2 found that all those who heard about CBE knew that it is done by doctors or nurses. 87.9% and 85.9% respectively knew the correct starting age of CBE and that CBE should be part of the routine medical checkup for women. Specific attitude items related to CBE showed that 90% of them believed that CBE is useful in detecting cancer early. 4.4% felt comfortable when obtaining it. The majority felt embarrassed to obtain a CBE. Mean knowledge and attitude scores for CBE of the study subjects were also mentioned in table 2.

In table 3, around three-quarters of the study subjects never practiced CBE throughout their lives. Only 5.5% of respondent women in this study adequately practiced CBE according to the recommendation.

Women who adequately practiced CBE had a higher mean knowledge score than those without adequate CBE practice (100 vs 44.2), the difference in mean score of the knowledge was highly significant (P<0.001) as demonstrated in table 4.

Table 1: Frequency distribution of ever heard of CBE according to socio-demographic variables of 657 selected women.

Socio-demographic variables	Ever heard of CBE				Total		P value
	Yes		No				
Age in years(Mean ± SD)	37.5±12.4		37.6±10		37.5±11.3		0.85 [NS] (t-test)
Categorical variables	**No.**	**%**	**No.**	**%**	**No.**	**%**	
Educational levels							<0.001
No formal education	25	(16.7)	125	(83.3)	150	(100.0)	(Chi-square)
Primary school	40	(32.0)	85	(68.0)	125	(100.0)	
Intermediate school	46	(36.8)	79	(63.2)	125	(100.0)	
Secondary school	112	(90.3)	12	(9.7)	124	(100.0)	
University/higher degree	117	(88.0)	16	(12.0)	133	(100.0)	
Employment status							0.007
Never worked	225	(48.2)	242	(51.8)	467	(100.0)	(Chi-square)
Was employed but not now	15	(50.0)	15	(50.0)	30	(100.0)	
Full–time employee	100	(62.5)	60	(37.5)	160	(100.0)	
Social classes							<0.001
High social class	166	(73.1)	61	(26.9)	227	(100.0)	(Chi-square)
Middle high class	34	(33.3)	68	(66.7)	102	(100.0)	
Middle low class	90	(42.5)	122	(57.5)	212	(100.0)	
Low social class	50	(43.1)	66	(56.9)	116	(100.0)	
Total	340	(51.8)	317	(48.2)	657	(100.0)	

CBE: clinical breast examination; SD: Standard Deviation

Table 2: Frequency distribution of positive knowledge and attitude items for CBE among 340 women who ever heard about CBE.

Positive knowledge items for Clinical Breast Examination	No.	%
CBE is the examination of the breast done by a doctor or a nurse	340	100.0
CBE should be started at an early age (20 years)	299	87.9
CBE should be part of the routine medical checkup for women	292	85.9
Knowledge score	Mean (SD) 47.2 (48.0)	Range (0 - 100)
Attitude items for Clinical Breast Examination	**No.**	**%**
Feeling embarrassed to obtain a CBE	320	94.1
Feeling comfortable when obtaining a CBE	15	4.4
Believe that CBE is useful in detecting cancer early	306	90.0
Attitude score	Mean (SD) 34.8 (34.3)	Range (0 - 95)

Table 3: Frequency distribution of CBE practice among 657 women.

Frequency of having Clinical Breast Examination	No.	%
Never	484	73.7
Less frequent than once per 5 years	15	2.3
At least once every 5 years	117	17.8
At least once in three years	11	1.7
At least once a year	30	4.6
Adequacy of practicing clinical breast examination		
Adequate**	36	5.5
Not adequate	621	94.5

**Every 3 years for women (20-39) years, an annual examination for women 40 years and older.

Table 4: Comparison of the mean knowledge score of CBE between those who adequately practiced it and those who did not.

Knowledge score for CBE*	Practice of CBE		P (t-test)
	Not adequate	Adequate**	
Mean	44.2	100	<0.001
SD	47.6	0	
N	621	36	

*Clinical Breast Examination.

**Every 3 years for age (20-39), and yearly afterward.

Discussion:

BC is the most frequently diagnosed cancer in women. Meanwhile, early diagnosis and management is a fundamental step for increasing survival and improving the quality of life. Therefore; this study aims to evaluate the knowledge, attitudes, and practices of CBE among women. Although BSE and mammography had been investigated in Iraq, there is limited research on CBE.

BC is the most frequent cancer in women. Even though, about half of the responders reported that they had ever heard about CBE, the majority never practiced it in their lives, and only 5.5 % of respondents adequately performed CBE. However, this rate of practice is considered good concerning previous studies done in Iraq [17].

Regardless of the frequency of practicing CBE, a study in Vietnam showed that 51 % of the sample ever practiced it [18] while 19.8% of women attending PHCCS in Najran, Saudi Arabia, visit their doctors for this examination[14]. There were 28.7% of Jordanian women who mention performing CBE otherwise [19]. Another study conducted among Saudi women found that 8.8% of eligible women performed CBE on a regular annual basis [13]. The low practice of BC screening may explain the late diagnosis and thereby high mortality rate of BC among Iraqi women [3]. This low rate of practice can be related to the low knowledge and attitude levels related to this screening behavior.

Although women in this study had a mean knowledge score of (47.2±48) for CBE, those women with adequate practice had a (100) mean knowledge score. The adequate practice of CBE was positively associated with knowledge of CBE. The fact that being knowledgeable about CBE was significantly associated with CBE adequate practice emphasizes the importance of increasing knowledge level to increase regular practice. Previous studies found that there was a significant association between knowledge about BC and adopting preventive practices [20,21]. Others found no significant effect of knowledge on the adequate practicing of CBE [22,23]. In addition, lack of knowledge about screening is the major barrier to increasing screening. These results support the importance of women's education about methods for early detection of BC and it is essential to disseminate the information in an easily understandable way. It was obvious that the majority of the study subjects were embarrassed about practicing CBE even though they believed in its benefit, because of the sensitive nature of the Iraqi community and their religious beliefs. This might be one of the reasons for inadequate practice in this study. Nevertheless, this study showed a limitation regarding the examination of only one item regarding barriers to CBE. Therefore, interventions for Iraqi women should highlight the benefits of CBE (i.e., early diagnosis of BC, increasing survival). On the other hand, barrier identification is a very important issue in intervention strategy.

Limitations:

There were some limitations in the current research. Firstly, the results of the present study were based on responses of present PHCCs attendant women in Baghdad. So the findings cannot be generalized to all women. Secondly, informational bias may have existed in that the knowledge, attitudes, and behaviors stated by the participants (recall bias); this could affect the precision of the data concerning their ability to recall previous events, behaviors, and expenses.

Conclusions and Recommendations.

The high incidence rate, the young age, and the late stage at presentation all made BC a health priority in Iraq.

The majority of women in the current study were not well informed on pertinent issues surrounding CBE. In addition, the majority were with inadequate practices. A positive relationship between knowledge and practice indicates a good chance of a successful awareness program regarding early detection in the future. Educational programs are highly recommended for motivating women to adhere with clinical breast examinations as well as breast self-examination.

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The Effect of General Anesthesia Induction Drugs on Cardiac Output of Patients in Azadi Teaching Hospital/Duhok/Iraq

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Abstract

Background: Cardiac output can be decreased by many factors whose effects may be exaggerated during induction of anesthesia **(**which is already insulted to have negative effect on cardiac output) till the point of cardiac stand still.

Aims: This study aims to answer the questions that "Is there any effect of general anesthesia induction agents on cardiac output? If there is any, which patient is affected more?".

The Study Design: It is a cross sectional study with convenient sampling procedure. According to the inclusion criteria, it includes patients planning to perform surgical procedure under general anesthesia while it excludes patients who refused to participate in the study or their surgical procedures had been canceled for certain reasons.

Method and Patients: The study targeted a population from Duhok province and its territories; 207 patients, were admitted to Cardiac Center Operation theatres from 12/9/2021 to 30/10/2021 and Azadi Teaching Hospital operation theatres from 2/11/2021 to 15/1/2022. The data were collected pre operatively after taking a verbal consent as age, sex, weight, chronic diseases and duration of chronic diseases. Foreword by using echocardiography machine pre and post general anesthesia induction ejection fraction would be obtained. All this information would put in previously designed excel form. This data had been analyzed by Microsoft Excel Worksheet and transferred to SPSS V. 23**(**IBM). Descriptive statistics **(**central tendency) and proportions of uni-variant variables were calculated. Paired t test for sample mean difference and ANOVA test for more than two group means were applied to test the mean differences. A P value of < 0.05 considered statistically significant**.**

Results: For the age of patients the mean was 40 years with range 77 years, minimum 1 year, maximum 78 year and standard deviation 15.731 years, for weight the mean was 71kg with range 130 kg, minimum 7kg, maximum 137kg, and standard deviation17.210 kg, for pre general anesthesia induction anesthesia the mean was 0.6055 %with range 0.45%, minimum 0.35%, maximum 0.80%, and standard deviation 0.06587%, for post general anesthesia induction the mean was 0.5531% with range 0.54%, minimum 0.24%, maximum 0.78% and standard deviation 0.087485, for duration of chronic diseases out of 41 patients the mean was 1.47 years with range 26 years**,** maximum 26 years, and standard deviation 3.802 years fortunately 166**(**80%) of patients were without any chronic diseases. The post induction ejection fraction significantly differs with the pre operation ejection fraction for **(**207) patients received anesthesia in Duhok hospitals during 2021. The average means difference was of 0.04499 **(**95% confidence interval, 0.04499, 0.05984.69). This difference is statistically significant at a ≤ .05 by the paired ᴛ test **(**two-tailed). In this study, patients underwent induction of anesthesia had an average of .05242 **(**standard deviation, .00377) change in ejection fraction.

Key words: induction of general anesthesia, cardiac output.

Introduction

Cardiac output (CO) is the volume of blood pumped by the ventricles during one minute; this is the way through which all human body parts gain oxygen and nutrients and get rid of waste products. CO is the product of heart rate (HR) and stroke volume (SV). The heart will respond by modulating one or both of the HR and SV when the demand of body's parts for oxygen increases, as during exercise. This processes under the regulation of a complex cooperation of the autonomic nervous system, endocrine, and paracrine signaling pathways [1].

So, any cardiovascular dysfunction has the potential to result in significant morbidity and mortality. This functional impairment has a variety of methods to be assessed and in turn guides diagnosis, prognosis, and treatment [2,3,4,5,6].

General anesthesia is using anesthetic agents to induce unconsciousness, amnesia, analgesia and the loss of autonomic system reflexes with or without skeletal muscle relaxation [7].

The concentration of halogenated agents, including sevoflurane, desflurane, isoflurane, enflurane, and halothane, all decrease the MAP in a dose-dependent manner [8,9,10]. This effect can be explained by decrease in systemic vascular resistance (SVR) except for halothane which also decreases the MAP but by directly relaxing myocardium which in turn decreases the CO that leads to decreasing MAP in a direct relation with dose [9,10,11]. Sevoflurane has demonstrated less impact on cardiovascular dynamic parameters than desflurane and isoflurane, leading to reduced morbidity and mortality [8,28].

Some intravenous anesthetics may act by increasing the concentration of the inhibitory neurotransmitter γ-aminobutyric acid (GABA) in the central nervous system (CNS), like etomidate, midazolam, propofol and thiopental. Meanwhile, ketamine antagonizes the effect of the excitatory neurotransmitter N-methyl-D-aspartate (NMDA) on N-methyl-D-aspartate (NMDA) receptors, and opioid agonists stimulate opioid receptors. Propofol is highly hydrophobic and distributes rapidly into the CNS and other tissues, which accounts for its rapid onset of action and its wide use [12].

The reduction in the cardiac output caused by anesthetic agents can be partially preserved by an increase in HR in healthy individuals while the presence of comorbidities, aging and concurrent medication may inhibit this compensation, unmasking the reduction in cardiac output [13].

An echocardiography is the use of standard ultrasound or Doppler ultrasound to form a dynamic medical image of the heart [14]. The echocardiogram gives the physicians the privilege to estimate the systolic function by calculating the CO and ejection fraction, as well as the diastolic function. Therefore, it is of potential importance in following-up patients with heart failure and their treatments[15,16]. Using pulsed- or continuous-wave Doppler ultrasound and echocardiogram can produce an accurate assessment of the blood flowing through the valves of the heart. The Doppler echocardiography technique can also be used for tissue motion and velocity measurement [17].

There are several types of echocardiography, transthoracic echocardiography, stress echocardiography and transesophageal chocardiography. Transthoracic echo is the most common type of echocardiogram test as it is painless and noninvasive diagnostic tool that needs minimal training in image acquisition and interpretation to estimate global left ventricular (LV) function with reasonable accuracy. Bedsides, transthoracic echocardiography (TTE) is increasingly

used by intensivists and anesthesiologists for cardiac evaluation of hemodynamically unstable patients [18].

American college of cardiology **(**ACC)/ American heart association **(**AHA) guidelines as well as European society of cardiology **(**ESC) guidelines document echocardiography as the single most beneficial test for the diagnosis of heart dysfunction since the presence of structural abnormality, dysfunction in systole or diastole, or a combination of these abnormalities have to be document-ted to establish a definitive diagnosis in patients present with resting or/and exertional symptoms of heart failure [19,20].

Methodology:

This is a cross sectional prospective descriptive study with convenient sampling procedure. The included patients were those who plan to perform surgical procedure under general anesthesia and verbally agree to be examined by echocardiography while the excluded were those among the above but refused to participate in the study or their surgical procedure had been canceled for any reason. This study targeted Duhok Province and its territories population.

Resources were all at the researcher's expenses except two echocardiography machines: one had been supplied by the Azadi Teaching Hospital**/ C**oronary Care Unit and the other one by the Cardiac Center in the same hospital. The ejection fraction was calculated by M Mode which is consisting of putting the cardiac prop in left lateral parasternal long axis view and moving this prop to be as much as possible in perpendicular position on the left ventricular image then to freeze the picture to activate the measuring which had measured both end diastolic **(**EDV) and end systolic **(**ESV) volumes and finally the ejection fraction would be resulting from the ratio of EDV-ESV/EDV.

In this study, 207 patients had been examined in Azadi Teaching Hospital; they were planned to undergo different operations. The effect of general anesthesia induction drugs on the cardiac function was represented by ejection fraction in the duration from 12/9/2021 to 30/10/2021 in cardiac center operation theatres and from 2/11/2021 to 15/1/2022 in Azadi teaching hospital operation theatres. The patients' assessment was conducted in ratio of 3 - 4 operation theatres fumigation days a week including weekends and some occasionally vacant days. The everyday examination included at least four patients in the operation theatre complex and one patient in cardiac center. It procedurally begins checking the operations list first, selecting the patients who best fit in for the study regarding type of anesthesia that expected to be given, the type of surgery and its duration, age, their sequence in the list **(**preferred not to be the first), and finally examining the patients who are fit by echocardiography.
Firstly, the data of the patient would be collected individually before being examined by echocardiography but after verbal consent. The data include name, age, gender, weight, chronic disease, and the drugs used for these chronic diseases and the duration of chronic diseases. The data would be admitted in excel form at the same examining night. Secondly, the ejection fraction of selected patients will be preoperatively measured in the pre anesthesia room in supine with 30 degree tilting to the left by LV study and M Mode. The resulted ejection fraction would admit also in the above excel form. Thirdly, when patients is taken to operation room to perform the surgical procedure, the ejection fraction would be measured again 3 to 5 minutes after induction of general anesthesia and before starting the surgical procedure in order to exclude the effect of

the last on ejection fraction. Routinely the patients had been vitally monitored by electrocardiography, pulse oximetry, non-invasive blood pressure, temperature and end-tidal CO2. Meanwhile the drugs of general anesthesia induction would be documented in details and then transferred to the same excel form. The collected data would be analyzed by Microsoft Excel Worksheet and transferred to SPSS V. 23(IBM). Descriptive statistics (central tendency) and proportions of uni-variant variables were calculated. A paired t test, for sample, mean difference and ANOVA test for more than two group means were applied to test the mean differences. A P value of < 0.05 is considered statistically significant.

The data on the general anesthesia induction drugs used by doctor for the patients had been collected. Hence, if the patient had taken specific drug the study would write (Yes) but if s/he hadn't taken the same specific drug the study would write (No). Those general induction drug agents include Propofol, Midazolam, Narcotic meant both Fentanyl and Morphine, Muscle relaxant meant both Rocuronium and Atracurium, Inhalation meant both Isoflurane and sevoflurane. The percentage of these general anesthesia drugs had been listed in Table (2).

The preoperative assessment of ejection fraction was the cause behind the surgical intervention postponement as it was too low to tolerate the negative inotropic effect of general anesthesia induction for three patients, one of them in the Cardiac Center and to in the Azadi Teaching Hospital.

It is worth noting that all the patients were quite cooperative and highly satisfied with assessment. However, the major problem that faced in the study was that there was no echocardiographic machine specially belong to the operation theater; so, it was necessary to bring the one in the Coronary Care Unit in the second floor to the first floor where the operation theater complex existed whenever patients' data had to be collected.

Results:

The study has found the standard deviation, mean, minimum, maximum of age, weight, pre general anesthesia induction ejection fraction and post general anesthesia induction ejection fractions, and duration of chronic diseases for all the patients (n=207) as follows:

- For the age of patients, the mean was 40 years with range 77 years, minimum 1 year, maximum 78 year and standard deviation 15.731 years;
- for weight, the mean was 71kg with range 130 kg, minimum 7kg, maximum 137kg, and standard deviation17.210 kg;
- for pre general anesthesia induction anesthesia the mean was 0.6055 %with range 0.45%, minimum 0.35%, maximum 0.80%, and standard deviation 0.06587%;
- for post general anesthesia induction, the mean was 0.5531% with range 0.54%, minimum 0.24%, maximum 0.78% and standard deviation 0.087485;
- for duration of chronic diseases out of 41 patients the mean was 1.47 years with range 26 years, maximum 26 years, and standard deviation 3.802 years fortunately 166(80%) of patients were without any chronic diseases. (Table 1)

Accordingly, it could be noticed that, with the patients who took morphine and rocuronium, the ejection fraction (CO) of the patients decreased about (0.15) more than with those who took other drugs, after morphine and rocuronium. Yet, the decrease in the ejection fraction was of about (0.13) in the patients who took

ketamine combination with other drugs like propofol, midazolam, atracurium, isoflurane only in three patients; the combination with propofol, fentanyl, atracurium, sevoflurane in two patients**;** the combination of ketamine with propofol, midazolam, fentanyl, atracurium, isoflurane in eight patients; and the combination of ketamine with propofol, midazolam, fentanyl, atracurium, and sevoflurane in two patients. Meanwhile combination of ketamine with midazolam, fentanyl, rocuronium and isoflurane had increased the ejection fraction in three patients. With patients who took propofol and midazolam, the ejection fraction was decreasing about **(**0.10) but fentanyl and isoflurane decreased about **(**0.09) of the patients ejection fraction. With the patients who took atracurium the ejection fraction was decreased about (0.08) less than the other general anesthesia induction drugs, inhalation anesthesia like sevoflurane decreased ejection fraction about **(**0.11).

Inversely, the combination of propofol, midazolam, fentanyl and sevoflurane increased ejection fraction in only six patients, two of them took rocuroniom in addition while the other two took atracurium instead, in addition, the combination of propofol, midazolam, fentanyl, isoflurane increased CO **(**ejection fraction) in only the two other patients: one of them had taken atracurium in addition. Finally, no change in ejection fraction had been noticed in two patients who took combination of propofol, midazolam, fentanyl and atracurium in addition to sevoflurane in one of them and isoflurane in the other (Table 2).

It can be seen that the means and standard deviations of the pre-operative ejection fraction and post induction ejection fractions for 207 patients were 0.6055, and 0.06587 and 0.5531 and 0.08748 respectively (Table 3).

The study displays the correlation between the two means of pre-operative ejection fraction & post induction ejection fraction of the study patients (n=207) which are indeed correlated positively with correlation coefficient of 0.786 at a p value = .000. (table 4)

The study also shows the average difference between the two values **(**paired differences mean = 0.05242), the 95% confidence interval around the difference **(**0.04499, 0.5984), the value of the computed t-statistic**(**13.918), and the actual p-value associated with the computed statistic **(**p = .000, or p < .001). (table 5)

This study gave some aside outcomes regarding the effects of using chronic diseases drugs on the changing of ejection fraction after induction of general anesthesia. Among these drugs, beta-blockers and unexplained antidiabetics owned the highest level of lowering cardiac output, followed by nitroglycerin and diuretics. Unexpectedly calcium channel blocker had the minimal decreasing factor on the cardiac output along with heparin (Table 6).

Hence, the post induction ejection fraction significantly differs from the pre operation ejection fraction for **(**207) patients who received anesthesia in Duhok hospitals during 2021. The average means difference was of 0.04499 **(**95% confidence interval, lower is 0.4499, upper is 0.5984.69). This difference is statistically significant at a ≤ .05 by the paired ᴛ test **(**two-tailed).

Table 1: Descriptive statistics of age, weight, pre general anesthesia induction ejection fraction and post general anesthesia induction ejection fractions, and duration of chronic diseases of the study patients(n=207)

	N	Range	Minimum	Maximum	Mean	Std. Error	Std. Deviation
Age of patients(Year)	207	77	1	78	40.00	1.093	15.731
Weight(kg)	207	130	7	137	71.00	1.196	17.210
Pre general anesthesia induction Ejection Fraction	207	.45	.35	.80	.6055	.00458	.06587
Post general anesthesia Induction Ejection Fraction	207	.54	.24	.78	.5531	.00608	.08748
Duration of Chronic Diseases(Year)	41	26	0	26	1.47	.264	3.802
Total	207						

Table 2: Pre general anesthesia induction Ejection Fraction, Post general anesthesia Induction Ejection Fraction, and Difference between pre and post induction ejection fractions for anesthetic drugs given to the study patients(n=207)

Anesthetic Drugs	Pre general anesthesia induction Ejection Fraction	Post general anesthesia Induction Ejection Fraction	Difference between pre and post general anesthesia induction ejection fraction
Propofol	.61	.55	.10
Midazolam	.61	.55	.10
Fentanyl	.61	.56	.09
Morphine	.49	.42	.15
Ketamine	.61	.55	.13
Rocuronium	.54	.48	.15
Atracurium	.62	.57	.08
Isoflurane	.61	.56	.09
Sevoflurane	.60	.54	.11
Total	.61	.55	.10

Table 3: The descriptive statistics of Pre general anesthesia induction Ejection Fraction, Post general anesthesia Induction Ejection Fraction, of the study patients(n=207)

Paired Samples Statistics		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	**Pre-Operative Ejection Fraction**	.6055	207	.06587	.00458
	Post Induction Ejection Fraction	.5531	207	.08748	.00608

Table 4: Correlation between the Pre general anesthesia induction Ejection Fraction & Post general anesthesia induction Ejection Fraction of the study patients(n=207).

Paired Samples Correlations		N	Correlation	Sig.
Pair 1	Pre-Operative Ejection Fraction & Post Induction Ejection Fraction	207	.786	.000

Table 5: The mean difference, and the 95% confidence interval of the Pre general anesthesia induction Ejection Fraction & Post general anesthesia Induction Ejection Fraction of the study patients(n=207).

		Paired Differences					T	df	Sig. (2-tailed)
		Mean	SD	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Pre-Operative Ejection Fraction - Post Induction Ejection Fraction	.05242	.05418	.00377	.04499	.05984	13.918	206	.000

Table 6: The means Pre general anesthesia induction Ejection Fraction, Post general anesthesia Induction Ejection Fraction, and Difference between pre and post induction ejection fractions for chronic disease drugs used the study patients(n=207).

		Pre general anesthesia induction Ejection Fraction	Post general anesthesia induction Ejection Fraction	Difference between pre and post general anesthesia induction ejection fraction
Chronic Disease Drugs	Angiotensin blocker	.56	.47	.17
	Nitroglycerin	.48	.38	.21
	Beta blocker	.52	.40	.24
	Diuretic	.47	.38	.20
	Anti-diabetic	.51	.39	.24
	Aspirin	.51	.41	.19
	Heparin	.55	.53	.04
	Anti-uric acid	.50	.44	.13
	Calcium channel blocker	.51	.49	.05
	Thyroxin	.63	.58	.08
	Total	.55	.47	.15

Discussion:

Hua *et al.*, (2017) study conducted at a London teaching hospital between June-November 2014. Patients of American Society of Anesthesiologists grade I-II aged between 18-45 years, had perform elective lower-limb arthroscopic surgeries examined to record HR, MAP, SV, CO, SVR and BIS continuously prior to induction and up to 3-minutes after anesthesia. The result of this study can be said to be the same result of the present study because they said HR, SVR, MAP, SV and CO were decreased by post general anesthesia induction. Their findings highlight the significance of involving cardiovascular assessment in routine perioperative monitoring [21].

Hubner *et al*., (2013) demonstrated that general anesthesia through decreased SVR, decreased myocardial contractility, decreased SV, and increased myocardial irritability, affects arterial and central venous pressures, CO, and varying heart rhythms. Specifically They document that systemic arterial pressure decrease by 20-30% after induction of general anesthesia, but blood pressure will return up about 20-30 mm Hg because of tracheal intubation. Compared with inhaled anesthetics the use of fentanyl, sufentanil, of alfentanil causes less myocardial depression. This depression is by venodilation which results in decreasing preload [22].

Homi *et al*., (1972), Filner and Karliner (1976), Dale et al, (1987) and Friesen (1983) show different effects of inhalation agent on CO. The decrease in arterial pressure by halogenated anesthetics results either from a reduction in CO that showed in (enflurane> halothane >> isoflurane) or decrease in SVR that came with use of (isoflurane > enflurane > halothane) [23,24,25,26].

Cahalan *et al*., (1991), and Brioni *et al*., (2017) stated that the patient's CO is indirectly related with concentrations of inhaled anesthetics [11,8].

Brioni *et al*., (2017), and Li and Yuan (2015) demonstrated that sevoflurane compared with desflurane and isoflurane, has less morbidity and mortality due to its low impact cardiovascular dynamic parameters [8,27].

Aguirre (2016) and Park et al, (2007) displayed that systemic hemodynamics as isoflurane, desflurane, and sevoflurane reduce MAP, (CO), and cardiac index in a dose-dependent fashion [28,29].

Alwardt *et al*, (2005) said that nitrous oxide, halothane, enflurane, isoflurane, desflurane, sevoflurane will decrease blood pressure, SVRs and CO with less effect of halothane on systemic resistance and isoflurane and desflurane on CO while HR will increase in enflorane, isoflurane and desflurane but decreased by halothane, nitrous oxide do not change all of them parameter and sevoflurane and do not change CO. Although isoflurane may result in the greatest decrease in SVR leads to arterial blood pressure decline, CO is preserved as the result of an active carotid baroreceptor reflex and decreased afterload [30].

Lippmann *et al*., (1986) mentioned that the decrease in CO may be quite correct in high risk patients among those who had taken general anesthesia induction, CO will be decreased more and in a degree higher than healthy individuals. This is completely agree with result of present study which documented that CO decrease more in the patients who had chronic diseases such as cardiovascular and endocrine diseases [31].

Anyhow, Green (2015) still thinks that most anesthesiologists continue to regard the decrease in MAP on induction due either to cardiac depression, as Kakazu and Lippmann propose, or to decrease in SVR. Furthermore, Green, believed that

the reduction in cardiac contractility has little to do with decrease in CO regarding the effect on preferentially reducing venous rather than arterial tone [32].

Bentley et al, (1989) and Goodchild and Serrao (1989) stated that venorelaxation and an increase in venous capacitance is the cause of venous return and SV decline resulted in decrease of CO and MAP. This result is similar to the results of the present in that propofol cause decrease of CO [33,34].

Petrun and Kamenik (2013) are to be congratulated for pointing out that the driving of decrease in MAP post-induction is the decrease in CO which is more evident with both propofol and etomidate [35].

Pagel and Warltier (1993) and Larsen *et al*., (1988) stated that propofol causes reduction in arterial blood pressure in proportion to dosage and plasma concentration. They found that this reduction was related to decrease in SVR and CO which already found in the present study [36,37].

Chen and Ashburn (2015) said that most opioids have low direct negative inotropic effect. As opioids are rarely the sole anesthetic agent used, interestingly mentioned that combination of opioid with other drugs especially with benzodiazepines effect on the cardiac function and cause decrease in cardiac function. This study is parallel with the present study. In addition, significant diminishing in cardiovascular parameters can be observed when opioids are administered with inhaled anesthetics [38].

Chen and Ashburn (2015), Benyamin *et al*., (2008), Shirani (2010) and Aghadavoudi (2015) summarize numerous studies that have investigated the harmful - effects of opioids on the body organs especially the cardiovascular system, especially when applied with benzodiazepines by causing decrease CO, bradycardia, histamine release, heart electrical disturbance and cardiac arrhythmia [38,39,40,41].

The effect of fentanyl, even after large doses, on hemodynamics like HR, MAP and CO is minimal. This is described by Bailey *et al*., (2000) [42].

Khanderia et al (1987) stated that benzodiazepines have less cardiorespiratory effects which include a slight decrease in CO and blood pressure. These effects are more evident when used in conjunction with narcotics [43].

Mehmet *et al*., (2014) displayed that haemodynamic variations are of three general anesthesia induction agents (thiopental, propofol, and etomidate) when used in conjunction with fentanyl. The decrease in CO was more marked with propofol than with etomidate or thiopentone. So they concluded that the combination of fentanyl with propofol is less safe than both the groups of fentanyl with etomidate and fentanyl with thiopental in terms of providing haemodynamic stability. Again, the result of the present study demonstrated that the combination of propofol with fentanyl can decrease CO [44].

Khan *et al*., (2014) said that ketamine could increase arterial pressure, HR and CO as opposed to other intravenous anesthetics due to central stimulation of the sympathetic nervous system [45].

Yet, it is said that ketamine has negative inotropic actions but this is to somehow reversed as it has a centrally mediated ability of catecholamine release, which appear as an increasing HR, blood pressure and CO (Traber et al, 1968) [46].

Elisha *et al*., (2022) determinated the cardiovascular effects[47]. Mazzeth *et al*., (2015) identified that ketamine, unlike other intravenous anesthetics, has a circulatory stimulant charachter, producing increases in systemic blood pressure, HR,

cardiac contractility and output, and central venous pressure [48]. Yet, Ivankovich *et al*., (1974) showed SVR responded, differently among patients undergoing cardiac catheterization and angiography, possibly because of patient variability in autonomic tone and disease states. Other studies have failed to show significant effects in SVR but have found evidence of an increase in pulmonary vascular resistance, pulmonary artery pressure, and right ventricular stroke work [49].

Kuipers *et al.,* (2001) proposed that recirculatory models can explain accurately first-pass pharmacokinetics and the influence of CO, which is obvious in drugs with a fast onset of effect. This explains what this present study said that rocuronium can decrease CO by 0.15 (15%) because the mean pre general anesthesia induction was 0.54 (54%) and the mean post general anesthesia induction was 0.48 (48%) so, the mean different between pre and post general anesthesia will be 0.15 (15%) [50].

Shiraishi *et al*., (2018) justified in their study that there was a statistically significant inverse correlation between the onset time of rocuronium and CO mainly in the elderly patients [51].

Gallo *et al*., (1988) explained that the cause of a statistically significant decrease in blood pressure at 2 minutes and a statistically significant increase in CO and decrease in SVR at 2, 5, and 10 minutes, was changes in serum histamine levels. Although histamine level did not change after vecuronium, there were no statistically significant differences between the two groups. The result of this study have the opposed result to present study because it state that CO decrease by using atracurium[52].

Conclusion: The overall effect of general anesthesia induction agents is negative inotropic with mean decreasing of 10% of baseline ejection fraction. This is a considerable level in patients of border line CO (heart failure). Anesthesiologist should give special caution when use the drugs of high negative inotropic effect like Morphine and Rocuronium.

Recommendation: it will be very informative if this study extended to individually examine the effect of each general anesthesia induction drugs on the CO or to be comparative study between groups of these drugs.

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Total Superficial Parotidectomy: Pros and Cons

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Abstract

Background: Total superficial parotidectomy is the most commonly used approach in excising the tumors that affect the superficial lobe of the parotid gland, whether they're benign or malignant.

The aim of the study is to evaluate the benefits and drawbacks of total superficial parotidectomy for parotid gland tumors within five years of follow-up.

Patients and methods: Nineteen patients with lateral facial swelling affecting the parotid region were included in this study. All of them operated under general anesthesia with oral endotracheal intubation, where Modified Blair Incision (lazy S incision) was utilized in all cases.

Anterograde dissection with facial nerve identification was accomplished with total superficial parotidectomy.

Results: Fifteen patients had benign parotid tumors, and only four patients had well-differentiated mucoepidermoid carcinoma.

Skin necrosis of the distal tip of the postauricular flap was the most commonly observed postoperative complication, it occurred in five patients; facial nerve weakness was observed in the another three patients.

Conclusions: total superficial parotidectomy is an efficient, safe technique for benign and malignant tumors affecting the superficial lobe of the parotid gland with minimum postoperative complications.

Keywords:

Pleomorphic adenoma, Mucoepidermoid carcinoma, Total superficial parotidectomy

Introduction

The most frequently affected salivary gland lobe by tumors is the superficial lobe of the parotid gland; most of these tumors are benign, and 60–70% of these benign tumors are pleomorphic adenomas [1,2]. While malignant parotid gland tumors are rare and exhibit varied biological behaviors, mucoepidermoid carcinoma is the most common malignant salivary gland tumor found in the parotid gland [2].

Pleomorphic adenoma, despite being a benign tumor, had an incomplete capsule. For this reason, surgical resection with a free resection margin is the best treatment option for both benign and malignant parotid gland tumors [1].

Multiple approaches were used to manage parotid gland tumors. Whether the tumor is benign or malignant, there is no standardized way to determine the extent of resection margin, which depends on many factors like the position of the facial nerve, the extent of the tumor, and its grade [3,4].

Previously, intracapsular dissection was used to treat parotid gland benign tumors; however, this approach ended with a high recurrence rate. [5]

Today, Superficial parotidectomy with identifying of the facial nerve main trunk or one of its branches in an anterograde or retrograde approach is a widely accepted method. This approach is commonly used for benign and malignant tumors confined to the superficial lobe of the parotid gland with no signs of facial nerve impairment. It involves the removal of all parotid gland tissues lateral to the facial nerve [6].

However, facial nerve dysfunction, Frey's syndrome, flap necrosis, and salivary leakage with this approach are possible [7,8,9,10].

Facial nerve impairment is one of the most significant adverse effects of parotid surgery, which can further impair the patient's quality of life. About 10-65% of patients may experience temporary facial nerve weakness, and 14% of patients experience permanent damage to the facial nerve.

This study aims to evaluate the benefits and drawbacks of total superficial parotidectomy for parotid gland tumors within five years of follow-up.

Patients and Methods

Nineteen patients who complained of lateral facial swelling were referred to the maxillofacial consultation clinic at the Alkinday teaching hospital from March 2014 to September 2018. This study was carried out according to ethical principles and in compliance with the Declaration of Helsinki, and the patients gave informed consent.

After taking a medical history and performing a clinical examination, patients were sent for an ultrasound examination for the swelling and showed a well-defined hypoechoic mass within the parotid gland. To confirm the diagnosis, a fine needle aspiration was performed, followed by a computed tomographic scan to determine the exact position and size of the tumor.

All patients were operated on under general anesthesia with oral endotracheal intubation, where Modified Blair Incision (lazy S incision) was utilized in all cases. The incision begins with a vertical arm in the pre-auricular region, continues through the anterior border of the mastoid, and terminates in the sub-mandibular region.

To securely identify the main trunk of the facial nerve, anterograde dissection with identification of the tragal pointer and posterior belly of the digastric muscle was performed.

The dissection continued lateral to the main trunk of the facial nerve, separating the tumor with a cuff of normal glandular tissues around it and sent for histopathological examination. Fig.1

After that, hemostasis for all bleeding points with the use of bipolar electro-diathermy was done. A vacuum drain was placed and inserted from behind the ear and fixated with sutures. Then watertight closure for all facial planes and skin don followed by packing and pressure dressing over the surgical site.

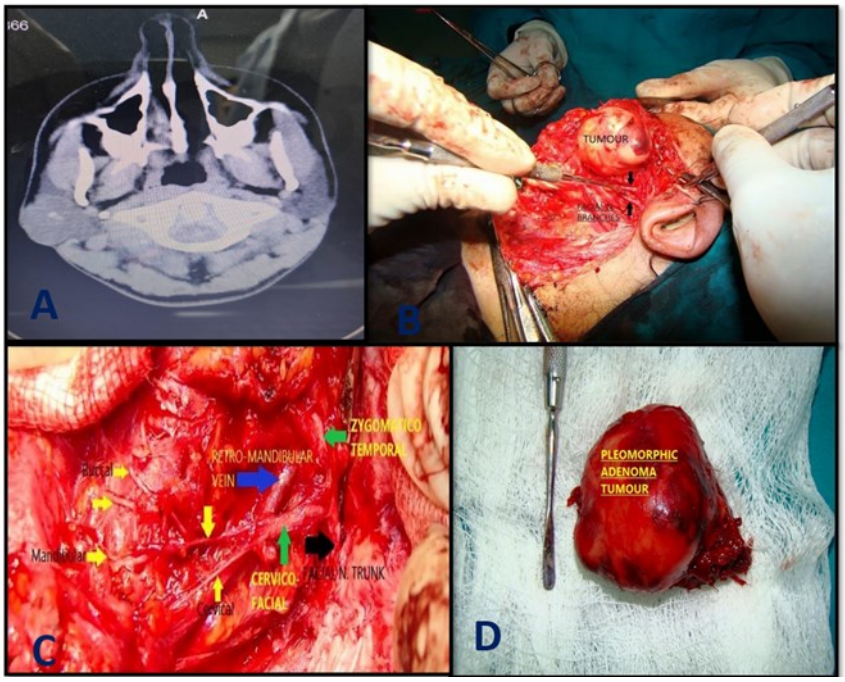

Fig.1 A: axial section of CT scan showing lobulated soft tissue mass within the posterior part of the superficial lobe of the left parotid gland, **B**: showing modified Blair incision with anterograde dissection identifying the main trunk of the facial nerve, **C**: total superficial parotidectomy with preservation of all facial nerve branches, **D**: the tumor mass with a cuff of normal parotid gland tissue.

Vacuum drains are checked every 12 hours for the amount of the collected fluids. The drain is removed when it collects less than 20 ml of fluids.

All patients were kept on Ceftriaxone 1 mg once daily, Decadron® 2 ampoules only (the first ampoule is given immediately after recovery and the second one given 12 hours later), and Paracetamol 1 gram three times daily for seven days.

Facial nerve function is evaluated immediately after recovery from general anesthesia and before developing facial swelling that may affect the function of the nerve in the next few hours.

Wound healing, the development of Frey's syndrome, and salivary leakage were evaluated in the next weeks of the follow-up period, which extended for three years.

Results

Nineteen patients (eleven females and eight males) were included in this study; patients' ages ranged from 19–67 years, with a mean age of 39 ± 14.49. All patients had unilateral facial swelling affecting the left side in 65% of the patients. They had been presented for 4.57 ± 1.83 years. The mean size of the parotid tumors was 4.35 ± 0.91 cm, as shown in Table (1).

After three months of monthly evaluations, the clinical assessment was completed every four months for the first year. then every year for the following two years, for a total of three years.

The ultra-sonographies were performed every six months for three years, and no computed tomography (CT) scan was performed in the follow-up period.

Table (1): Patients characteristics.

Item		No.
Mean age ±SD		**39 ± 14.49**
Gender	**Male**	8
	Female	11
Affected side	**Left**	12
	Right	7
Duration of presentation		4.57 ± 1.83 years
Mean size of the parotid tumors		4.35 ± 0.91 cm.

The histopathological results from Fine Needle aspiration (FNA) preoperatively and excisional biopsy of the total superficial lobe of the parotid gland postoperatively were accurate in 18 cases out of 19.

Fifteen patients had benign parotid tumors (13 pleomorphic adenomas, 2 Warthin's tumors), and only four patients had well-differentiated mucoepidermoid carcinoma. The histopathological features of the pleomorphic adenoma group showed the presence of cartilaginous to myxoid tissue with benign-looking epithelial components surrounded by benign intact salivary gland lobules suggesting the diagnosis of pleomorphic adenoma. While in mucoepidermoid carcinoma, there has been a long-standing facial swelling for more than seven years, with sudden and painful, rapid growth in the last month before visiting the maxillofacial consultation clinic. With no facial nerve involvement.

Only three patients complained of temporary weakness of the mandibular branch of the facial nerve, and it resolved within three months. All of them had mucoepidermoid carcinoma.

Another patient developed a neuroma of the great auricular nerve branch, which was resolved by keeping the patient on gabapentin for three months.

Skin necrosis of the distal tip of the postauricular flap was observed in 5 patients and associated with salivary fluids discharge from the necrotic flap tip. It was controlled by giving the patient an anticholinergic drug with packing and pressure dressing for three weeks. Three of those patients had been diagnosed with pleomorphic adenoma and two of them with mucoepidermoid carcinoma.

At the end of the three years of follow-up, all patients were satisfied with the results, with no signs or symptoms of recurrence.

Discussion

Salivary gland tumors represent 3-10% of the head and neck tumors [(2)]. The most frequent benign tumor affecting the parotid gland is a pleomorphic adenoma, while the most frequent malignant tumor is mucoepidermoid carcinoma.

Failure to perform complete excision of these tumors ends in catastrophic consequences; these should be weighed against the possible drawbacks associated with total superficial parotidectomies like facial nerve weakness, facial scarring, Frey's syndrome, flap necrosis, and salivary leakage.

In this study, 11 out of 19 patients were females, with the female-to-male ratio being 1.7:1. This finding was on par with other studies [11,12,13], but in contrast to the other studies [14, 15,16].

Venkatesh et al. reported that there is a predilection for the left parotid gland to be affected more than the right one [17], and this coincides with the findings of this study. While the predilection was for the right side noticed in another study in Iraq.[13] However, no explanation drowns for this finding in the literature; the author thought that the limited number of patients included in these studies might lead to such findings.

In this study, 78.9 % of the patients had benign parotid tumors, and this finding is comparable to the known percentage of benign and malignant tumors affecting the parotid gland [1,2].

Stathopoulos *et al.* (2018) found that partial superficial parotidectomy is a highly efficient technique for excising benign parotid gland tumors by minimizing the complications associated with total superficial parotidectomy. However, he concludes that it is preferred to do more extensive surgical intervention (total superficial parotidectomy) when the tumor size exceeds four cm [5].

The mean size of the parotid tumors in this study is 4.35 ± 0.91 cm. these large-sized tumors are associated with a long history of parotid facial swelling (4.57 ± 1.83 years), and they need extensive surgical dissection to guarantee full tumor removal with a cuff of healthy salivary glandular tissues to prevent disease recurrence, which has been achieved in all 19 patients included in this study after five years of follow-up.

Fine needle aspiration provides a preoperative diagnosis for parotid tumors with an accuracy rate ranging from 90-95% of the cases [18]. This study showed an accuracy rate of 94.7%, which is comparable to the known accuracy rate of FNA.

According to Jin H et al., one of the most common causes of facial palsy after parotid surgery is the presence of deep-seated parotid tumors, large-sized tumors, revised parotid surgeries, or total parotidectomy [19].

15.7% of the patients in this study ended with temporary facial nerve weakness, and all of them had mucoepidermoid carcinoma; this may be explained by the fact that these malignant tumors in this study had a long-standing history of facial swelling with the sudden onset of painful rapid growth, resulting in large sized tumors.

The major postoperative complication in this study was the necrosis of the distal tip of the flap at the postauricular area with resultant salivary fluid discharged from this area. This complication occurs in 26.3% of the patients, notably in the first eight patients included in this study.

In the subsequent 11 patients, neither flap necrosis nor salivary fluid discharges were noticed. This was achieved by prescribing an anticholinergic drug with packing and pressure dressing for three weeks for all patients postoperatively.

Despite the limitations of this study (small sample size, short follow-up time), it can be concluded that the total superficial parotidectomy is an efficient, safe technique for benign and malignant tumors affecting the superficial lobe of the parotid gland with minimum postoperative complications.

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Detecting Phenotypic and Genotypic of the Antibiotic Resistant Salmonella enterica Serotype Paratyphi Isolated from Blood Samples in Najaf Province /Iraq

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Abstract

Background & Objectives: Salmonella Paratyphi is a leading cause of human paratyphoid fever in developing countries, causing deaths in humans worldwide. There are several paths for catching paratyphoid fever, but the close contact between patients and healthy humans is so far the most frequent cause of human infections. No study is found about the antibiotic resistance (phenotypic and genetic) of S. Paratyphi isolated from patients in Al-Najaf Province/Iraq, to the researcher's best knowledge. Hence, this study aimed to determine the prevalence of S. Paratyphi isolates from blood specimens and the antibiotic resistance determinants of them, as well as the genetic relationship among isolates.

Methods and Results: Blood specimens from 1743 patients with suspected enteric fever were cultured for the identification of Salmonella enterica during the period from first April to the end of October 2017. 107 (6.14%) S. enterica isolates were recovered and only two (1.87%) of isolates were S. enterica serovar Paratyphi B. These two isolates (ST39 and ST89) were tested against 23 antibiotics using the disc diffusion method on Muller-Hinton agar and the genotypic antibiotic resistance determinants by PCR. ST39 isolate was sensitive to all antibiotics while ST89 isolate was resistant to only cefepime, piperacillin and tobramycin. ST39 isolate did not carry integrons (1 or 2) and any resistance determinants, while ST89 isolate carried integron class1 as well as blaTEM, blaCTX-M and aac(6')-lb genes.

Conclusions: The findings of S. Paratyphi isolates with integron 1 and resistant antibiotic genes indicating public health risks.

Key words: aac(6')-lb genes, blaCTX-M, blaOXA, blaSHV, blaTEM, ESBLs, and S. Paratyphi,

Introduction

Paratyphoid fever which is a specific

disease for humans, is a type of enteric fever caused by Salmonella enterica, subspecies enterica serovar Paratyphi A, B and C. S. Paratyphi A, B and C are differentiated by their various surface antigenic structures [1]. The symptoms of paratyphoid fever are similar to those of typhoid fever, making these two conditions difficult to differentiate clinically [2,3]. S. Paratyphi B infections can cause enteric fever (paratyphoid fever) or gastroenteritis. In some cases, serious complications can occur (septicaemia, meningitis). The most affected age group is infants, young children and immunocompromised patients [4]. Clinical reports show that S. Paratyphi can persist in the gallbladder of asymptomatic carriers [5].

The main factor in the development of antibiotic-resistant strains is the ability of the bacterium to acquire and spread the extra-chromosomal DNA through mobile genetic elements, such as plasmids, transposons and integrons [6,7,8]. The increased prevalence of antibiotic-resistant bacteria has led to a great interest of researchers in the genetic mechanisms of resistance offered by these bacteria. Environmental factors influence the development of antimicrobial resistance in bacteria. Studies have shown that bacteria isolated from faecal-contaminated areas have more resistance to antibiotics due to their acquisition of resistance genes from faecal-associated bacteria. Therefore, contaminated foods by faeces containing S. Paratyphi will be more serious [9]. Hence, The Enterobacterial Repetitive Intergenic Consensus polymerase chain reaction (ERIC-PCR) technique is used to identify genetic diversity in bacteria by separating specific chromosomal segmen-ts. These chromosomal segments are various in different species, genus and strains. The ERIC sequences depended on the amplification of the chromosomal segments, which is appear by gel electrophoresis method as genomic bands (fingerprints) in different molecular weights. This method is used to reveal the epidemiological relationship between bacterial isolates and their degree of genetic diversity [10,11,12]. The aim of this study is to determine the prevalence of S. Paratyphi isolates, the phenotype and genotype of their antibiotic resistance, and to identify the integrons and the genetic relationship among isolates.

Methods:

Sample Collection and Isolation

A total of 1743 blood samples were taken from patients with suspected enteric fever, in Najaf hospitals, Iraq; they all were aseptically collected during the seven months period of the study from April to October 2017. They were subjected to isolation by being cultured in brain heart infusion broth and incubated at 37°C for 5-7 days. Each BHI medium was sub-cultured on blood agar and incubated at 37˚C for 24 hr. to give bacteria more chance to grow [13]. From blood agar colonies, the pure colony was subcultured on the selective media, XLD agar, and incubated at 37˚C for 24 hrs.

Identification of S. Paratyphi B

A typical colony from each XLD agar was identified by using standard biochemical tests and confirmed by using the Vitek 2 compact system [14,15]. All the identified bacterial isolates were preserved in 15% glycerol nutrient broth and stored in the deep freeze at −20°C. Positive isolates were sent to the Central Health Laboratory in Baghdad to confirm the final identification

Susceptibility Testing

Depending on the recommendations of the Clinical and Laboratory Standards (CLSI) [16], twenty-six antibiotic discs of various classes were chosen for the Kirby-Bauer

disc diffusion method [17]. The isolates of S. Paratyphi and E. coli ATCC 25922 (as a control strain) were tested to determine the antibiotic sensitivity patterns.

Each isolate grown on XLD agar was inoculated in 2-3 ml nutrient broth and incubated at 37°C for 18 hours. According to the turbidity of McFarland tube, a sterile cotton swab was used to spread the suspended culture onto a Müller-Hinton agar, then antibiotic discs were dispensed on plates among which the distance is 15 mm at least, and incubated at 37°C for 18-20 hrs. The diameter of the zone around each disc was measured and compared according to the breakpoints of each type of the antibiotic in CLSI in order to determine their being sensitive (S), intermediate (I), and their resistance (R).

Primers Oligonucleotide Design

The primer sequences of blaTEM, blaSHV, and blaCTX-M genes were obtained from Bali et al. (2010) [18] while blaOXA gene was obtained from Guerra et al. (2001) [19], aac(6')-lb gene was obtained from Akers et al. (2010) (20), intl-1 and intl-2 genes were obtained from Dillon et al. (2005) [21], and ERIC gene was obtained from Smith et al.(2007) [22]. As in Table 1.

Table 1: PCR primers of *bla*$_{TEM}$, *bla*$_{SHV}$, *bla*$_{OXA}$, *bla*$_{CTX-M}$, *aac(6')-lb*, *intl-1* and *intl-2* and ERIC genes with their references.

Target	Primer name	Oligo sequence (5'-3')	Product size (bp)	Reference
bla$_{TEM}$	TEM-F	TTTCGTGTCGCCCTTATTCC	403	Bali *et al*. (2010)
	TEM-R	ATCGTTGTCAGAAGTAAGTTGG		
bla$_{SHV}$	SHV-F	CGCCTGTGTATTATCTCCCT	293	Bali *et al*. (2010)
	SHV-R	CGAGTAGTCCACCAGATCCT		
bla$_{OXA}$	OXA-F	ACCAGATTCAACTTTCAA	598	Guerra *et al*. (2001)
	OXA-R	TCTTGGCTTTTATGCTTG		
bla$_{CTX-M}$	CTX-M-F	CGCTGTTGTTAGGAAGTGTG	754	Bali *et al*. (2010)
	CTX-M-R	GGCTGGGTGAAGTAAGTGAC		
aac(6')-lb	F	TATGAGTGGCTAAATCGAT	395	Akers *et al*. (2010)
	R	CCCGCTTTCTCGTAGCA		
	intI1- F	CAGTGGACATAAGCCTGTTC	160	Dillon *et al*. (2005)
intl-1	intI1- R	CCCGAGGCATAGACTGTA		
intl-2	intI2 -F	CACGGATATGCGACAAAAAGGT	789	Dillon *et al*. (2005)
	intI2 -R	GTAGCAAACGAGTGACGAAATG		
ERIC	ERIC-1	ATGTAAGCTCCTGGGGATTCAC	variable	Smith *et al*. (2007)
	ERIC-2	AAGTAAGTGACTGGGGTGAGCG		

Detecting Encoding Genes by PCR Technique

According to the results of the antibiotic resistance, five types of primers were chosen to reveal ESBLs genes (blaTEM, blaSHV, blaOXA and blaCTX-M) and aac(6')-lb gene as well as intl-1, intl-2 and ERIC genes (Table 1). The DNA was extracted by using a Promega Wizard Genomic DNA Purification Kit which is used as the template in the PCR technique. These templates were stored at -20°C in a sterile Eppendorf tube.

A PCR assay was used for detecting the antibiotic-resistant genes in the total volumes of 25µl containing 1 µl of each primer, 2 µl of template DNA, 12.5 µl of Taq Master Mix (Bioneer AccuPower Gold PreMix, Korea), and 8.5 µl PCR grade water. Thermocycler Biosystem was adjusted as in Tab. 2.

On 1.5% agarose gels, the PCR products and DNA-size ladder (100-1500 bp; GeneDireX INC, USA) were analyzed with electrophoresis which was performed at 60-70 V for 90 minutes with antibiotic resistance encoding genes and 150 minutes with ERIC genes. To evaluate the target product size according to the ladder, the bands of PCR products and the ladder were visualized by ultraviolet light.

Table (2): Programs of PCR thermocycling conditions for all primers used in the present study.

Gene name	Temperature (˚C)/ Time				
	Initial denaturation	Cycling condition			Final extension
		denaturation	annealing	extension	
TEM	94/5 min	94/30 sec	60/30 sec	72/50 sec	72/5 min
		No. of cycles = 35			
SHV	94/5 min	94/30 sec	60/30 sec	72/50 sec	72/5 min
		No. of cycles = 35			
OXA	94/5 min	94/30 sec	55/30 sec	72/50 sec	72/7 min
		No. of cycles = 35			
CTX-M	94/5 min	94/30 sec	60/30 sec	72/50 sec	72/5 min
		No. of cycles = 35			
aac(6')-lb	94/15 min	94/45 sec	55/45 sec	72/45 sec	72/10 min
		No. of cycles = 34			
intl-1	94/5 min	94/30 sec	55/30 sec	72/1 min	72/7 min
		No. of cycles = 35			
intl-2	94/5 min	94/30 sec	62/30 sec	72/1 min	72/10 min
		No. of cycles = 30			
ERIC	95/3 min	95/30 sec	51/1 min	72/2 min	72/5 min
		No. of cycles = 35			

Results

The Isolation and Identification of Salmonella Paratyphi B

A sum of 1743 blood samples were obtained from patients with suspected enteric fever from the main hospitals in Najaf province during the period from April to October 2017. The conventional biochemical tests of the culture verified by Vitek 2 compact system has shown that 107 (6.14%) isolates were recovered as Salmonella enterica and only two (1.87%) of the isolates were S. enterica serovar Paratyphi B.

Antimicrobial Susceptibility of S. Paratyphi B Isolates

The two S. Paratyphi isolates were evaluated for susceptibility to 26 different antibiotic discs out of 11 antibiotic classes (according to CLSI / 2020 guidelines as resistant, moderate resistant, and susceptible).

It appears that the 1st isolate (ST89) exhibited resistance only to tobramycin and piperacillin and intermediate resistant to piperacillin/tazobactam and cefepime, but sensitive to the others while the other isolate (ST39) was sensitive to all antibiotics but intermediate resistant to tobramycin and cefepime.

Detecting the Antibiotic Resistance Encoding Genes by PCR

1. ESBLs Genes (blaTEM, blaSHV, blaOXA, blaCTX-M):

ST89 S. Paratyphi isolate exhibited resistance to piperacillin and intermediate resistant to piperacillin/tazobactam and cefepime; therefore, it was chosen to reveal the presence of ESBLs genes by using blaTEM, blaSHV, blaOXA and blaCTX-M genes. So, it yielded amplification products with blaTEM gene (Fig. 1a) and yielded amplification products with blaCTX-M gene (Fig. 1b) while blaSHV and blaOXA genes were absent.

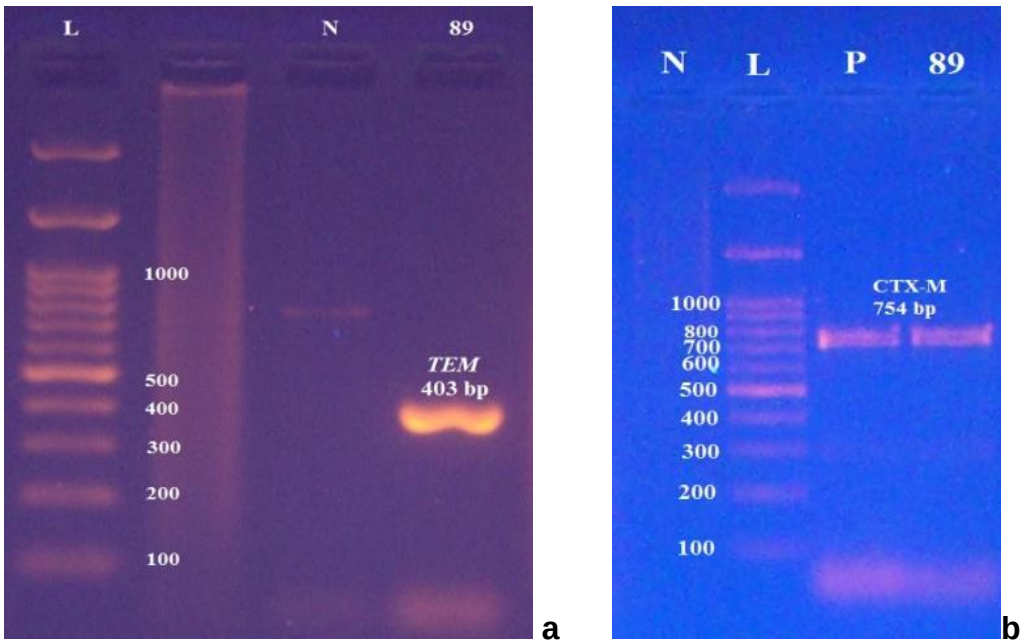

Figure 1: Gel electrophoresis of PCR product showing ESBLs genes (*bla*$_{TEM}$ and *bla*$_{CTX-M}$ genes).

2. Aminoglycoside Resistance Genes

ST89 *S*. Paratyphi B isolate showed positive results with primer *aac(6')-Ib* (Fig. 2).

Class I and II integrons and their distribution among S. Paratyphi B

Both S. Paratyphi isolates were tested for the carrying class 1 and class 2 integrons, by PCR technique with specific primers for the intI-1 and intI-2 integrase genes. Only ST89 isolate were found to be carrying class 1 integron, while class II integron was not found in all isolates.

The isolate of integron-positive S. Paratyphi B was found carrying blaTEM, blaCTX-M and aac(6')-Ib genes while the isolate of integron-negative S. Paratyphi B had no antibiotic resistant genes.

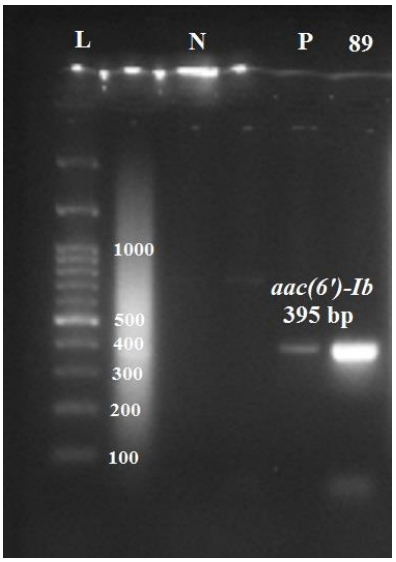

Figure 2: Gel electrophoresis of PCR product showing *aac(6')-Ib* gene.

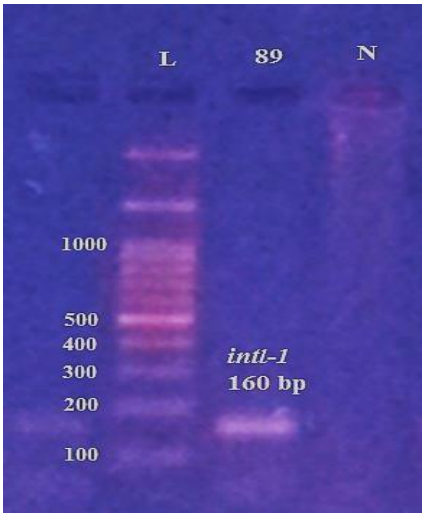

Figure 3: Ethidium bromide-stained agarose gel of monoplex PCR amplified products from extracted DNA of *S*. Paratyphi B isolates and amplified with Intl-1 genes primers. The electrophoresis was performed at 70 volts for 1:30 hr. Lane (L), DNA molecular size marker (100 bp ladder), Lanes (89) show positive results with Intl-1 gene. Lanes (39) show negative isolate with Intl-1 gene.

Detecting the epidemiological relationships between isolates by ERIC-PCR

The results of ERIC-PCR fingerprinting of the two S. Paratyphi B isolates has shown two PCR amplicons. The numbers of amplified bands range between 2-4 bands with molecular size range between 100 bp and 700 bp (Fig. 4).

As in Fig. 4, the dendrogram construction based on ERIC-PCR banding including two S. Paratyphi isolates has produced two patterns with different clusters at 19.8% similarity.

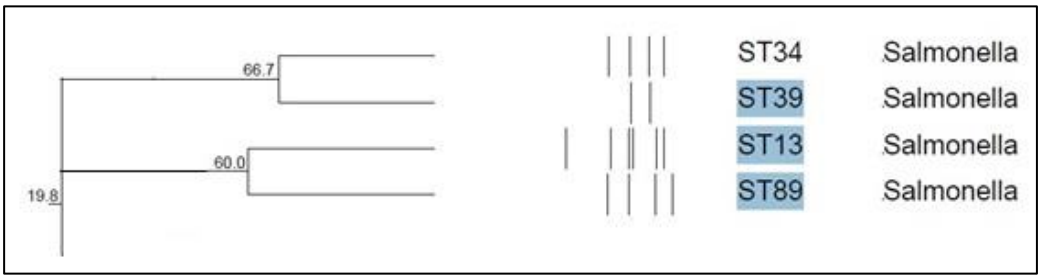

Figure 4: Dendrogram showing two different ERIC-PCR fingerprints of *S*. Paratyphi B isolates at 80% similarity.

Discussion:

During the study period, the examined blood samples revealed that the prevalence rate of S. Paratyphi B was 1.87%, and this result was in agreement with the studies of Issa et al. (2006) [23] in Najaf which was one isolate (1%) from 91 positive isolates; Thewaini and Mohameed (2006), in Al-Hilla (5/ 68, 7.35%)[24] and Singh and Cariappa (2016) in India shows only one (0.01%) isolate [25], as well as Malaysia studies during the years from 1990 to 2000 which were between 3.3-5.5% of the total numbers of S. enterica [26] while in AlQadesiah (2007), 20 from 65 (30.77%) of Salmonella were positive isolates [27].

S. Paratyphi B is the human pathogens mostly isolated from poultry [28]. The results of antibiotic susceptibility test revealed that one of the two S. Paratyphi isolates (ST89) has shown resistance to two antibiotics (tobramycin and piperacillin) and intermediate resistance to other two antibiotics (piperacillin/tazobactam and cefepime). However, the other isolate (ST39) have shown intermediate resistance to other two antibiotics (tobramycin and cefepime). The resistance to these antibiotics could be either because of the inhibition of antibiotics by the acquired genes or gene mutations; it indicates the use of these antibiotics in the region.

Detecting the Antibiotic Resistance Encoding Genes by PCR

Molecular characterization revealed that ST89 isolate harbored the blaTEM, blaCTX-M and aac(6')-Ib genes. Several studies have shown the emergence of Salmonella strains containing ESBLs that carry out ESBL genes worldwide [29]. However, to the researcher's best knowledge, no other study has investigated the molecular characterization of S. Paratyphi B strain harboring the antimicrobial resistant genes in Iraq.

Spread of Class 1 and Class II Integrons Gene Among S. Paratyphi:

Due to differences among countries in the consumption of types of antibiotics, different resistance against these antibiotics appeared; accordingly, integrons appeared [1,30]. In this study, class 1 integrons found in only ST89 isolate while class 2 integrons was absent.

ERIC-PCR Fingerprinting

The ERIC genotypes of isolates were used to show the epidemiological relationship of the recovered strains. ERIC analysis revealed different patterns among the two S. Paratyphi B isolates. The similarity ratio between ST89 and ST39 isolates was 19.8% which indicates that these isolates were from different sources.

In Najaf, variety of infection sources may happen because it has a feature that especially makes it a center of attraction for many, including the year-round attraction of many pilgrims or visitors, some of them come to tourism, including religious tourism, cultural tourism and business tourism. It has also become a hub for displaced people from hot cities in Iraq, where many displaced families have planned to live, because of stability. In addition to the presence of many universities, colleges and religious and academic institutions, many students from all over the world are drawn to study and research, making the area a continuous movement of passengers arriving and departing from different countries around the world.

Conclusions

This study has shown that the S. serovar Paratyphi B, recently acquired resistance determinants like blaTEM, blaCTX-M and aac(6')Ib genes as well as intl-1, constitutes major anxiety for public health. Further, surveillance and researches are very necessary to understand their epidemiology and to limit the prevalence of antibiotic resistant Salmonella spp.

Recommendations:

According to this research, the recommendations are:

1. The continuous monitoring of paratyphoid dissemination and antibiotic resistance of isolates.
2. Educating food staff and consumers about paratyphoid fever transmission methods.
3. Tracking paratyphoid fever cases among travellers to developing countries.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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Data Availability

All datasets generated or analyzed during this study are included in the manuscript and/or the Supplementary Files.

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Prevalence of Small Round Cell Tumors in Pediatric Age Group in the last 10 Years Registered in Al- Najaf Governorate

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Abstract

Malignant small round cell tumors (MSRCT) are referred to as tumors made up of malignant small round cells. The cells in this type of neoplasms are tiny, rounded, and largely undifferentiated. Ewing's sarcoma (ES), peripheral neuroectodermal tumor, rhabdomyosarcoma, non-Hodgkin lymphoma, retinoblastoma, neuroblastoma, hepatoblastoma, and nephroblastoma are a few of the more common ones. The aim of this study is to estimate the prevalence and types of pediatric small round cell tumors in Najaf Province/Iraq, over the 10 years period between 2010-2019.

Method: This is a retrospective observational study. Cases were collected from pathology laboratories in As-Sadr Medical City and some private laboratories in Najaf over a 10 year-period extending from 2010 to 2019.

Results: A 6366 pediatric surgical biopsy cases were reported during the study period and this represent 8.7% of all cases. Out of these cases, 108 cases with small round cell tumors (SRCT) have given a prevalence rate of 17 per 1000 pediatric cases and 1.5 per 1000 of total (73504) adult and pediatric cases during the same period. The mean age of these SRCT cases was 6.3± 1.6 (range: one month-19) years. The higher proportion of cases was reported in the age of 1-5 years, contributed for 43.5%. Male to female ratio is 59/108 vs. 49/108, respectively, the male to female ratio being at 1.2 to 1.0.

Conclusions: The mean age of SRCTs cases was 6.3± 1.6, ranging from one month to 19 years. The higher proportion of SRCTs cases was reported in the age ranging from 1-5 years; with a ratio of males to females being 1.2 to 1.0.

Keywords: Ewing's sarcoma, Malignant small round cell tumors, retinoblastoma.

Introduction

Malignant small round cell tumors (MSRCT) are referred to as tumors made up of these cells[1]. The cells in this type of neoplasms are tiny, rounded, and largely undifferentiated. Ewing's sarcoma (ES), peripheral neuroectodermal tumor, rhabdomyosarcoma, non-Hodgkin lymphoma, retinoblastoma, neuroblastoma, hepatoblastoma, and nephroblastoma are a few of the more common ones[2]. Small cell osteogenic sarcoma, granulocytic sarcoma, and intraabdominal desmoplastic small round cell tumor are further differential diagnosis for small round cell tumors (SRCT). Due to their undifferentiated or primitive nature, tiny round cell tumors are particularly challenging to identify. It is typically simple to diagnose tumors that exhibit good differentiation, but when a tumor exhibits poor differentiation, it may be impossible to identify the diagnostic morphological features[2]. Around the world, cancer is the primary cause of mortality in children; each year, 300,000 children between the ages of 1 day and 19 years are given a cancer diagnosis.[3]. Leukemias, brain malignancies, lymphomas, and solid tumors, like neuroblastoma and Wilms tumor, are the most prevalent types of childhood cancer[3]. In many low- and middle-income countries (LMICs), only approximately 20% of children with cancer are cured, compared to more than 80% in high-income nations[4].

Materials and Methods

Cases were collected from pathology laboratories in As-Sadr Medical City and some private laboratories in Najaf over a 10-year period extending between 2010 and 2020. The study included only pediatric patients (1day - 19 years) of age who were diagnosed with SRCT. Elective data bases were reviewed over the 10 years period, extending from 2010 to 2020. A total 73504 surgical biopsy cases were reported, 6366 (8.7%) represent pediatric cases; furthermore, 108 cases diagnosed as SRCTs. Study group: 108 SRCT pediatric cases, the range of age of these cases was one day-19 years .

Results

During the 10 year-period, 2010 – 2019, a total of 73504 cases were reported in the department of Pathology in As-Sadr Medical City in Najaf Province and in some private laboratories in there including both pediatric and adult cases. Among them, 6366 pediatric cases were reported which represented 8.7% of all cases. Out of the 6366 pediatric cases, 108 cases with SRCT were giving a prevalence rate of 17 per 1000 pediatric cases and 1.5 per 1000 of total (73504) adult and pediatric cases during the same period (Table 1, Figures 1,2).

In 2010, the total surgical biopsy cases were 6143, pediatric cases were 306, and SRCT cases were 10 (27.8 prevalence per 1000 pediatric cases, and 1.6 prevalence per 1000 total cases).

In 2011, the total surgical biopsy cases were 5086, pediatric cases were 484, and SRCT cases were 4 (8.3 prevalence per 1000 pediatric cases, and 0.8 prevalence per 1000 total cases).

In 2012, the total surgical biopsy cases were 6960, pediatric cases were 634, and SRCT cases were 4 (6.3 prevalence per 1000 pediatric cases, and 0.6 prevalence per 1000 total cases).

In 2013, the total surgical biopsy cases were 4715, pediatric cases were 348, and SRCT cases were 12 (34.5 prevalence per 1000 pediatric cases, and 2.5 prevalence per 1000 total cases).

In 2014, the total surgical biopsy cases were 9773, pediatric cases were 1083, and SRCT cases were 7 (6.5 prevalence per

1000 pediatric cases, and 0.7 prevalence per 1000 total cases).

In 2015, the total surgical biopsy cases were 5817, pediatric cases were 502, and SRCT cases were 10 (19.9 prevalence per 1000 pediatric cases, and 1.7 prevalence per 1000 total cases).

In 2016, the total surgical biopsy cases were 8086, pediatric cases were 634, and SRCT cases were 13 (20.5 prevalence per 1000 pediatric cases, and 1.6 prevalence per 1000 total cases).

In 2017,the total surgical biopsy cases were 8836, pediatric cases were 740, and SRCT cases were 25 (33.8 prevalence per 1000 pediatric cases, and 2.8 prevalence per 1000 total cases).

In 2018, the total surgical biopsy cases were 10086, pediatric cases were 778, and SRCT cases were 10 (12.9 prevalence per 1000 pediatric cases, and 1.0 prevalence per 1000 total cases).

In 2019, the total surgical biopsy cases were 8002, pediatric cases were 803, and SRCT cases were 13 (16.2 prevalence per 1000 pediatric cases, and 1.6 prevalence per 1000 total cases) (Table 1).

Regarding the characteristics of the 108 SRCT pediatric cases , the mean age of these cases was 6.3± 1.6 (range: one month-19) years. The highest proportion of cases was reported in the age of 1-5 years, contributed to 43.5%, (Table 2). Males were more dominant than females; 59/108 vs. 49/108, respectively, with a male to female ratio of 1.2 to 1.0, (Table 3). No significant differences between both genders in all types of tumors (P>0.05) (Table 4). Across the age, Neuroblastoma, Wilms tumor and Retinoblastoma were noticeably more common in the younger age group., (P. value < 0.05). Ewing sarcoma was much more common in the older age group (P<0.05). No significant differences across the age in other types of tumors, (P>0.05) (Table 5).

Table1: Frequencies and Prevalence rates of SRCT in pediatric cases during the period 2010-2019.

Year	Total cases	Pediatric cases	SRCT	Prevalence per 1000 pediatric cases	Prevalence per 1000 total cases
2010	6143	360	10	27.8	1.6
2011	5086	484	4	8.3	0.8
2012	6960	634	4	6.3	0.6
2013	4715	348	12	34.5	2.5
2014	9773	1083	7	6.5	0.7
2015	5817	502	10	19.9	1.7
2016	8086	634	13	20.5	1.6
2017	8836	740	25	33.8	2.8
2018	10086	778	10	12.9	1.0
2019	8002	803	13	16.2	1.6
Total	73504	6366	108	17.0	1.5

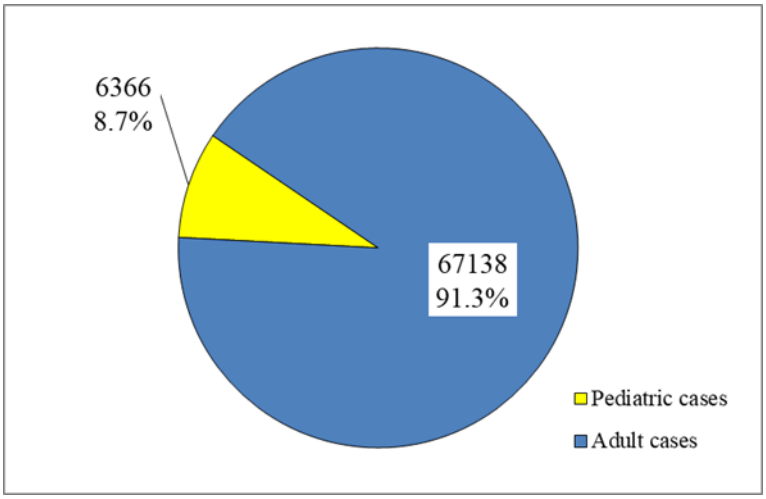

Figure 1: Overall cumulative prevalence rate of tumors pediatric cases during the period 2010-2019 in Najaf

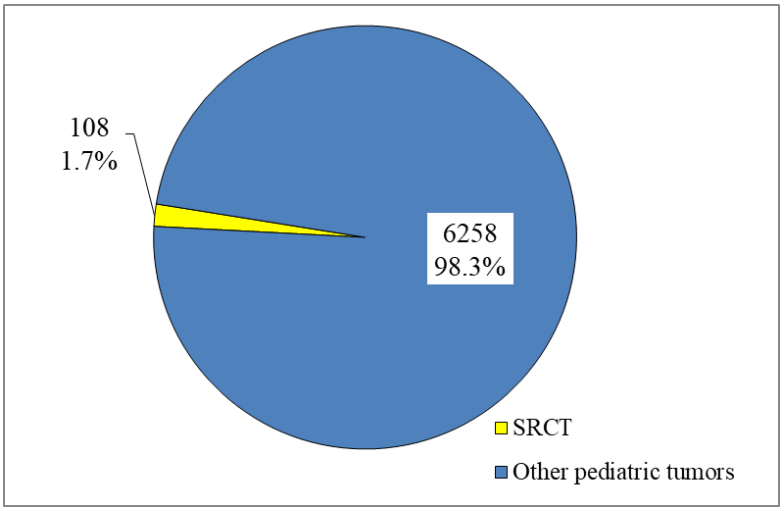

Figure 2: Overall cumulative prevalence rate of SRCT among all pediatric tumors during the period 2010-2019 in Najaf

Table 2: Distribution of 108 small round cell tumor pediatric cases in the last 10 years (2010-2019) according to Age

Age (year)	No.	%
< 1 year	18	16.7
1 – 5	47	43.5
6 – 10	15	13.9
11 – 15	18	16.7
15 – 19	10	9.3
Mean ± SD	6.3 ± 1.6	-
Range	One month- 19 years	

SD: standard deviation

Table 3: Distribution of 108 small round cell tumor pediatric cases in the last 10 years (2010-2019) according to gender

Gender	No.	%
Male	59	54.6
Female	49	45.4
Total	108	100
Male: Female ratio	1.2 : 1	-

Table 4: contrast among types of tumors based on gender of patient

Type of tumor	Total number	Male	Female	P. value*
Neuroblastoma	26	10	16	0.239
Wilms tumor	22	13	9	0.394
Ewing sarcoma	20	9	11	0.655
Retinoblastoma	17	8	9	0.808
Medulloblastoma	9	7	2	0.096
Alveolar rhabdomyosarcoma	4	3	1	0.317
Embryonal rhabdomyosarcoma	4	3	1	0.317
Hepatoblastoma	3	3	0	0.102
Lymphoblastic lymphoma	3	3	0	0.102
Total	108	59	49	0.220

Table 5: contrast among types of tumors based on age of patient

Type of tumor	Total No.	Age (years)					P. value
		< 1 year	1 – 5	6 – 10	11 - 15	> 15	
Neuroblastoma	26	12	10	2	2	0	**0.005 sig**
Wilms tumor	22	2	15	5	0	0	**0.002 sig**
Ewing sarcoma	20	0	2	3	10	5	**0.028 sig**
Retinoblastoma	17	2	14	1	0	0	**0.001 sig**
Medulloblastoma	9	0	5	2	1	1	0.189 ns
Alveolar rhabdomyosarcoma	4	0	0	0	1	3	0.317 ns
Embryonal rhabdomyosarcoma	4	0	1	2	1	0	0.779 ns
Hepatoblastoma	3	2	0	0	1	0	0.564 ns
Lymphoblastic lymphoma	3	0	0	0	2	1	0.564 ns
Total	108	18	47	15	18	10	**0.001 sig**

Discussion

In the present study, the most common type of SRCT was Neuroblastoma while the least common was Hepatoblastoma and Lymphoblastic lymphoma. Neuroblastoma was also common in other cancer registries compared, where it was more prevalent in a Japanese study published in 2017 [5], also in the western Australia pediatric cancer registry in 2008 [6] and pediatric cancer registry in England 2015 to 2016 Report [7]. It is worth noting that in the present study, Ewing sarcoma was the third most common SRTs while it moved to the last of the list in the Japanese study published in 2017 [5] and in the western Australia pediatric cancer registry in 2008 [6] while in another study done in Dohuk, Iraq (2020), it was reported that the Ewing sarcoma at the top of the list [8].

In regard to the tumors comparison according to gender, it has been found that neuroblastoma was more common in female gender (16 female,10 males) in the present study in contrast to pediatric cancer registry in England[7] where the incidence is slightly more in males. This study also describes the prevalence of neuroblastoma in Southern-Eastern Europe (SEE)[9]. However, in the western Australia pediatric cancer registry in 2008[6] the incidence was equal in both genders, Wilm's tumor was more common in male in our present study (13 males, 9 females) compared to the results of the western Australia pediatric cancer registry in 2008[6] , in contrast to the pediatric cancer registry in England 2015 to 2016 Report[7] where Wilm's was reported to be more common in females. Besides, in a study done by J.S. Ali et al., in sulaimanyah, Iraq (2018), they found that willms tumor is more common in females (29 female, 21 males)[10].

Ewing sarcoma in the present study females were reported to be more common than males (11 females, 9 males) while Munlima Hazarika et al, reported that Male: Female ratio was 1:1 in a study in 2020[11] . In contrast to the pediatric cancer registry in England 2015 to 2016 Report[7] , in which Ewing sarcoma is reported more in males, the same result was reported by Sazgar H. Majeed et al.,in Iraq (2019) [12] they reprted that from 31 pediatric ES patients overall 58% were male, and 42% were female. Retinoblastoma was slightly more in females in the present study (9 females, 8 males) which was similar to the result of Joshua F. A. Owoeye et al…who reported that male to female ratio of 1:1.2.in his study in 2008 [13] , in contrast to the reports of the western Australia pediatric cancer registry in 2008[6] , in which the incidence more in males than females.

Rhabdomyosarcoma was more common in male gender in the present study (6 males, 2 females) which was similar to the reports of registries of the western Australia pediatric cancer registry in 2008[6] and also similar to results of Häußler, S. M.,et al study in 2017 [14], including 28 patients (17 males, 11 females). Medulloblastoma in the present study was more common in male gender (7 males, 2 females); this is similar to results of Fruehwald-Pallamar, J., et al study [15] who reported that the ratio of male/female was 1.5:1 (38 males ,26 females). They also reported that males are more likely than females to have MB, with a male: female ratio of 1.8:1.

Lymphoblastic lymphoma in the present study was more commen in males (3 males, 0 females); this is comparable to the study of PATEL, Amol, et al in 2019 who found that male : female ratio of 2.25:1[16] and also comparable to the study of Sergio Cortelazzo ,et al. in 2017 who

report that males are more likely than females to have LBL, with a male to female ratio of 1.4..[17] Hepatoblastoma in our presnt study was more common in male gender (3males, 0 females) this result was comparable to what reported by Dawooda, L. J.,et al, in basara Iraq (2015)[20] . In regard to the comparison of tumors in relation to age groups, Neuroblastoma in the present study was significantly more common in children less than 1 year age group and (1-5 years) which was similar to Japanese study published in 2017[5] . Wilms tumor was more common in the age group (1-5 years) in a significant manner in the present study, similar to the reports of the comparable three registries (japan,WA, and England)[5-7] ; also similar to J.S. Ali et al., 8 in sulaimanyah, Iraq (2018) [10].

Ewing was significantly more common in the age group (11-15 years) in the present study with a P value of 0.028, which was similar Japanese study published in 2017 [5] and pediatric cancer registry in England 2015 to 2016 Report published in 2016[7]; it is also similar to study of Sazgar H. Majeed et al.,in Iraq (2019)[12] who reported that the average patient age upon diagnosis was 13 years. Retinoblastoma was more common in the age group (1-5 years) in the present study with a significant P value of 0.001; it was similar to a Japanese study published in 2017 [5], and to the western Australia pediatric cancer registry in 2008[6] ,pediatric cancer registry in England 2015 to 2016 Report published in 2016.[7] and report of Mohammed Faranoush, et al., in Tehran 2020[18].

Rhabdomyosarcoma in the present study Adolescents had a higher prevalence of alveolar RMS compared to younger children who had a higher prevalence of embryonal type. This result is similar to what reported by Perez, Eduardo A., et al.[19] Medulloblastoma in the present study was more common in (1-5 years) group, followed by (6-10 years) age group similar to a Japanese study published in 2017[5].

Lymphoblastic lymphoma in the study was more prevalent in the (11-15 years) age group but was not significant statistically, this is similar to what is reported by PATEL, Amol, et al (2019)[16], who found that median age was (12 years) while in Japan pediatric registry was more common in the (5-9 years) age group. These differences may be due to different environmental factors. Hepatoblastoma in the study was more prevalent in the (<1 year) age group, which was comparable the Japanese and England cancer registries [5,7] , while the study of Dawooda, L. J.,et al, in Basra- Iraq (2015)[20] showed more prevalence in (1-4 years) age group.

Conclusion:

The mean age of SRCTs cases was 6.3± 1.6 (range: one month-19) years. The highest proportion of SRCTs cases was reported in the age ranging from 1-5 years. Ratio of males to females 1.2 to 1.0. Neuroblastoma was the most common type while lymphoblastic lymphoma was the least one.

Conflict of Interest: None

Source of Funding: None

Ethical Clearance: Compliance with ethical standers.

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A Comparison of Tubular Minimal Invasive Surgery and Conventional Surgery in The Treatment of Patients Suffering from Single Level Lumber Disc Herniation (Short Term Follow Up)

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Abstract

Background :
Lumbar disc herniation is frequently-occurring and the most common spine-related disease in orthopedic surgery. However, nearly more than 50% of affected persons usually respond to conservative treatment. Furthermore, there is another group of patients who are suffering from incapacitating low back pain and sciatica although they have been treated for more than 6 weeks or who are suffering from early or progressive neurological impairment that required another approach far from the conservative treatments**.**

Aim of the Study
The present study is designed to unveil the most reliable procedure which should be most adopted for single level lumbar disc herniation in Iraqi patients **.**

Patients and Methods
A total of 40 patients who were suffering from back pain radiated to the lower limb were included in the present investigation. Out of them, 20 patients underwent open discectomy and the other 20 patients underwent tubular discectomy **.**

Results:
1**-**At the 10th day of postoperatively assessment, an obvious statistically significant decrease in the mean total Oswestry low back pain disability score was recorded in micro-tubular discectomy compared with the open discectomy (P<0.001)**.**
2**-**At the 6th month of postoperatively, the mean total Oswestry low back pain disability score was increased in both groups; nonetheless, there has still been a decrease in the micro-tubular discectomy group in comparison with that of open discectomy group (P<0.001).

Keyword: lumber disc herniation, micro-tubular discectomy, Open disctomy

Introduction:

The herniated disc occurs when the gel-like center of person's disc ruptures out through a tear in the tough disc wall. The gel material is irritating to the patient's spinal nerve, causing like a chemical irritation. Patients usually suffer from a pain as a result of the spinal nerve inflammation and swelling caused by the pressure of the herniated disc, which usually tends to decrease over time; patients then experience partial or complete pain relief. On the other hand, it was established that to deal with lumbar disc herniation, the open microdiscectomy was most reliable surgical treatment [1].

However, such an approach has now been replaced by the most recent one which is what was called minimally invasive procedures [2,3]. The main reasons behind the new trend is that while the open microdiscectomy is conducted by mobilizing the muscles laterally off the spinous process and lamina using a unilateral retractor, the new minimally invasive procedures relay on dilating the paraspinous muscles and using tubular retractors without stripping the muscles off the spinous process[4,5,6]. Obviously, such a new approach is now being recommended by many orthopedic surgeons because they thought that dilating the muscles rather than stripping them decreases the surgical morbidity [7,8,9]. Furthermore, it was established that the minimally invasive approach will have a great impact on the patients themselves. The patients with this approach will recover more quickly because of less tissue trauma [10], less postopertive pain, and finally lower blood loss.

Patients and Methods

Patient Selection

A total of 40 patients who were suffering from back pain that radiated to the lower limb were clinically diagnosed by a consultant physician according to standard patient's criteria and confirmed by MRI examination were included in the present study. All patients had a single level lumber disc with posterolateral herniation. Out of the 40 patients, 20 underwent open discectomy and the other 20 patients underwent tubular discectomy. The two groups were randomly selected with regard to the type of surgical operation, open discectomy or tubular discectomy, to avoid any bias in the selection that could affect the statistical outcome.

The present study was approved by the local Institutional Review Board of the University of Kufa, Faculty of Medicine in accordance with the 1964 Helsinki declaration and the revised form of 2015 and its later amendments. All the patients were informed of the aim of the present work and the possibility of publication of the results of the outcome of the surgery; all the patients willingly agreed to participate and a signed a written consent to indicate their willing to participate.

This prospective cohort study has been conducted during the period between February 2020 till June 2021. During that time, a follow up post-operation , on day 1, day 10, 6th week and 6th month, has been recorded with a special attention to the patients' pain and their return to work simultaneously.

All the surgical operations and the subsequent follow up were conducted by the same team which consist of two orthopedic surgeons and all surgeries in both approach were done by that team.

Criteria of Patients Selection

1- Patient with clinical examination signs of nerve root compression proved by MRI study.
2- Patient who do not respond to conservative treatment until 6 weeks.
3- Patient between 20 – 60 years old.

4- Patient with a single level lumbar disc herniation.

Exclusion Criteria

1- Patient with back pain but without radiculopathic symptom
2- Pregnant female patients
3- Patient with spinal stenosis
4- Patients whose dynamic x- ray and clinical examination show unstable symptom.
5- Multi-level disc herniation on MRI
6- Central disc herniation (cauda equina syndrome)

Surgical Procedure

1- Tubular Discectomy

All cases were performed under general anesthesia with endotracheal tube and in prone position. Before turning the patient to the prone position, the anesthesiologist shouldensure that intravenous line and endotracheal tube are secure and that appropriate personnel are available to prevent injury during the turn. A pad of cotton was placed on the patient face to avoid any injury to the face especially eyes in prone position. The head is positioned in horseshoe headrest, Complications of the prone position to which there must be constant attention are retinal ischemia and blindness from orbital compression. The abdomen of the patient was free to decrease the intra-abdominal pressure and decrease bleeding during laminotomy. After that, flexion to lumbar spine is done to make the discectomy easier by opening the disc space to allow pituitary forceps to get in easily in the disc space and start draping.

Then under fluoroscope determines the level of the prolapse disc by a lateral view and using a k- wire as a guide. After determining the required level, an anteroposterior view is taken by fluoroscope to ensure whether the exact site was right or left according to the spinous process.

One finger-breadth (1.5 c m) lateral to the midline on the symptomatic side of the patient at the appropriate disc level. All of the patients receive an antibiotic of a third generation cephalosporin one hour before skin incision as prophylactic dose. Typically, the surgeon stands on the side of prolapsed disc and fluoroscopic screen is located contralateral to the surgeon. An assistant is also standing on the contralateral side.

Then, the lamina appear then fenestration is done by starting with the inferior edge of the superior lamina of the surgical level, at the insertion of the ligamentum flavum, and continue laminotomy medially and laterally and cranially according to the surgical target, until complete visualization of the ligament. Then, flavectomy is done and the lateral part of the root will be in the field. Then we use root retractor to protect the root and insure that we are in the wanted disc space by aid of fluoroscope. Then discectomy done with pituitary rongeurs

After completing the decompression, the surgical field is washed with saline solution, and with garamycin amp 80mg in the disc space, to rule out any bleeding points. Hemostasis can be achieved with bipolar coagulation and the use of hemostatic agents, such as bone wax and gel foam. Complete hemostasis before closing is important as hematoma can cause compression of the neural elements, muscular pain, fibrosis and infection. Usually no drain is placed in lumbar tubular decompressive surgeries. Then, suturing is done layer by layer (fascia, subcutaneous and skin).

2- Open Discectomy

At the same position of tubular microdiscectomy, the level is determined by the aid of fluoroscope, 5-6 cm skin

incision is made mid-line, the fascia is opened, then the paraspinal muscle is stripped from spinous process, and then, according to clinical and MRI finding, we go direct to the site of pain without removing the spinous process. Then, a fenestration is done in the lamina and laminotomy is done to one side and then the flavectomy and the discectomy are done. Besides, the surgical site was irrigated with normal saline and the disc space was injected with 80 mg ampule of gentamycin. After that, a fat pad is taken from the subcutaneous layer and placed over the dura to decrease adhesion.

Both groups, open and tubular, received the same treatment to avoid any bias regarding VAS score which are:

1- Antibiotics (3rd generation cephalosporin) for 5 days .

2- Analgesia **a**- Paracetamol vial 1gm 8 hrs; **b**- Narcotics in form of TRAMADOL amp single dose day zero post op

3- fluid (Glucose Saline 1 pint 8 hrs.)

Results:

General characteristic of the studied groups:

As a baseline characteristic of the studied groups, eight persons, 21-30 years old, underwent a micro-tubular discectomy accounting to 40.0%; seven cases underwent an open discectomy representing 35.0% of the total cases. Furthermore, seven cases, aged 31-40 years, were subjected to a micro-tubular discectomy (35.0%) while six cases were subjected to an open discectomy representing 30% of the total cases. Again, three patients, 41-50 years old, experienced a micro-tubular discectomy and four persons experienced an open discectomy accounting 15.0% and 20.0% respectively. Finally, only five patients who were more than 50 years old were involved in the present investigation; two of them underwent an open-tubular discectomy while the other three underwent an open discectomy representing 10.0% and 15.0% respectively. In all of the compared cases above, no significant differences were observed (P = 0.922).

On the other hand, the mean age standard deviation (±SD) were (35.6 ± 9.2) for the micro-tubular discectomy and (36.4 ± 10.4) for the open discectomy, with no significant difference being found (P= 0.800).

Table 1 shows the demographic characterization of the patients in the present investigation: 14 males patients underwent micro-tubular discectomy and 12 males underwent open discectomy accounting to 70.0% and 60.0% of the total cases respectively. However, this study involved only 14 female patients: six cases underwent micro-tubular discectomy (30.0%) while 8 underwent open discectomy accounting to 40.0%. No significant difference was recorded with regard to gender (P=0.507).

As Table 1 shows, 18 married male patients underwent micro-tubular discectomy (90.0%) while 17 married male patients underwent open discectomy (85.0%). Yet, only two unmarried patients were subjected to micro-tubular surgery (10.0%) and three unmarried underwent open discectomy (15.0%). Again, no significant difference was recorded (P=0.723).

Finally, as for the occupation of the patients, five employed patients were exposed to micro-tubular discectomy and six employed ones were exposed to open discectomy representing 25.0% and 30.0% respectively. On the other hand, 15 unemployed persons underwent micro-tubular discectomy (75.0%) and 14 unemployed (70.0%) were subjected to open discectomy. No significant difference was observed with regard to the

occupation of the patients (P=0,723) (Table 1).

Table 1: Baseline characteristics of the studied groups

Variable		Tubular discectomy		Open Discectomy		P. value*
		No.	%	No.	%	
Age (year)	21 - 30	8	40.0	7	35.0	
	31 - 40	7	35.0	6	30.0	0.922
	41 - 50	3	15.0	4	20.0	
	> 50	2	10.0	3	15.0	
	Mean age ± SD	35.6 ± 9.2		36.4 ± 10.4		0.800
Gender	Male	14	70.0	12	60.0	0.507
	Female	6	30.0	8	40.0	
Marital status	Married	18	90.0	17	85.0	0.723
	Unmarried	2	10.0	3	15.0	
Occupation	Employed	5	25.0	6	30.0	
	Unemployed	15	75.0	14	70.0	

SD: standard deviation

*In all comparisons P. value is not significant

Site and level of the disc prolapse of the study groups

The total number of patients who had a left site disc prolapse surgical intervention were 20 cases; 11 were exposed to micro-tubular discectomy, accounting for 55.0%, and nine patients underwent open discectomy, representing 45.0% of the total cases. Likewise, the total number of cases who required right site surgical intervention were 20 cases as well. However, nine patients were exposed to micro-tubular discectomy and 11 cases went through open discectomy, accounting for 45.0% and 55.0% respectively. As indicated in Table 2, no significant difference was observed (P=0.527).

Out of the 20 cases exposed to micro-tubular discectomies, 11 patients underwent surgery at vertebral level of L5-S1 (55.0%), 8 had surgery at L4-L5 (40.0%), one experienced surgery at L3-4 (5.0%), none at L2 – 3 to an open discectomy. Out of the other 20 patients, 9 had surgery at L5-S1 (45.0%), ten had a surgery at L4-5 (50.0%), none at L3-4, and one at L2-3 (5.0%). A statistical analysis was conducted to see whether there was a significant difference between the two groups; in fact, no significant difference in the number of surgeries was observed (P=0.490) (Table 2).

Comparison of mean total Oswestry low back pain disability score of the study groups at different assessment points

The result of a comparison of mean total Oswestry low back pain disability scores of the studied group at different assessment points was grouped in Table 3. The mean total of Oswestry Low Back Pain Disability score for the 10 sections of the

Comparison of mean total Oswestry low back pain disability score of the study groups at different assessment points

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questionnaire was not significantly different in both groups pre-operatively as the mean was 35.05 ± 6.28 in micro-tubular and 33.20 ± 7.27 in open discectomy group,

Table 2: Site and level of disc prolapse characteristics of the studied groups

Variable		Tubular discectomy		Open discectomy		P. value
		No.	%	No.	%	
Site	Left	11	55.0	9	45.0	0.527
	Right	9	45.0	11	55.0	
disc prolapse level	L2-3	0	0.0	1	5.0	0.490
	L3-4	1	5.0	0	0.0	
	L4-5	8	40.0	10	50.0	
	L5-S1	11	55.0	9	45.0	

*In both comparison P. value is not significant

(P. value >0.05). At the 10th day assessment, a significantly lower total scores were reported in micro-tubular than open discectomy group, (P. value < 0.001). At the postoperative 6th week, a significant reduction was reported in both groups; however, the total mean score in micro-tubular discectomy group was significantly lower than that in the open discectomy group, (P value=0.003). At the postoperative 6th month, the total score increased in both groups; nonetheless, it is still lower in micro-tubular than open discectomy group, (P value<0.001) (Table 3).

Levels of disability in both study groups pre- and postoperatively:

Table 4 shows the levels of disability reported in both study groups pre- and postoperatively. It was obvious, that the level of disability (minimal, moderate and severe) which has been assessed revealed that in preoperative stage, the number of patients who were suffering from minimal disability and underwent micro-tubular discectomy was only one patient out of 20 cases accounting to 5.0%. However, the same number of cases (one patients) underwent open discectomy (5.0%). Out of the 20 cases, 15 persons were of moderately disability exposed to minimal micro-tubular discectomy (75.0%) while 17 moderately disable patients went through open discectomy representing 85.0% of the total cases. As for severe disability, 4 subjects were exposed to micro-tubular surgery and only 2 persons underwent open discectomy accounting to 20.0% and 10.0% respectively (Table 4). The results here show no significant difference between both groups at baseline level (P = 0.763).

Table 4 also reveals the assessment points of the level of disability after 10 days postoperatively; none of the patients still have sever disability in both groups, but those who became with minimal disability were more frequent in micro-tubular than open discectomy group, (P<0.001). Nonetheless, at the 6th week and 6th month post operatively, all patients became with minimal disability, (Table 4).

Table 3: Comparison of mean total Oswestry Low Back Pain Disability score of the study groups at different assessment points (Pre and postoperatively)

	Tubular discectomy		Open discectomy		P. value between groups (unpaired test)
	Mean	SD	Mean	SD	
Preoperative	35.05	6.28	33.20	7.27	0.394
Postoperative 10 days	20.30	2.45	30.70	2.58	<0.001 sig
Postoperative 6 weeks	1.05	0.94	2.40	1.60	0.003 sig
Postoperative 6 months	3.80	1.32	7.60	1.93	<0.001 sig
Percentage of reduction	89.2%	6.2%	77.1%	7.3%	0.032
P. value with group (paired t test)	< 0.001 sig		< 0.001 sig		

Table 4. Levels of disability reported in both studied groups pre and postoperatively

Assessment point	Disability level	Tubular discectomy		Open discectomy		P. value* between groups
		No.	%	No.	%	
Preoperative	Minimal	1	5.0	1	5.0	0.673 ns
	Moderate	15	75.0	17	85.0	
	Severe	4	20.0	2	10.0	
Postoperative 10 days	Minimal	12	60.0	0	0.0	**< 0.001 sig**
	Moderate	8	40.0	20	100.0	
Postoperative 6th week	Minimal	20	100.0	20	100.0	-
Postoperative 6th month	Minimal	20	100.0	20	100.0	-
P. value* within group	**<0.001 sig**			**<0.001 sig**		

sig: significant, ns: not significant
Chi square test used in comparisons between and within groups

Discussion

The present study is supported by the work of Kulkarni et al [11] who published his prospective study in 2014 using 188 consecutive patients exposed to tubular retractors for the treatment of herniated disc. All his patients were discharged within 24 to 48 hours' post-surgery. He concluded further after 1 week, 6 weeks, 3 months, 6 months, 12 months and 2 years by using VAS scale for leg pain which showed improving from 4.14 – 0.76 and also the mean VAS scale for back pain which showed improvement from 4.1 to 0.9. Furthermore, he reported that Oswestry disability index (ODI) changed from 59.5 to 22.6, that the microscopic-endoscopic discectomy (MED) is highly effective in the treatment of herniated discs with the advantage of minimal

postoperative morbidity and early postoperative recovery:

On the other hand, the present investigation is in disagreement with most recent work (Yadav et al. Medicine (2019) 98:50) who used VAS and ODI scores for clinical effectiveness assessment after the use of micro discectomy and open-lumber discectomy. They found a significant difference clinically and statistically between the VAS and ODI scores of the 2 groups after the first day postoperatively. After six weeks and six months follow up of both groups, the results were of a clinical improvement significant in each group but statistically not significant. Their work suggested an improvement in ODI in both groups. Further work has been published in 2016 by He J et all. 2016 [(12)], using meta-analysis protocol involving 501 patients and concluded that there were no any significant differences in the ODI and VAS between the micro-endoscopic and the open discectomy though the micro-endoscopic discectomy was associated with much less blood loss comparing with the open discectomy.

Indeed, as stated earlier our results showed equivocally, though ODI was not significant between both groups pre-operatively, at the 10th day assessment a significantly lower total score reported in micro-tubular than open discectomy group, (P. value < 0.001); at 6th week postoperatively, a significant reduction reported in both groups. However, the mean total score in micro-tubular discectomy group was significantly lower than open discectomy group, (P. value = 0.003). At the 6th month postoperatively, the total score increased in both groups; nonetheless, it is still lower in micro-tubular than open discectomy group, (P. value < 0.001), (Table 3 and Figure1). On the other hand, the current results also showed, beyond doubt, that a significant reduction was reported in VAS score in both groups with the time postoperatively, but the reduction in VAS score was more obvious in micro tubular group (P<0.001). Suggesting that the present work prefers the use of micro-tubular approach due to the differences in ODI scores between them in favor of the micro-tubular discectomy. Figures 1, and 2 demonstrate the change in mean total Oswestry low back pain disability and VAS score of the studied groups pre and postoperatively showing the change in mean total of ODI and VAS of patients who underwent micro-tubular approach in contrast with those patients who underwent open discectomy.

Conclusions and Recommendations:

The present study demonstrated an advantage in favor of minimal invasive tubular discectomy over the open discectomy techniques. Furthermore, much evidence and intensive research is highly recommended and powered by random and large clinical samples before any final conclusion could be reached to use this approach as standard treatment strategy for the lumber disc herniation.

Conflict of interests:

The authors declare that they have no conflict of interests.

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Evaluating Skull base Defect Reconstruction after Endoscopic Transsphenoidal Approach among Iraqi Patients

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Abstract

Background: Endoscopic skull base surgery is a well-established technique for the treatment of skull base pathologies. Once the resection is complete, reconstruction of the sellar floor is performed. Fat and fascia lata are used in an underlay fashion and then the dural sealant is placed over the repair.

Aim of the study: The study aims to assess the reconstruction of skull base defects after trans sphenoidal endoscopic surgery.

Patients and Methods: A total of 15 patients, 11 females & 4 males, were exposed to a cross-sectional study. The age of the participant ranged between 13 to 73 years old. The present work was carried out at Al-Hayat Private Hospital for the period starting from October 2017 to October 2021. All patients were followed up for at least 6 months' duration to assess the final outcome of the surgical operation. All the patients were informed of the aim of the study and they willingly agreed to participate; written consents were obtained from all of them.

Results: No CSF leak happened postoperatively in the patients. In spite of the small group of patients in the study, it can be concluded that the way of reconstructing the skull base has been effective

Key words: Skull base defects, Skull base pathology, trans sphenoidal.

Introduction

The nose develops from a number of mesenchymal processes around the primitive mouth during the fourth week of gestation. Collections of neural crest cells undergo proliferation and form the nasal placodes. Sinking of the nasal placodes leads to formation of the nasal pits which further deepen to form the nasal sac. Adjacent mesoderm cells proliferate to give rise to the medial and lateral nasal prominences of the frontonasal process which surround the nasal pit and sac to eventually become the nares. The maxillary processes grow anteriorly and medially to fuse with the medial nasal prominences and frontonasal process to close off the nasal pits and form separate nasal cavities. The primitive nasal cavity and mouth are initially separated by the bucco nasal membrane which gradually thins as the nasal sacs extend posteriorly and eventually breaks down to form the choanae. The lateral nasal prominences form the nasal bones, upper lateral cartilages and lateral crus of the lower lateral cartilages[1]. Tumors and pathologies in the skull base are a challenging problem to all surgeons due to difficult approaches and access in addition to high morbidity and mortality rate. With the increase in the popularity of skull base surgeries , transsphenoidal endoscopic surgery become important and used technique due to its flexibility with respect to classical techniques. These approaches allow to widen the surgical management horizon for many tumors even the more aggressive ones. However, reconstruction after resection in skull base surgeries and its potential for complications could affect patients quality life and satisfaction with the outcome[2,3]. Therefore, the present study tried to evaluate the procedure of reconstructing the skull base defects after transsphenoidal endoscopic surgery among 15 Iraqi patients who were operated on; data were collected in combined (retro-prospective) design.

Patients and Methods

Study design

This cross sectional study has been conducted during the period from 2017 to 2021 with follow up for 6 months duration. All cases performed at Al-Hayat Private Hospital in Najaf. All participants were informed about the study, and a written consent was obtained. A total of 15 patients, 11 females & 4 males, whose age ranged between 13 to 73 years, were included in this study.

Inclusion criteria

The patients subjected to present study were exposed to the same criteria which include :

a- preoperative evaluation
b- Surgical technique
c- Post-operative management

Exclusion criteria:

None.

Preoperative assessment

The following parameters were adopted prior to all the surgical protocol. Again, the same parameters were monitored for up to six months after the surgery .

Clinical parameters:

Signs and symotoms: like headache,, double vision watery rhinorrhea, etc.

Hormonal Analysis: The analysis included testosterone, follicle stimulating hormone (FSH), estradiol, cortisol, free thyroxin, corticotrophin, luteinizing hormone (LH), prolactin (PRL), thyrotropin (TSH), and growth hormone (LH).

Imaging:

Magnetic resonance imaging (MRI): All the patients were exposed to MRI to identify precisely tumor criteria prior to surgical intervention. Again, the patients were

referred for Coronal and axial computerized tomography (CT) where a CT scan helps in the evaluation of nasal cavity and paranasal sinuses anatomy, type of sphenoid sinus pneumatization and the attachment of its septa.

Ophthalmologic examination:
This examination was applied to symptomatic patients with optic chiasma compression.

procedure:
All cases were undergoing surgical operations under general anesthesia with endotracheal tube, and placement of throat pack. Endoscopic sinus surgery and skull base surgery sets should be prepared. The patient is placed in the supine position, with the operating table raised to 30 degrees and the head slightly extended is performed under general anesthesia with safe hypotension, maintaining a mean arterial pressure of approximately 70mm Hg. lumbar drain during and after the operation in all the patients were not put.

A 4 mm diameter and 180 mm length rigid endoscope, with zero, 30 and 45-degree lenses, applied to variable steps of the surgery were used. All patients underwent extended endoscopic end nasal transsphenoidal surgeries (EETS) which include the following steps :

A- a two nostril approach
B- removal of the middle turbinate
C- posterior septectomy
D- excision of vomer and sphenoid sinus walls to enable a wide access of the skull base for the so called four handed, two surgeons approach .
E- The sphenoid bone plenum, tuberculum Sella and upper and mid thirds of the clivus were dissected relative to the tumor invasion.
F- Multiple layer reconstruction was carried out for the repair skull base defect by using adipose tissue graft, fascia lata graft, (Gelfoam®) and dural sealant (Duraseal®).
G- fascia lata and/or fat were harvested by superolateral thigh incision.

The defects of the dura and the sella were plugged tightly with the fat and fascia lata and enforced by gelfoam and Duraseal. The fascia lata graft applied both intradural and extradural. Finally, the Duraseal was applied to the area and occluding the sphenoid sinus with the Duraseal .

The Dura Seal Sealant system consists of two dilute aqueous precursor liquids that crosslink to form a solid gel within 1-2 seconds of spraying. The resulting polyethylene glycol (PEG) based hydrogel sealant is adherent to tissue, strong enough to withstand elevated CSF pressures during the dura heals, and then breaks down and absorbs within 4-8 weeks. Following absorption, the liberated PEG molecules are then cleared primarily through the kidneys.

The gel also contains Blue dye, which allows accurate determination of applied sealant thickness and coverage. The PEG based hydrogel composition makes the sealant highly tissue compatible

All patients admitted to the ward, had Merocel® nasal packs inserted and removed at day 5 postoperatively, then the patients were discharged home (at day 6), and advised to have bed rest & avoid exercises and heavy lifting, and taken the following treatment:

A. Intravenous triple antibiotic (cephalosporin, gentamicin and metronidazole) .
B. Acetaminophen infusion on need.
C. Acetazolamide 500mg injection
D. Dexamethasone ampule
E. Desmopressin (in those who develop Diabetes Insipidus).
F. And patients are monitored for vital signs and measuring the urine output.

Post- operative assessment:
All patients assessed postoperatively at 10 days, 1st month, 3rd month and 6th month for monitoring the following parameters:

1 (-symptoms of hypotension and diabetes insipidus .
2 (-Hormonal Analysis:
The analysis included testosterone, follicle stimulating hormone (FSH), estradiol, cortisol, free thyroxin, corticotrophin, lutei-nizing hormone (LH), prolactin (PRL), thyrotropin (TSH) & growth hormone (LH).
3- (Imaging by MRI: To evaluate the extent of surgical resection.
4- (Ophthalmologic examination: This examination was applied to symptomatic patients with optic chiasma compression.
5- (-Histology biopsy was taken from the lesions for histopathological examination .

Statistical analysis:
All the obtained data were statistically evaluated by using statistical package for social sciences (SPSS version 26). Variables presented as frequencies (No.), percentages, mean and standard errors accordingly. Mean scores for items calculated as the average score of responses of patients toward items out of 6. Overall mean score calculated as the average of mean score for all items. Fisher's exact test was used to compare frequencies while Wilcoxon non-parametric test was used to compare the mean scores (pre vs. post-operative). Level of significance set at 0.05 and less to be significant. Finally, results were presented in tables and figures with an explanatory paragraph for each by using Microsoft Office Word and Excel Software version 2016.

Results

A total of 15 patients were enrolled in this study with a mean age of 36 (range: 13 – 73) years. Females were dominant with a ratio of 2.75 to one, (Table 1).

A computed tomography scan revealed that Pituitary macroadenoma was the more frequent detected pathology among the studied group which contributed to about 53.3% (8/15). Left sphenoid sinus mass in 2 patients (13.3%), other findings are less frequent, (Table 2).

Magnetic resonance imaging revealed macroadenoma, Invade Right cavernous sinus, encase carotid artery in 3 (20%) of patients for each, Press on optic chiasma in 2 (13.3%) patients; other findings are less frequent, in one patient for each (Table 3).

Macroadenoma was the more frequent Histopathological finding, it was reported in 7/15 (46.7%), Prolactinoma in 2 patients (13.3%), other findings are less frequent, in one patient for each, while 4 patients (26.7%) had negative Histopathological finding, (Table 4).

Table 5 shows a significant change in the mean score of patients' concerns about their appearance; it improved from a score of 4 to 5.7 postoperatively, (P. value < 0.05, significant). Also there was an improvement in concerns about weight and change in skin appearance but the difference did not reach statistical significance (P>0.05, not significant); patients reported that they did not have any concerns regarding easy bruising at pre- and postoperative, in both the mean score was 6/6. However, the comparison of overall mean score of patients concern revealed a significant increase (improvement); 5.05 at preoperative to 5.88 postoperative, (P<0.05), (Table 5). This was included in the patient's questionnaire to evaluate the effect of pituitary adenomas on the patient quality of life and post operatively and to assess patient improvement clinically.

Table 1. Age and gender distribution of the studied group

Variable		Value
Age (year)	Mean	36.0
	SD	15.9
	Range	13 – 73
Gender N (%)		Female 11 (73.3)
		Male 4 (26.7)

Table 2. Preoperative - Computed tomography scan findings of the studied group

CT finding	No.	%
Pituitary macroadenoma	8	53.3
Left sphenoid sinus mass	2	13.3
RT ethmoid sinus defect	1	6.7
Micradenoma	1	6.7
Mass in the right ethmoid extend to skull base	1	6.7
Defect in roof of RT.ethmoid sinus	1	6.7
CSF leak ,defect in right sphenoid sinus	1	6.7
Total	15	100.0

Table 3. Preoperative-Magnetic resonance imaging findings of the studied group

MRI finding	No.	%
Macroadenomas confined to the sella turcica	3	20.0
Macroadenomas with cavernous sinus invasion and/or carotid encasement	3	20.0
Macroadenomas compressing the optic chiasm	2	13.3
Ethmoid mass with intracranial extension	1	6.7
Defect with meningocele	1	6.7
CSF leak	1	6.7
Craniopharyngioma	1	6.7
Microadenoma	1	6.7
Left sphenoid meningoencephalocele	1	6.7
Defect with no meningocele	1	6.7
Total	15	100.0

Table 4. Preoperative -Histopathological findings of the studied group

Histopathology finding	No.	%
Macroadenoma	7	46.7
Prolactinoma	2	13.3
Craniopharyngioma	1	6.7
Extracranial meningioma	1	6.7
None	4	26.7
Total	15	100.0

Table 5. Comparison of pre and post-operative scores of patients' concerns

Item	Preoperative		Postoperative		P. value
	Mean	SE	Mean	SE	
Appearance	4.0	0.72	5.7	0.12	**0.026 ***
Weight	5.4	0.41	5.9	0.07	0.109
Changes in skin appearance	4.8	0.64	5.9	0.09	0.084
Easy bruising	6.0	0.00	6.0	0.00	1.00
Overall mean score for all items	5.05	0.39	5.88	0.07	0.025*

Score range 0-6, with 0 score for Too much concern about item, 6 score for not at all, *significant difference, SE: standard error of mean

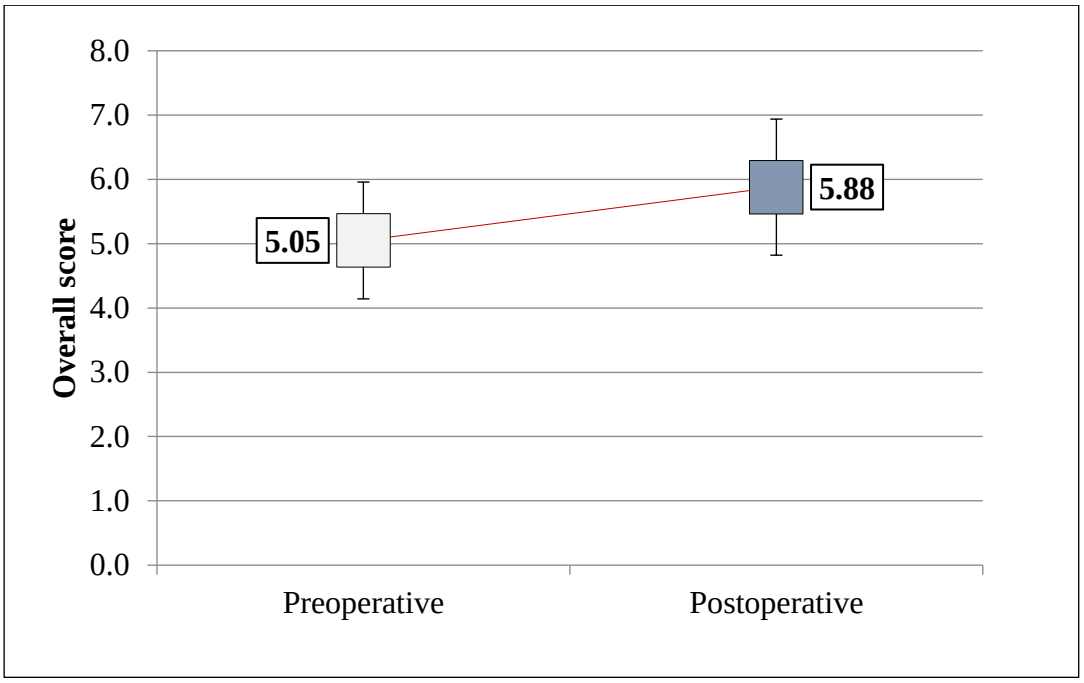

Figure1. A Comparison of pre- and post-operative overall scores of patients' concerns

There is a significant change in the mean score of patients' condition when they asked to rate the interference of their problem with their activities and life. In all items, the patients' scores increased significantly at postoperative evaluation, and the overall mean score was 1.89 at preoperative improved significantly to 5.78 at postoperative (P=0.001) about their appearance; it improved from a score of 4 to 5.7 postoperatively (P. value < 0.05, (Figure 1).Fig. 2 summarizes the mean scores of patients' problem at pre- and postoperative, where Headache, Rhinorrhea and Peripheral vision improved significantly (P<0.05). Other items were also improved where none of the patients further experienced a problem, at postoperative, but the difference did not reach the statistical significance. From a preoperative point of view, in some items such as crustations, diplopia, muscle weakness, swallowing food , irritability and inability to control anger, patients had no problem at all. The overall mean score for all items was improved but the difference was statistically insignificant, (Figure 2).

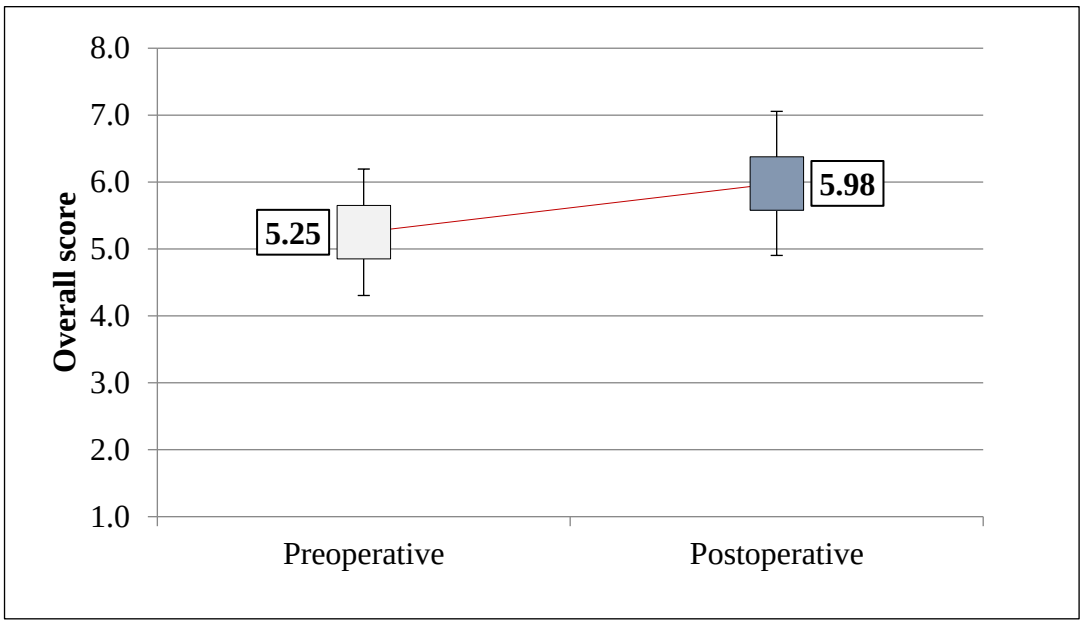

Figure 2: Comparison of pre and post-operative overall scores of patients' problems

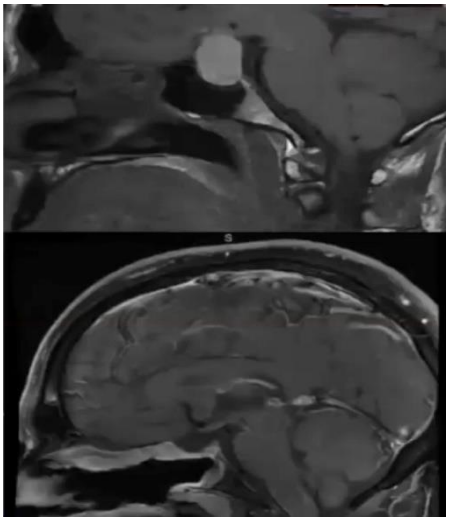

Figure 3. pituitary gland adenoma pre and postoperatively.

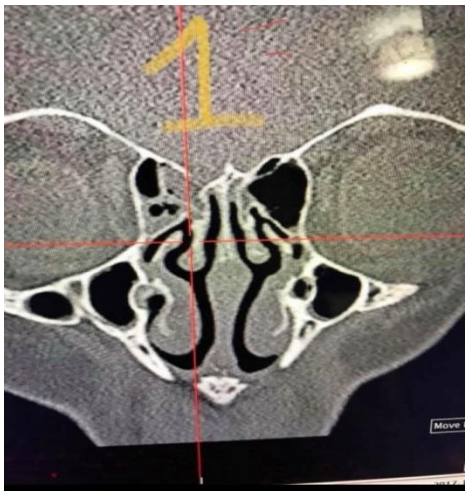

Figure 4. traumatic anterior skull base defect.

Discussion

It is well documented by many institutes that tumors and pathologies which affect skull base are too difficult to manage and considered to be the most obstacles to the majority of the surgeons. These obstacles attributed to the difficult approaches in addition to the high mortality and morbidity rates.

However, those difficulties have been eased by the invention of endoscopic trans sphenoid approaches which led to a lower rate of morbidity and mortality as a consequence[4] of the above approaches. The present study aims to evaluate the procedure of reconstructing skull base defects after trans sphenoidal endoscopic surgery among 15 Iraqi patients who were operated on. The data were collected in combined (retro-prospective) design (Table 1). The findings showed that the morbidity was significantly improved. They are in line with other investigators who reached the same conclusion [4].

On the other hand, CSF rhinorrhea is the most common complication following trans sphenoidal surgery (TSS) for pituitary tumors resection [4]. As a matter of fact, the cerebrospinal fluid leak through the nose is considered to be a popular problem that could be noticed after any trans sphenoid approach[4]. It has been shown equivocally that the frequency of this complication was in the range of 0.5% up to 15.0%. The non-adenoma tumor plus the existence of any leak during surgery associated with higher incidence of leak postoperatively in TSS. However, in the revision cases, it has been shown that the risk also increases if the patients exposed to radiotherapy [4]. However, according to the present study, the incidence of CSF leak is of zero percentage (0%) which attributed mostly to the low number of sample or low pressure pathologies or related to type of the reconstructed technique.

Furthermore, it has been reported that the incidence of Meningitis complication is about 0,4% - 9% [5]. Indeed, in the present study, no postoperative meningitis has been noticed because of either the absence of CSF leak in the present cases or probably the use of triple antibiotics which has been adopted in here though other investigations revealed that any postoperative CSF after leak could be an important factor for the presence of Meningitis after surgical operation [6]. On the other hand, further work reported a rare complication of postoperative CSF leak after the TSS (tension pneumo-

cephalus)[7]. No tension pneumocephalus complication was noticed during the course of the present investigation. It has been reported that Meticulous closure of the sellar defect has been applied to minimize or prevent any complications. Thus, cartilage, adipose tissue etc. has been used widely for Sella turcica reconstruction. This approach obviously aimed at preventing any postoperative CSF fistulas [8,9]). Indeed, the present study stress the use of fat, facia lata grafts, and dural sealant during skull base defect repair.

Conclusions:

The present study is in favor of the combination of fat graft, fascia lata graft, duraseal and gelfoam in the endoscopic repair of skull base defect though a much larger sample is highly recommended before any final conclusion could be reached.

Competing interests:

We have no competing interest to declare.

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