Assessment of the clinical concern about the non-malignant thyroid disorders in Sulaimani city – Kurdistan Region – Iraq

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الخلاصة

خلفية ألبحث: اضطرابات الغدة الدرقية-غيرالخبيثة مشكلة شائعة في أجزاءكثيرة من العالم ويؤثر على أعضاء مختلفةمن جسم الأنسان. ثبت أنه يؤدي إلى تخلف في النمو البدن و العقل. إن نسبة أنواعها السريرية تختلف في مناطق نقص اليود والمناطق المليئة باليود من العالم. تعتبر محافظة السليمانية ، إقليم كوردستان - شمال العراق منطقة جبلية معروفة ناقصة اليود.

الهدف: أجريت هذه الدراسة بغرض رؤية تقييم طيف السريري والاجتماعي لهذه الحالات وارتباطه مع فحوصات الدم المصلية للغدة الدرقية في السليمانية.

المنهجية: أجريت هذه الدراسة التحليلة المستقبلية على مرضى حالات السريرية والاجتماعية وعامل الخطر العائلي وكذلك التحاليل الدموية المختلفة في المرضى الذين يحضرون العيادة الجراحية الخاصة في السليمانية. شملت على 115 مريض (101 أنثى و 14 ذكر) من اضطرابات الغدة الدرقية غير الخبيثة خلال فترة ستة أشهر من 1 تموز إلى 31كانون الاول 2018. وقمنا بتقسيم المرضى إلى ثلاث مجموعات حسب إفراز هرمون الغدة الدرقية

النتائج: من 115 مريض (نسبة الإناث/الذكور:1/7) وجدنا التصنيف الوظيفي على النحو التالي: فرط 44.3٪، قصور35.7 ٪ ومع تضخم الغدة الدرقية السريرية أو العقيدات ولكن طبيعي وظيفيا 20 ٪. ألاعمارالأكثر شيوعًا للحالات تتراوح بين20-40 عامًا يليها العشرين عامًا القادمة. الحالة الزوجية للإناث وعددالولادات ومناطق جغرافية مختلفة في المحافظة لا تلعب دورًا مهمًا في اضطرابات الغدةالدرقيةالمختلفة.كان مؤشر كتلة جسم المرضى فوق وزن الطبيعي في (88.7 ٪) منهم. اما في تاريخ العائلي لاحظنا (اضطرابات الغدة الدرقية في 47.85 ٪ وماجلب الانتباه هو سرطان الغدة الدرقية 5.2٪ ومرض السكري 18.3٪). التشخيص بالموجات فوق الصوتية مفيدة لتحديد المظهر والحجم والسطح وعُقدة الغدة الدرقية. كان متوسط مستوى الهيموغلوبين (Hb) وكريات دم البيض ومعدل سكون كريات دم الحمر ضمن القيمة العادية (WBC&ESR) ما يقرب من نصف المرضى لديهم نقص فيتامينD.

الاستنتاج: كون محافظة السليمانية منطقة جبلية ناقصة اليود وباضافة اليود في ملح المستخدمة هنا نلاحظ تغير عرض وظيفي لاضطرابات الغدة الدرقية مقارنة مع عصر قبل الملح باليود. فرط نشاط الغدة الدرقية هو أكثر زيارات اولية للطبيب من قصورالغدة الدرقية. من ناحية أخرى تظهر في سن مبكرة وخاصة في الإناث. لم نجد اي فرق لانتشارالمرض بين مركز المدينة ومحيطها ولا في المناطق الريفية الجبلية العالية والتلال. سرطان الغدة الدرقية ومرض السكري وما قبل السكري أكثر شيوعا بينهم وعائلاتهم.

التوصيات: نحتاج تقييما دقيقا لدراسة تأثير الملح المخلوط باليود على تغيير عادات اضطراب الغدة الدرقية. في تاريخ العائلي لهذه المرضى ينبغي أن نكون على دراية الأقارب ليس فقط من الدرجة الأولى ولكن أيضا من الدرجة الثانية. واقترح دراسات أوسع نطاقا لهذه الاضطرابات الهامة.

ABSTRACT

Background: Non-malignant thyroid disorder is a common problem in many parts of the globe and affects different organ systems of the human body even proved to cause growth and mental retardation .These disorders are differences in frequency of clinical forms in iodine deficiency and iodine replete areas of the world. Sulaimani city, Kurdistan Region- North Iraq is a known mountainous iodine deficient region.

The aim: This study was undertaken with an objective to assess the spectrum of clinical concern of non-malignant thyroid disorders in correlation with thyroid serological blood tests in Sulaimaniyah city**.**

Methodology: A cross sectional study was conducted for the clinical presentation, risk factors and different hematological investigations in patients attending surgical private clinic in Sulaimaniyah. on 115 patients (101 female & 14 males) of non malignant thyroid disorders during the period of six months from July 1st to December 31st 2018. They were subjected to detailed clinical examination and biochemical blood tests.

Result: From 115 patients (female/male ratios: 7/1) presented with the functional classification thyroid disorder as follows: Hyperthyroidism 44.3%, hypothyroidism 35.7% and with clinical thyroid enlargement or nodule but euthyroid (functionally with normal thyroid function tests) 20%. The most common age of presentation is between 20-40 years, followed by 20 years. Female marital state, number of childbearing and a different geographical region in the city has no significant role in the different thyroid disorders. Body Mass Index (BMI) in 88.7% of the patients was above normal.

Conclusion: Thyroid disorders appear in earlier age especially in female than male patients. There is neither prevalence difference of the disease of Sulaimaniyah city center and periphery of the city nor in high mountain area and hill areas in rural area. Co- morbid Diabetes mellitus (DM) and pre-diabetes are more common in thyroid disorders and their families than normal. Thyroid cancer is more common in thyroid disorder families than the normal population.

Recommendation: Accurate evaluation of the effect of salt iodination on changing thyroid disorder habits. In family history of thyroid disorders not only first degree, but second degree relatives also should be aware of. Further wider studies suggested for these important disorders. These warrants further study.

Keywords: thyroid disorders, non-malignant, Sulaimaniyah, thyroid function tests, thyroid related antibodies, thyroid clinical presentations, family history thyroid related disease.

Introduction

Thyroid gland is the largest endocrine gland in the body that secretes hormones to regulate body metabolism. Imbalance in the secretion of these hormones can cause many disorders, which range from thyroid enlargement to life threatening diseases, such as thyroid cancer. (1)The diseases either lead to change in thyroid hormones secretion or structural changes such as in goiter with or without abnormal thyroid function. Thyroid disorders are prevalent condition affect 5% of the population [(2)] and world wide it is most abundant endocrine disorders after diabetes mellitus.[(3)] The functionally thyroid disorders may present, in relation to hormone production, as hypothyroid, hyperthyroid state in addition to gland enlargement (diffuse or nodular) with or without abnormal level hormone secretion . Thyroid disorders are leading causes of morbidity worldwide and remain under reported causes of premature mortality [(4)] Iodine nutrition is a key determinant of thyroid disease risk; however, other factors, such as ageing, smoking status, genetic susceptibility, ethnicity, endocrine disruptors and the advent of novel therapeutics, including immune checkpoint inhibitors, also influence thyroid disease epidemiology.[(5)] Iodine deficiency, autoimmune diseases (Graves' disease, Hashimoto disease and postpartum thyroiditis), pregnancy and other less common inflammation causes are the main cause of non-malignant thyroid disorders and goiter.[(6)] Most thyroid diseases are euthyroid then hypothyroid followed by hyperthyroid.[(7)] In iodine full areas most thyroid disorder persons have autoimmune disease (atrophic primary hypothyroidism, Hashimotto thyroiditis, Graves disease) in contrast to these, the most common cause of thyroid disorders is iodine deficiency. Almost one third of the world's population lives in iodine deficient areas and in areas of severe deficiency prevalence of goiter may reach 80% & populations with particular risk are remote and live mountainous area.[(1)] Further, the world health organization in (2012) estimates that 2 billion people worldwide still have iodine deficiency.[(8)] Goiter is a common disease in Iraq and it is more common in the North.[(9)] A national survey conducted in 1993 among 3004 school students in Iraq showed a prevalence of 24–44% for goiter.[(10)] This study, investigated the influence of socio-demographic characteristics on the clinical diagnosis of thyroid disorders with blood tests and sonographic relation in and associated factors in Sulaimaniyah – Kurdistan – Iraq.

Aim and objectives: This study was undertaken with an objective to assess the spectrum of clinical concern of non-malignant thyroid disorders in correlation with thyroid serological blood tests in Sulaimani city**.**

Methodology

Study design: A cross sectional study was conducted for the clinical presentation, risk factors and different hematological investigations in patients attending surgical private clinic in Sulaimaniyah.

Data collection:

Data were collected from patients attending private clinic for 6 months from July 1st 2018 to December 31st 2018. They were subjected to detailed clinical examination and biochemical blood tests. Accordingly, patients divided into three groups of thyroid diseases (hyper-functioning, hyperthyroidism, normal functioning (Euthyroid) and hypo-functioning (hypothyroid). Then other factors correlated. In addition to these complete blood count (CBC),

which includes hemoglobin level (Hb) and white blood cell (WBC), Erythrocyte Sedimentation Rate (ESR), lipid profile test and vitamin-D3 (Vit D) in some other cases were done. Ultrasonography (U.S.) was performed for suspicious nodular or enlarged thyroid glands

Study criteria: Through a pre-prepared questionnaire for this purpose. The inclusion criteria of the cases made on clinical suspicion of thyroid disorders and accordingly related blood investigations done. Age, Gender, Body Mass Index (BMI) and Socio-demographic state of the patients are determined.

Exclusion criteria: pediatric group under age of 16 years, patients from other cities of Iraq and malignant thyroid diseases in which period our enforced only one case.

Study analysis: Data were analyzed through by using SPSS-V21 (statistical package for social science-Version 21). At the beginning, descriptive statistic (frequencies and percentages) & inferential statistic like the Chi square test was used to find an association between studying variables. A P-value of <0.05 considered to be statistically significant.

Result

The present study showed of all 115 patients who attend private clinic and presented with thyroid disorders. The total mean age for both genders =37years, but Female means age alone is 33.42 and Male mean age is 38.93**.** The total female: male ratio is (7/1).

Table (1): Gender relation to diagnosis, age and BMI classification

	Female no.(%)	Male no.(%)	Total no. (%)	P-value
Association between Gender & Diagnosis				
Hyperthyroid	42(41.6)	9(64.3)	51(44.3)	0.225
Euthyroid	22(21.8)	1(7.1)	23(20.0)	
Hypothyroid	37(36.6)	4(28.6)	41(35.7)	
Total no.(%)	101(100.0)	14(100.0)	115(100.0)	
Age classification (years)				
< 20 y	3(3.0)	1(7.1)	04 (3.5)	0.133
20 – 40	63(62.4)	5(35.7)	68 (59.1)	
40 – 60	30(29.7)	8(57.1)	38 (33)	
> 60	5(5.0)	0(0.0)	05 (4.3)	
Total	101(100.0)	14(100.0)	115(100.0)	
BMI clssiffication				
Under weight	3(3.0)	0(0.0)	3(2.6)	0.214
Normal BMI	8(7.5)	2(14.3)	10(8.7)	
Over weight	22(21.8)	7(50.0)	29(25.2)	
Class I obesity	33(32.7)	3(21.4)	36(31.3)	
Class II obesity	24(23.8)	1(7.1)	25(21.7)	
Class III obesity	11(10.9)	1(7.1)	12(10.4)	
Total no.(%)	101(100.0)	14(100.0)	115(100.0)	

On the basis of clinical and thyroid function tests patients grouped as follows: Hyperthyroidism 44.3%, hypothyroidism 35.7% and Euthyroid (with clinical thyroid enlargement or nodule) 20%. In both genders presentations with hyperthyroidism is more than the other two categories.

The table above shows that 59%of the participants are aged between 20-40 years, followed by 33% of them aged of the next two decades.

Body Mass Index (BMI): BMI was calculated based on the formula: BMI = Weight (Kg)/ {Height (m)} ^{2} . For BMI classification, the WHO –Europe table nutritional status used for categorizing the patients. Nearly One third (31.3%) of the patients are Class I Obese. One quarter (25%) of the patients is overweight. One fifth (21.7%) of the patients are Class II Obese (Serious obesity). One tenth (10.4%) of the patients are Class III Obese (severe obesity). Only 2.6% are underweight.

Table (2): Patient's Demographic data

Demographic data	Frequency	Percentage (%)
Occupation		
Housewife	81	70.4
Employee	23	20.0
Student	5	4.3
Shop keeper	4	3.5
Farmer	2	1.7
Total	115	100
Residence		
Sulaimani Centre	47	40.9
Qaladza+ Rania	17	14.8
Halabja+ Hawraman	8	7.0
Arbat	5	4.3
Chamchamal + Bazian	15	13.0
Saidsadiq + Penjween	9	7.8
Kalar + Darbandixan	14	12.2
Total	115	100.0
Marital state		
Married	93	80.9
Single	22	19.1
Total	115	100.0

Occupation: Housewives 70.4%, followed by employee 20% and 10 % others. **Residence:** Only 40.9% are from the city center of Sulymaniyah. **Marital state**: 80.9 %of patients are married.{ married male 9 (64%), to married female 84 (83%)} **Signs and symptoms:** Commonest signs and symptoms at presentation of the patients (in decreasing order) were: weakness, palpitation, anxiety, shortness of breath, hotness, anterior

neck mass, sweating, tremor, menstruation irregularity, anterior neck tightness and heaviness, numbness, weight loss, constipation, headache palpable thyroid , hair loss, dimness , hoarseness of voice, weight gain, aches, eyelid puffiness, tender thyroid, feeling cold , pallor, snoring, carpal tunnel syndrome, dysphagia , exophthalmos, irritability, depression, growth retardation, leg edema.

Table (3): Association between Gender and (Hba1c, lipid profile)

	Female no.(%)	Male no.(%)	Total no. (%)	P-value
Association between gender and HbA1c (no. 56)				
Normal	43(86)	5(83.3)	48(85.7)	0.665
Prediabetic	3(6.0)	0(0.0)	3(5.4)	
Diabetic	4(8.0)	1(16.7)	5(8.9)	
Total	**50(100)**	**6(100)**	**56(100)**	
Association between gender and lipid profile (no. 52)				
Normal	26(61.9)	7(70.0)	33(63.5)	0.464
High	16(38.1)	3(30.0)	19(36.5)	
Total	**42(100.0)**	**10(100.0)**	**52(100.0)**	

The tables (1 & 3) showas that there is no significant association between gender and the factors of age, BMI, diagnosis, HbA1c and lipid profile.

Table (4): Different thyroid functional classification relation to other factors (dyslipidemia, Hb., WBC, ESR & vitamin D)

	Hyperthyroid	Euthyroid	Hypothyroid	Total (%)
Dyslipidemia (n=52)				
Dyslipidemia	6 (11.5%)	2 (3.8%)	11 (21%)	19(36.5%)
Association between thyroid disorders and mean (Hb, WBC, ESR)				
Hblevel gm/dl. (female/male)	12.14 /12.9	12.1/12.5	12.0/14.9	12.1/13.43
WBC (female/male)	8.57/7.81	7.36/3.8	8.0/6.22	8.0/6.22
ESR (female/male) (n=61)	28.8/23.3(26/6)	18.125/0(8/0)	28.1/3.5(19 /2)	25/13.4(53/8)
Association between thyroid disorders and Vitamin D3 (ng/ml) in n=67				
Deficiency (up to 20) F/M	17 (15/2)	8 (8/0)	10 (9/1)	35 (32/3)
Insufficiency (21-29) F/M	6 (5/1)	4 (3/1)	5 (4/1)	15 (12/3)
Sufficient (30-149) F/M	4 (4/0)	4 (4/0)	8 (7/1)	16 (15/1)
Toxicity (>150) F/M	0 (0/0)	0 (0/0)	1 (1/0)	1 (1/0)
Total: F/M	27 (24/3)	16 (15/1)	24 (21/3)	67 (60/7)

Blood investigations:

The TSH is low at 44.3% of the patients, high at 35.7% and normal in 20% of them. FT3 low in 16.7% of the patients, high at 23.1 % and normal in 60.3% of them. FT4 low in 20.6 % of the patients, high at 29% and normal in 50.5% of them.

The HbA1C of 56 patients show normal value in 85.7%, 8.9% Diabetic and 5.4% pre-diabetic. Lipid profile, any one of lipid profiles were abnormal accordingly categorized into high or low group, and we found two-third of the patients that investigated for this test are belonging to normal profile and only one-third have a high lipid profile.
Anemia is defined as hemoglobin (Hb) levels lower than 12 g/dl in women and 13 g/dl in men.[11] In altogether our patients mean Hb level was within normal range 12.26 gm/dl (female 12.1 gm/dl , male 13.43 gm/dl). In hyperthyroid male patients mean Hb level was just below the lower normal limit (12.9 gm/dl) but in female within normal limit (12.4gm/ dl). In euthyroid patients it was within normal limit in female (12.1gm/dl) but below the normal limit in male (12.5gm/dl) patients. In hypothyroidism the female mean Hb level was at the lower normal limit (12gm/dl) in contrast to male patients that was normal value (14.9gm/dl). In other words mean Hb female patients lowest in hypothyroid to higher in euthyroid then hyperthyroid, but in male patients from euthytroid to hyperthyroid and lastly hypothyroid.
White Blood Cells (WBC): The White Blood Cell (WBC) Count of 4,500-10,000 white blood cells per cubic millimeter regarded as an approximate Normal Range. Mean total 8 cell/mm^3 [female: 8.1 cell/mm^3 , male: 7.3 cell/mm^3]. All over Mean WBC for both sexes is normal 8 cells/mm^3 and same for all different disease are within normal limit with higher in female than male, but male mean WBC in euthyroid cases was below normal level (3.8 cell/mm^3).
Erythrocyte Sedimentation Rate (ESR) : Mean total patients ESR is 19.2mm/hr. Mean ESR in females is 25mm/hr but in male patients 13.4mm/hr. Mild elevated ESR in male hyperthyroidism 23.3mm/hr but with normal value in all other male and female patients. The lowest mean level of ESR seen in hypothyroid male patients 3.5mm/hr, and the highest mean level found in hyperthyroid females 28.8mm/hr. Still the last two readings are within normal value.
Vitamin D3: Nearly half of the patients have vitamin D3 deficiency, more in hyperthyroid than hypothyroid followed by euthyroid patients. The other half of the patients equally have either sufficient or insufficient vitamin D3 levels, but sufficient vitD3 were twice in hypothyroid to hyperthyroid patient, only one female patient has vitamin D3 toxicity due to over oral use of this type of medicine.

Ultrasound: The findings according to sonographist's impression of total 78 patients were:
1.Nodularity: no nodule in 51%, single nodule 19% but multiple nodules in 30%.
2.Normal appearance 23%, thyroiditis 73% and Graves disease 4%.
3.Surface: heterogeneous 68% but homogenous 32%.
4. The Size of the gland: normal 46%, enlarged 28% and smaller than normal in 26%.

Table (5): family history of medical diseases among thyroid disorders.

	Hyperthyroid	Euthyroid	Hypothyroid	Total (%)
Family history of medical diseases (n=80)				
Hyperthyroidism	7	2	9	18(15.7)
Hypothyroidism	13	6	12	31(27)
Thyroid carcinoma	3	0	3	06(5.2)
Diabetes Mellites	9	5	7	21(18.3)
Hypertension	3	1	0	04(3.5)

Family history (first and second degree relatives) of chronic diseases: Thirty five patients (30.45%) have no family history of any of the mentioned diseases in table but the remaining 80 patients (69.55%) has these diseases. Thyroid disorders 47.85% (hypothyroidism 27% + hyperthyroidism 15.65% + malignant thyroid diseases 5.2%). Diabetes mellitus 18.3%. Hypertension 3 .5% **.**

DISCUSSION:

The most common cause of thyroid disorders worldwide is iodine deficiency, leading to goiter formation and hypothyroidism. In iodine-replete areas, most persons with thyroid disorders have autoimmune disease.[12] The high prevalence rate of thyroid disorders around the world and also in Iraq seems to associate with iodide deficiency. Since 1965 till end of the previous century, many studies shown iodine deficiency, thyroid disorders more in north of Iraq than middle and south of the country[13]. Using iodizing salt started in Iraq since 1990 continues till now and this policy affects the frequency and the type of different thyroid disorders in this community. Being Sulaimaniyah city, a mountainous iodine deficient area and using iodine – salt supplement here and all Iraq changed functional presentation of thyroid disorders comparing to an era before salt iodination. Hence hyperthyroidism is more seen at present than hypothyroidism. In this study, the high frequency of first time patients presentation of thyroid diseases seen in form of hyperthyroidism followed by hypothyroidism and then euthyroid in the form of thyroid enlargement or nodules in spite of that, these differences are statistically not significant at (P-value =0.226). Our result is in agreement with the study done in Baghdad [13] by AL-Faisal, A. et al. As hyperthyroidism is more than hypothyroidism but not in that euthyroid goiter is more than hyperthyroid cases, reminding that their study included only women, this may prove that difference. Adding iodine supplement to salt with a probability of environmental pollution may cause changes in the behaviors of thyroid disorder in our country. Our patients, living in the mountainous iodine deficient area by using iodinated salt, have a mixed behavior of presentation of iodine depleted and iodine replete regions of the world. Reminding that some thyroid diseases, especially autoimmune type, present with hyperthyroidism in an early state, then by time, will change to hypothyroidism in the end phase of the disease. In addition to high iodine intake regions and this may be the cause of that in other studies hypothyroidism is more common. This presentation differs from society to another also increased with age progress with the prevalence of 1-2% in the world to 4-5% in the developed countries. [4, 14, 15]

Regarding the gender, it is well known that thyroid disorders predominantly affect females. We found the frequency of the thyroid disorders is seven times higher in female than male. This is near and similar to other studies, females to male ratio is (6:1). This female predominance in their prevalence could be due to effects of female sex hormones, prolactin and estrogen, the last hormone has a direct effect on thyroid tissue and enhance the development of goiter, nodule and cancer in women, moreover of the X chromosome which may play a role. [2,16,17].

In terms of age, the age range was above 16 years**.** The peak age of the diseases, six of ten patients, aged is between 20-40 years, followed by three of ten patients age of the next two decades. In female patients higher number seen in same manner age groups, but in male patients more seen in 40-60 years (57.1%) followed by younger age 20-40 years age (35.7%). These results are statistically not significant (P Value = 0.133).

Total age means for both genders is 37 years, but Female mean age alone earlier is 33.42 and Male mean age is 38.93. The total mean age in hyperthyroid or hypothyroid patients are same 36.5 but for euthyroid age mean is 39. These results are shown that female patients are more prone to thyroid disorders at an earlier age than male, which mostly related to their physiology and gonad hormones. These results are in agreement with other studies by R.D. Olmos et al. From Brasil in 2015 [2,18] on the other hand disagree with two other study findings by Jimmy Antony et al 2014 and Maheshwari P et al. 2017 . [17,19] We can observe that we are more prone to thyroid diseases at an earlier age than other developed countries and its cause may be multi-factorial including diet, genetics and water supply.

In regards to occupation, housewives were 70.4% followed by employee 20%. it is logic to be found more in these groups as thyroid diseases more seen in women and most of our city women are housewives, who are not employed. Though there is some studies referred to cosmetics containing thyromimetic substances used by females may play a role in thyroid disease and in other different employees may be related type of stress of works and burden of life may prone them to this disorders but actually till now this is not proved and still no study done in our region to support or reject these findings.[20,21]

In terms of residency, as the prevalence and incidence of thyroid disorders depends on geographic areas and most importantly the amount of iodine intake of the population [19]. In the current study, Only four out of ten of the patients are from the city center of Sulymaniyah. In comparing association of residence, geographical area for the diagnosis of the thyroid diseases between the center of Sulaimiyah and periphery, we found that there is no significant difference (P-value : 0.282). This can mention that the disorder is related to water supply and food type consumption, which are now nearly same in these different places. Regarding rural areas of Sulaimaniyah, we found that there is no difference between high mountainous area & low mountainous (hill) area in the prevalence of the disease.

The highest BMI range was found in 88.7% of the patients and only 2.6% are underweight. According to these findings most of our patients are above normal range weight and this may be related to the community body mass index for, which we couldn't find a study in our population the BMI distribution. On the other hand, most of our patients, especially females have sanitary

type of life with less care to exercise and self body weight alert. In spite of the fact that many patients of this study presented with hyperthyroidism still high BMI is clearly seen among most of patients with thyroid disorders. So patients BMI before acquiring the disease to be compared to BMI after getting the thyroid disorder is more informative as overt thyroid dysfunction affects body weight. Clinical hypothyroidism causes an increase in body weight, while hyperthyroidism reduces it.[22] At the same time obesity, especially central obesity, is related to many endocrine abnormalities, including thyroid dysfunction (thyroid hormone regulates energy, thermogenesis and plays a important role in metabolism of glucose and lipid), food intake and the oxidation of fatty acids and mild thyroid dysfunction causes significant changes in body weight regarded as a risk factor for overweight and obesity. [23] Both gaining weight and losing weight are well known conditions of functional thyroid disorders either hypothyroid or hyperthyroid conditions.

Most of thyroid disorders, clinical signs and symptoms are not clear or specific all times, can be found with other different non thyroidal diseases in human beings. Symptoms of thyroid diseases in the normal aging and the elderly people are very similar. Generalized weakness and easy fatigability are main presentation than other symptoms in most age groups and depend on the type of the thyroid dysfunction. This supports other studies done for elderly patients. [24,25] We found that these findings can be the presentation for most of other age group patients complaining these disorders as well and may superadded by palpitation, anxiety, feeling shortness of breath, hotness, anterior neck mass in these patients .
The two common endocrinopathies found in the general population are diabetes mellitus and thyroid disorders. As thyroid hormone is insulin antagonist and thyroid disorders may have an effect on dyslipidemia and vascular endothelial dysfunction these may boost the cardiovascular disease risk in diabetic patients. [26] Furthermore, diabetes mellitus affects thyroid function tests to variable extents and several reports documented a higher than normal prevalence of thyroid dysfunction in the diabetic population. Some studies demonstrated an overall prevalence of 11% and 13.4% of thyroid diseases in diabetics. [15,27]**.** In our study, we found the correlation in the opposite direction, that Diabetes mellitus also common in thyroid disorder patients when we detected HbA1C of our patients. The combined diagnosed diabetic and pre-diabetic patients reaching about 13.3% (8.9% Diabetic and + 5.4% pre-diabetic). Autoimmunity has been implicated to be the major cause of thyroid-dysfunction associated diabetes mellitus also same thing is true for diabetes in thyroid disorder patients with a normal population prevalence Type2 DM is 3.16%.[28] This indicates a fourfold increase in susceptibility of thyroid disorders patients to gain DM than the normal population. Regarding the definition of first degree relatives (FDR) includes the parents, siblings, or children of an individual and second degree relatives (SDR) includes aunt, uncle, grandparent, grandchild, niece, nephew, or half-brother or –sister].**[29]** Chronic disease history in (first and second degree relatives) of the family among our patients shown: Thyroid disorders, 47.85% (hypothyroidism 27% + hyperthyroidism 15.65% + malignant thyroid diseases 5.2%). Hypothyroid is nearly twice hyperthyroid in the family and this is expected as the end stage of most of all types of thyroidits is hypothyroidism. Nearly half of our patients have a family history of at least one of these thyroid disorders including

malignant thyroid disease. Surprisingly, we noticed that family history of thyroid cancer reaches 5.2% of our patients. Comparing this with the fact that approximately 1.2% of the population will be diagnosed with thyroid cancer at some point during their lifetime, based on 2013-2015 data.[30] This fourfold high prevalence of different thyroid cancers among families needs more family genetic evaluation and detailed precise investigation for those with a family history of thyroid disorders. At the same time during history taking of thyroid disorder patients we should take family history of both first and second degree relatives because we found four times thyroid cancer is common in families of thyroid disorders than the normal population. Other family related disease which found to be not overlooked is Diabetes mellitus which again common in family members of thyroid disorder patients reaching 18.3%. This may support combined genetic, autoimmune and environmental factor may play a role. This needs more wide and meticulous study.

High-resolution ultra sound US, which is non-invasive, widely available, less expensive, and does not use any ionizing radiation is the most wide imaging modality available for examination of the thyroid gland and associated abnormalities. In several early autopsy surveys, up to 50% of patients had thyroid nodules. But the incidence of thyroid nodules is very high on US, ranging from 50% to 70% [31,32] In our study ultrasonography findings were shown, only half of the patients have a single thyroid nodule or multiple nodules, with multiple nodules more than single nodule of ratio 3 : 2. This result goes side by side with previous mentioned autopsy and US study findings. Because of high specificity US can differentiate normal thyroid from Graves' disease or Hashimoto's thyroiditis. Endocrinologists recommend a radioactive iodine uptake test to determine if someone has Graves' disease in addition to the serology and US [33,34,35] On reminding that the radioactive iodine uptake test is not available in our region and nearby Iraqi cities at the moment, we diagnosed only 4% of the cases of Graves disease on US bases. These to be corresponded to clinical and serological findings. Some study shown that the ultrasound can detect early changes in autoimmune thyroid diseases even before thyroid antibody positive (TPO Ab) in autoimmune thyroid diseases [31] In our patients nearly one quarter normal appearance but the remaining of eighteen times thyroiditis than Graves disease at diagnosis mentioned. These encourage the US, non invasive useful investigation, to be done by expert hands to help early and easier diagnosis. Similarly, it is helping in some extent to exclude malignancy or to do a more invasive test like fine needle aspiration to reach the diagnosis.
In terms of Lipid profile, among this study population, patients were normal in about two-third of the patients (63.5%) but higher than normal range (at least one of them) in another one-third (36.5%). Comparing this with the study on Iraqi young adult (20 – 40) hyperlipidemia where the prevalence was 75%. [36] Our result of dyslipidemia is same as prevalence in Chinese (34%) and less than Iranian (51.8%) people.[37,38] We found that in general thyroid disorder do not increase risk of dyslipidemia and the vice versa may be true. And this will not go in the same direction of that dyslipidemia is more commonly detected in elderly patients with thyroid abnormalities as reported by Gesing A in 2012. [24] and the age factor may be the cause of this discrepancy. Dyslipidemia more seen in hypothyroid than hyperthyroid and euthyroid patientients.[39]

With regards to the value of **Thyroid stimulating Hormone (TSH)** Thyroid-stimulating hormone (TSH) is a glycoprotein hormone secreted by the anterior pituitary and is used to classify our patients into three categories of hyperthyroid, euthyroid and hypothyroid in which the subclinical conditions of hyper or hypothyroid are included in overt state of each of them. In the negative feedback mechanism TSH is central and a little variation in thyroid function leads to dramatic changes in TSH secretion it is regarded as screening tests[40] and it's shown that over 95% accuracy patients thyroid state can be classified accordingly. The diagnosis of thyroid dysfunction was TSH dependent on first line investigation after clinical examination of our patients. [19, 41] In this study, TSH is low at 44.3% of our patients, high at35.7% and normal in 20% of them. This specifies that functionally hyperthyroid presentations are more than hypothyroid. This may be explained by the transitional zone of the low iodine region that supplied with iodine salt state of these years and sometimes may be hyper-iodine-salty food ingestion in some families may be the risk factor of increasing hyperthyroidism as iodine excess may lead to thyrotoxicosis. This needs reevaluation of iodine-salt supply and more detailed investigation of our hyperthyroid patients to find any possibility of iodine over feeding, in addition to thyroid autoimmune diseases. Interms of **FT3 and FT4**: Because it doesn't depend on thyroid binding protein changes, after TSH test, FT4 is regarded as the second line test to investigate TSH abnormality conditions, or where TSH measurements are known to be unreliable. In contrast to that only indication of free T3 (FT3) measurement, in addition to the occasional patient on T3 replacement monitoring, is to diagnose T3-toxicosis if FT4 is not above the reference range in a patient with a low serum TSH. [41] Our results shown mostly these two free hormones go side to side for diagnosing the functional state of thyroid hormones and this supports these previously mentioned studies. Regarding **anemia, s**ome studies said that anemia, which is associated with a decrease in hemoglobin concentration is a frequent clinical condition accompanying thyroid disease. Thyroid dysfunction induces different effects on blood cells, such as anemia, erythrocytosis, leukopenia, thrombocytopenia and in rare cases cause pancytopenia. Although anemia and thyroid dysfunction often occur simultaneously, the causative relationship between them still not clear, but mostly through erythropoiesis by thyroid hormone stimulation and at the same time iron deficiency anemia may affect the negative thyroid hormone status.[42,43,44] In altogether our patients mean hemoglobin level were within normal range 12.26 (female 12.1, male 13.43). Only in hyperthyroid male patients mean Hb was just below the lower normal limit (12.9**)** but in female within normal limit (12.4). In other words , in female patients the lowest mean Hb seen in hypothyroid with higher in euthyroid then hyperthyroid, but in male patients from euthytroid to hyperthyroid and lastly hypothyroid. These findings are not going parallel with these mentioned studies, but support contra idea of other studies that found the abnormal thyroid hormone levels is a rather infrequent finding among adults with anemia. [45,46] Still no concrete relation found between thyroid disorder and anemia. Regarding **White Blood Cell (WBC) count,** all over Mean WBC for both sexes is normal 8000 cell/mm^3 and at the same time for all different these thyroid diseases are within normal limit, Higher normal level in female than male but male mean WBC in euthyroid cases was below

normal level (3.8 cell/mm^3). This agree with other studies that shows WBC count did not have significant differences in thyroid diseases and gender differences but mild decrease in WBC detected in euthyroid male patients is not reaching state of agranulocytosis which can lead to sever serious infection and this low level may be temporary.[46,47]
In regards to **Erythrocyte sedimentation rate (ESR)** which is one of the popular Acute-phase reactants that involve in pro-inflammatory molecules in different inflammatory diseases. The normal ESR value range is 0-22 mm/hr for men and 0-29 mm/hr for women. We observed that the mean total patients ESR are 19.2mm/hr. In female patients is 25mm/hr but in male patients 13.4mm/hr. We agree with a study by Hou X etal. In 2015 who stated that ESR in patients with nodular goiter was normal reading [42] but disagree with another study by Savas E etal. who mentioned that ESR was significantly elevated in patients with hypothyroidism, hyperthyroidism and in patients with autoimmune and non-autoimmune thyroid disease in a significant extent.[48]
This doesn't confirm the role of inflammation in the pathogenesis of all these thyroid dysfunctions regardless of type of the thyroid dysfunction but maybe only in some of them. We regard that ESR is not a good, strong and dependable marker for diagnosis and follow up of thyroid disorders except in few cases like inflammatory thyroid diseases and is temporary.
Vitamin D3 deficiency is a global health problem. Over a billion people worldwide are vitamin D deficient or insufficient. Both vitamin D3 and thyroid hormone bind to similar steroid hormone receptors (VDR) in which a different gene predisposes to AITD. We found that nearly half of our patients have vitD3 deficiency and this is still within normal range of the disease prevalence reported in a study in Iran that described the prevalence of vitamin D deficiency among adult population was 14-59% and in the USA, Canada and Europe is 30-50% with higher percentage in middle east. The other half of the patients nearly equally have either sufficient or insufficient vitD3 levels. In spite of many studies reported that patients with Hashimoto's thyroiditis and hypothyroidism had lower vitamin D3 levels still there is no clear, powerful studies support the direct relation between vitamin D3 deficiency and thyroid diseases or potential role and effect of vitamin D3 in prophylactic and treatment of thyroid disorders.[14,49,50]

Conclusion:

Functional presentation of thyroid disorders changed from the era before of salt iodination and hyperthyroidism is more seen at present than hypothyroidism with mixed behavior of presentation of iodine depleted and iodine replete regions of the world. Thyroid disorders here appear in an earlier age, especially in female than male patients. Marriage and total higher number child bearing do not increase risk of thyroid disorders. There is no prevalence difference in Sulaimaniyah city center and rural area. Furthermore, any difference in high mountainous area and hill areas. Co- morbid Diabetes mellitus and pre-diabetes are higher in thyroid disorders than the normal population and the autoimmune state may be the explaining factor for this. Besides Diabetes found more in families of these thyroid disorder patients. Family history of thyroid disorders we should take history of first and second degree relatives because nearly half of the patients have at least one of the relatives ha thyroid disorder and we found thyroid cancer is four

times more common in thyroid disorder patients' families than the normal population. Ultrasonography inexperienced hand is helpful to reach the diagnosis. The ESR and WBC counts are not a good indicator for diagnosis and follow up of thyroid disorders except in a few cases.

Recommendation:

Accurate evaluation of effect of salt iodination on changing thyroid disorder habits. Searching for possibility of seasonal variation of flu and viral pathogen infection cross antigen with thyroid receptors for the autoimmune thyroid diseases. In family history of thyroid disorders not only first degree, but second degree relatives also should be aware of. Improved public awareness and understanding of thyroid disorder is essential among people for earlier diagnosis and treatment of thyroid disorders. These warrants further study.

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