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CONTENTS

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IMPACT OF SERUM AMYLOID A IN EARLY DETECTON OF ENDOTHELIAL ENGARY BY PERCUTANEOUS CORONARY INTERVENTION

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ABSTRACT

Background: Evidence of elevated serum levels of inflammatory and restenosis markers afterpercutaneous coronary intervention (PCI), including balloon angioplasty and stenting has been reported in various population. The utility of serum amyloid A in early diagnosis of endothelial cell damage of coronary arteries by cardiac ballooning and stenting still uncertain. The aim of the present study was to determine the validity of serum amyloid A in early diagnosis of endothelial cell damage of coronary arteries by cardiac ballooning and stenting.
Methods Serum amyloid A and high sensitive c-reactive protein (Hs-CRP) was determined in a sample of 137 patients attended diagnostic cardiac angiography unite at Sulaimaniyah Center of Heart disease,68 cases were previously diagnosed with coronary artery lesions, underwent coronary ballooning and stenting, and 69 patients with chest pain underwent diagnostic angiography, free of coronary artery lesion participated in this study . The alteration in serum amyloid A and Hs-CRP levels was estimated before and after 4 hours from procedure.
Results: The comparison between cases and controls showed that the 2 groups did not differ significantly with respect to age, gender, ethnicity, hypertension, diabetes mellitus and smoking.The pre- and post-operative mean values of Hs-CRP were similar in cases and controls. The post-operative cases exhibited significantly higher serum amyloid A levels than controls and the difference was statistically significant (p=0.001).The usefulness of serum amyloid as a screening test for endothelial injury was assessed by calculating its validity with regard to cut-off point of Hs-CRP. The post-operative cases with Hs-CRP > 3 mg/l had a higher prevalence 54.0% of amyloid A compared with those of Hs-CRP <3 mg/l. (46.0%, p=0.001).
Conclusions: It is evident from this study that post-operative cases underwent coronary ballooning and stenting had high serum amyloid Aproteinlevels. It thus indicates the needs for determining serum amyloid A in patients at risk of early coronary endothelial injury.

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Keywords: Amyloid A, Hs-CRP, Coronary endothelial damage

Serum amyloid A (SAA) is protein which regarded as a major component of the acute-phase inflammatory response synthesized by the liver and also from some extrahepatic source response to infection, inflammation, injury, and stress dramatically 1000-fold greater than normal within 5-6 hours after

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stimuli. It can be regarded as proatherogenic and proinflammatory marker[1]. Percutaneous coronary intervention (PCI) including balloon angioplasty and stenting has become a first line management of stable angina and acute coronary syndromes; however restenosis is still occurring in approximately 30% of all patients after procedure as unfavorable physiological response to stent implantation[2].

Serum cardiac markers provide diagnostic and prognostic information that may reflect critical elements involved in the evolution of an acute coronary syndrome. With inflammation now recognized as contributing to atherogenesis, inflammatory proteins have been investigated as potential indicators of underlying atherosclerosis as well as unstable athermanous lesions[3]. Elevated levels of C-reactive protein (CRP), the protypical acute phase protein are associated with adverse cardiovascular outcomes in patients with stable and unstable ischemic heart disease and as well as healthy men without clinical vascular disease. Similar to CRP, serum amyloid A is found to identify a population of patients who remain at increased mortality risk[4]. It has been reported that amyloid A represent the inflammatory marker of the coronary stenosis with highly predictive of the risk for cardiovascular events even within 3 years, while the level of Hs-CRP was not associated with cardiovascular heart disease[5]. Serum amyloid A, also an important acute phase protein, has an expanded dynamic range with different kinetics compared with CRP and is reported to be a more sensitive indicator of inflammation in some non-cardiovascular inflammatory conditions[6]. However, serum amyloid A has not been examined as extensively in endothelial damage of coronary arteries by cardiac ballooning and stenting.

METHODS

A case control study was conducted at Sulaimaniyah Center of Heart Disease, Sulaimaniyah Teaching Hospital in Kurdistan Region during the period November 2014 to February 2015. A heterogeneous group of 137 adult patients of both sexes (91 males and 46 females) who attended cardiac angiography unit in the above center were included. Of these 68 patients previously diagnosed with coronary artery lesions (48 males and 20 females), underwent coronary ballooning and stenting (case group). The reminder (n=69) were patients with chest pain admitted to the center for diagnostic coronary angiography (43 males and 26 females), served as a control group. Protocol involved that: all patients undergo percutaneous cardiac angiography; during the period of the study were interviewed

and informed about the nature of the study. After the patients signed an informed consent form, pre and post cardiac intervention blood samples were collected for Amyloid A and Hs-CRP measurement. The study protocol was approved by the scientific research and ethics committee of the Kurdistan Board of Medical Sciences. Permission was obtained from administrative authorities of Sulaimaniyah Center of Heart Disease and Sulaimaniyah Central laboratory and doctor Saman laboratory.

The specimen collection from the patients was carried out using venous blood collected in two different times, first one were taken before patients undergoing cardiac interventions, usually were around 7:30 AM to 10:30 AM, while the second specimen were taken after 4 hours from cardiac intervention, usually were around 12 PM to 4 PM. Five millers of blood has been taken from each patient and transfer in plain tube. The blood specimens left a room temperature for 20 mints, and then centrifuged at 3000 rpm for 10 minutes. Serums were separated and pipetted in to plain tubes for storage at -40 0C, till the day of analysis. Serum amyloid A was measured using enzyme-linked immune sorbent assay (ELISA),kit assay manufactured by Shanghai YEHUA biological technology Company. Quantitative Hs-CRP protein measurement was done by using Cobas Hs-CRP reagent kit in c 311 Cobas analyzer. The assay system uses immune-turbidometric method through latex particles coated with antibody specific to human CRP (monoclonal anti CRP antibody) aggregated in the presence of CRP from the sample forming immune complex.

Statistical analysis was performed using SPSS version 18 software for windows. Data are presented as mean+SDE. Differences in frequencies for categorical variables were assessed by the chi-square test. We compared the groups using the independent-sample t-test. A p-value of less than 0.05 was considered statistically significant in all data analyses.

RESULTS

The baseline characteristics of the 137 men and women included in the analysis are shown in table 1. Overall, males comprised 66.4% of the study subjects and females comprised 33.6% of the study population. Age group subjects in 50-69 years had a higher incidence as compared to the other age groups. The majority of the study subjects were Kurd ethnicity. The cases and controls did not differ significantly with respect to age, gender, ethnicity, hypertension, diabetes mellitus and smoking.

Baseline characteristics for the cases and controls with previous cardiac history are presented in table 2. None of the control

had any history of traditional cardiac intervention including previous and current stent implantation number. Increasing mean stent number values were exhibited in the study cases (0.26 to 1.87).

Table 1: Baseline characteristics of controls and cases

Variables n (%) n (%) Age (years)	Controls (n =69)	Cases (n=68)	*P* value
<50	16(23.2)	10(14.7)	0.289
50-59	21(30.4)	20(29.4)	
60-69	25(36.2)	24(35.3)	
≥70	7(10.1)	14(20.6)	
Gender			
Males	43(62.3)	48(70.6)	0.305
Females	26(37.7)	20(29.4)	
Ethnicity			
Kurd	66(95.7)	48(70.6)	0.11
Others	3(4.3)	8(11.8)	
Hypertension			
Yes	43 (62.3)	41(60.3)	0.808
No	26 (37.7)	27(39.7)	
Diabetes mellitus			
Yes	23(33.3)	23(33.8)	0.952
No	46(66.7)	45(66.2)	
Smoking			
Yes	11(15.9)	15(22.1)	0.361
No	58(84.1)	53(77.9)	

Table 2: Baseline characteristics of cardiac history in cases and controls

Variable	Controls (n=69)	Cases (n=68)	*P* value
Previous stent number	0.00 ± 0.00	0.26±0.07	0.002
Operated vessel number	0.00 ± 0.00	1.35±0.04	0.001
Current stent number	0.00 ± 0.00	1.87±0.09	0.001
Balloon inflation mean pressure	0.00 ± 0.00	15.84±0.13	0.001

Results: SEM

The comparison between cases and controls are summarized in table 3. As expected, the post-operative cases exhibited significantly higher serum amyloid A levels compared to controls. However the difference was not statistically significant (p=0.064). A significant difference has been noted in amyloid A levels (p=0.01) in post-operative cases as compared to pre-operative group.

Table 3: Serum Hs-CRP and Amyloid A levels in cases and controls

Markers	Controls (n=69)	Cases (n=68)	*P* value
Hs-CRP (mg/l)			
Pre-operative	9.30±2.75	7.72±2.06	0.705
Post - operative	9.20±2.71	8.18 ±2.19	0.809
Difference	-0.10 ±0.02	0.45±0.02	0.180
Amyloid A (mg/dl)			
Pre-operative	9.50±0.69	10.65±1.09*	0.405
Post-operative	9.86 ±0.68	12.59±1.20	0.064
Difference	0.36±0.01	1.94±0.38	0.001

Results: SEM, * Pre- vs post-operative, p=0.01

The usefulness of serum amyloid as a screening test for endothelial injury was assessed by calculating its validity with regard to cut-off point of Hs-CRP (table 4). The post-operative cases with Hs-CRP > 3 mg/l had a higher prevalence 54.0% of amyloid A compared with those of Hs-CRP <3 mg/l. (46.0%, p=0.001).

Table 4: Comparison of post-operative Serum Amyloid A with cut-off value of Hs-CRP among the studied subjects

	Hs-CRP post-operative			
	≤3mgL	>3mg/l	Total	*P* value
Amyloid post-operative,	n(%)	n(%)	n(%)	
Normal	54(43.9)	69(56.1)	123(100.0)	0.001
High	9(64.3)	5(35.7)	14(100.0)	
Total	63(46.0)	74(54.0)	137(100.0)	

DISCUSSION

This study provided definitive evidence that post-operative cases underwent coronary ballooning and stenting had high serum amyloid Alevels. The best difference of amyloid A was in the pre- and post-operative cases. However, no such a difference was observed with regard to Hs-CRP.

As percutaneous coronary angiography is a novel non-surgical technique for opening coronary arteries occlusion, by using a set of specialized balloons and stents, the procedure may stimulate immune system and causing variable degree of inflammation response upon inflation by balloon and implanting the stent[7,8]. Restenosis has been occur in many patients after percutaneous coronary intervention, as a result of inflammatory process, which is start by endothelial injury followed by intimal proliferation, and smooth muscle migration in the corresponding vessel[9]. So inflammatory proteins will be a hall mark of prediction of early endothelial injury and expectation for late outcome. It is therefore, in this study the impact of serum amyloid A in early detection of endothelial injury in comparison with Hs-CRP was carried out. For both, cases who underwent coronary artery angioplasty by inserting balloon or stent and controls who underwent only diagnostic coronary angiography, serum amyloid A and Hs-CRP were estimated before and after 4 hours from procedure. The pre- and post-operative serum amyloid A values ranged from 1.25 to 13.75 mg/dl and from 3.1 to 48.79 mg/dl, respectively. In addition, the post-operative cases exhibited significantly higher serum amyloid A levels than controls and the difference was statistically significant with a p value=0.001.

Considering the difference in risk factors across countries, cases underwent coronary ballooning and stenting have significantly higher levels of acute phase proteins compared with non-ballooning or stenting (control group). This withstanding that the majority of study population are Kurdish ethnicity (92%), hypertensive (61.3%), and with diabetes mellitus (33.6%). This will associated with higher coronary plaque burden aggressive coronary disease[10].

Because Kurdish ethnicity were more contribute in this study, this may lead us to have a queries for looking to other unmeasured underlying risk factors associated with aggressive coronary disease, regarding this ethnicity for

example negative emotion and anxiety, and this is in agreement with other studies in different ethnicity specially Hispanic[11]. However, none of the control group has history of previous stent, whereas some of cases had history of previous stent with P value =0.002.

As the inflammatory proteins are circulating freely in the serum of patients in response to much acute or chronic inflammatory process, we collected a blood sample in two occasions for each control and case group, to exclude any baseline elevation of inflammatory protein. Our results shows Pre- and post-operative serum Hs-CRP values ranged from 0.7 to 224.3 mg/l and from 0.81 to 221.1 mg/l, respectively. The mean values of Hs-CRP were similar in cases and controls with p value =0.180, which was statistically not significant, in agreement with other study that show decreasing inflammation response by using drug eluting stent[12]. The finding was also in agreement with other study that shows a decrease inflammatory response by clopidogrel preoperatively[13]. Additionally all patients in case group were treated with unfractionated heparin as an anticoagulation agent to prevent coagulation and lead to inhibition of inflammatory response[14].

The usefulness of serum amyloid A protein as a screening test for endothelial injury was assessed by calculating its validity with regard to cut-off point of Hs-CRP. We noticed that post-operative cases with Hs-CRP>3mg/l (as a high risk for coronary artery injury) had a higher prevalence 54.0% of amyloid A by comparison with those of Hs-CRP <3 mg/l. (46.0%, p=0.001), which was statistically significant.

These finding is a positive step to support serum amyloid A as better sensitive marker for early inflammatory process and endothelial injury in comparison with Hs-CRP for late coronary stent outcome.

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پوختە

ئاستێ (Amyloid A) دناف خوینێدا ژبو دەست نیشانکرنا پێشوەخت یا پیچبونا دەمارین دلی لدەف نەخوشێن پێداچون ددەمارێن دلی دا (PCI) بو هاتیە ئەنجامدان

پاشەکی و ئارمانج: بلندبونا ئاستێ هێمایێن کولبونێ و دوبارە تەنگبونێ پشتی نشتەرگەریا پیداچونێ ددەمارێن دلی دا وەك بالون و توربێ یا هاتیە تومارکرن ل دەف گەلەك جڤاکان. بکارئینانا ئاستێ (Amyloid A) دناف خوینێدا ژ بو دەست نیشانکرنا پێشوەخت یا پیچبونا دەمارین دلی لدەف نەخوشێن پێداچون ددەمارێن دلی دا (PCI) بو هاتە ئەنجامدان ب رێکا بالون و توربێ هەتا ڤی دەمی نەیا دوپاتکریە.

ریکێن ڤەکولینێ: ئاستێ (Amyloid A) و(Hs-CRP) هاتە سنورکرن دنمونەیەکا پێکهاتی ژ١٣٧ نەخوشان ئەوین سەرەدانا هوبا وێنەکرنا دەمارێن دلی ل سەنتەرێ سلیمانیێ یێ نەخوشیێن دلی پشکداری دڤێ ڤەکولینێدا کربو. ٦٨ نەخوش بەری دەمێ ڤەکولینێ هاتبونە دەستنیشانکرن کو ئیشێن دەمارێن دلی هەنە و پێداچون ددەمارێن دلی دا ب ریکا بالون و توربێ بو هاتبو ئەنجامدان، ئو ٦٩ نەخوش ئیشانا سینگی هەبو وینەکرنا دەماران یا دەستنیشانکرنێ بو هاتبو ئەنجامدان بەلێ بێت ڤالا بوون ژ ئیشێن دەمارێن دلی. گورانکاری د ئاستێ (Amyloid A) ئو (Hs-CRP) هاتنە هەژمارتن بەری و چوار دەمژمێران پشتی نشتەرگەریێ.

ئەنجام: بەراوردیکرن دناڤبەرا نەخوشێن دلی ئو بێن ڤالا ژوان دیارکر کو چ جودایی ب رەنگەکێ بەرچاڤ نینە دگەل ژیی، رەگەزی، نفشی، بلندبونا فشارا خوینێ، نەخوشیا شەکرێ، ئو جگارە کیشانێ تیکرایێ ئاستێ (Hs-CRP) یێ وەك هەڤبو ل دەف هەردوو گروپان بەری و پشتی نشتەرگەریێ، ئاستێ (Amyloid A) بلندتر هاتە دیارکرن ب شیوەکێ بەرچاڤ ل دەف نەخوشێن دلی پشتی نشتەرگەریێ ژ ئەوین ڤالا ژنەخوشیین دەمارین دلی (p=0.001). مفادایا بکارئینانا ئاستێ (Amyloid A) دناف خوینێدا وەکو پشکنینەکا لیگەریانێ بو بریندارببونا شانێن ژناڤدا یێن دەمارێن دلی هاتە هەلسەنگاندن ب هەژمارتنا ڤالیدیتیا وێ دگەل خولەکا هەڤبرینێ یا (Hs-CRP) . نەخوشین پشتی نشتەرگەریێ ئەوێن ئاستێ (Hs-CRP) پتر ژ (3 mg/L) ریژەکا بلندتر یا بەربەلاڤبونێ (54.0%) یا (Amyloid A) پشتی بەراوردی کرن دگەل وان کەسان یێن ئاستێ (Hs-CRP) کێمتر ژ (3 mg/L) (P=0.001, 46.0%).

دەرئەنجام: ئاستێ پروتینێ (Amyloid A) بلند هاتە بەرچافکرن دڤێ ڤەکولینێدا لدەف نەخوشێن پێداچون ددەمارێن دلی دا (PCI) بو هاتیە ئەنجامدان ب ریکا بالون و توربێ. ژبەر ڤێ چەندێ یا گرنگە ئاستێ (Amyloid A) بهێتە سنورکرن ل دەف نەخوشین مەترسی هەی بو بریندارببونا شانێن ژناڤدا یێن دەمارین دلی یا پێشوەخت.

الخلاصة

مستوى (Amyloid A) في مصل الدم في التشخيص المبكر لتلف الشرايين القلبية عند مرضى التداخل القسطاري (PCI)

المقدمة والاهداف: ارتفاع مستويات مؤشرات الالتهاب وأعادة التضييق بعد التداخل القسطاري (PCI) كالبالون والشبكية اصبحت مؤشرات مدونة في مجتمعات مختلفة. استخدام مستوى (Amyloid A) في مصل الدم في التشخيص المبكر لتلف الخلايا المبطنة للشرايين القلبية بسبب البالون و الشبكية غير مؤكدة لحد الان.

طرق البحث: حددت مستوى (Amyloid A) و(Hs-CRP) في نموذج من ١٣٧ مريض زارو وحدة تلوين الشرايين القلبية التشخيصي في مركز السليمانية لأمراض القلب ٦٨ منهم تم تشخيصهم قبل ذلك بمرض الشرايين القلبية وخضعوا للتداخل القسطاري بواسطة البالون والشبكية و٦٩ منهم عانوا آلام في الصدر وخضعوا لتلوين الشرايين القلبية ولكن لم يكن لديهم أمراض الشرايين القلبية شاركوا في هذه الدراسة. تم قياس التغيير في مستوى مصل الدم لكل من (Amyloid A) و(Hs-CRP) قبل وبعد أربعة ساعات من العملية.

النتائج: بينت المقارنة انه لا يوجد اختلاف ملحوظ بين المجموعتين أخذاً بنظر الاعتبار كل من العمر، الجنس، العرق، ارتفاع ضغط الدم، مرض السكر والتدخين. معدل القيمة لـ(Hs-CRP) قبل وبعد العملية كان متشابها بين المجموعتين. مرضى الشرايين القلبية بعد العملية أظهروا مستوى أعلى للـ(Amyloid A) من اللذين ليس لديهم مرض الشرايين القلبية وكان الاختلاف ملحوظاً احصائياً (P=0.001). تم تقييم فائدة فحص الدم للـ(Amyloid A) كفحص مسحي لتلف الخلايا المبطنة للشرايين القلبية بواسطة حساب صلاحية الفحص مع الاخذ بنظر الاعتبار نقطة حد الفصل لـ(Hs-CRP). مرضى الشرايين القلبية بعد العملية مع مستوى (Hs-CRP) أكثر من (3 mg/L) كانت لديهم نسبة انتشار اعلى (54.0%) من مستوى (Amyloid A) مقارنة مع اللذين لديهم مستوى (Hs-CRP) اقل من (3 mg/L) (46.0%, P=0.001).

الاستنتاج: شوهدت في هذه الدراسة أن مرضى الشرايين القلبية الذين خضعوا للبالون والشبكية كان لديهم ارتفاع مستوى البروتين (Amyloid A) في مصل الدم بعد عملية التداخل القسطاري، ولذلك تحديد مستوى الـ(Amyloid A) أصبح مشروطاً في المرضى الذين لديهم نسبة خطورة عالية لجرح الخلايا المبطنة للشرايين القلبية المبكر.

SERUM GAMMA GLUTAMYL TRANSFERASE LEVELS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME; RELATION TO OXIDATIVE STRESS

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ABSTRACT

Background: There is increasing evidence on the association between high serum gamma glutamyl transferase (GGT) levels and oxidative stress in women with polycystic ovary syndrome (PCOS). The aim of this study was to examine serum GGT levels in a sample of women with PCOS and to ascertain the relation to oxidative stress.

Methods: A case control study included forty women who were clinically diagnosed with PCOS according to Rotterdam criteria and twenty apparently healthy women served as a control group. Following clinical diagnosis, anthropometric measurement was calculated including height, weight and body mass index (BMI). Serum gamma glutamyl transferase, high sensitive C-reactive protein (hs-CRP) and malonyldialdehyde (MDA) were measured.

Results: The women with PCOS exhibited significantly higher serum GGT, hs-CRP and MDA levels than did the healthy women (p=0.04, p=0.05, p=0.05) respectively. The correlation between serum GGT levels and hs-CRP was significant among women with PCOS (p=0.05).

Conclusion: Our results suggest that mild elevation of serum GGT may be related to oxidative stress in women with PCOS particularly obese.

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Keywords: Polycystic ovary syndrome, gamma glutamyl transferase and oxidative stress.

Polycystic Ovary Syndrome (PCOS) is a common metabolic endocrinopathy of the female reproductive system characterized mainly by chronic anovulation associated with other symptoms such as elevated androgen levels (hyperandrogenemia), insulin resistance and hirsutism1. Although the precise etiology of PCOS is not fully understood, studies indicate that both genetic and environmental factors results in dysfunctions in hypothalamic pituitary axis (HPA) and excessive androgen levels leading to hormonal imbalance represented by decrease in follicular stimulating hormone (FSH) and elevation in luteinizing hormone (LH) which in turn eventually results in anovulation[2,3].

Previous studies focused on a variety of PCOS aspects mainly the relationship between anovulation and oxidative stress. Studies concluded that there is existence of

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low grade chronic inflammation as well as oxidative stress that contribute to the PCOS pathogenesis through altering LH/FSH ratio[4]. However, gamma glutamyl transferase (GGT) which is expressed in the cell membranes of various tissues and plays a pivotal role in glutathione and leukotriene metabolism, has been linked to various disorders including insulin resistance and cardiovascular diseases[5,6,7]. Studies suggest that both cellular and serum GGT levels may play an important role in generating reactive oxygen species (ROS) and subsequently considered as a predictable and sensitive marker for oxidative stress[8,9]. The aim of this study was to examine the serum GGT levels in women with polycystic ovary syndrome as well as examining its reliability as a marker for oxidative stress.

METHODS:

After receiving an approval letter from the research committee at Duhok College of Medicine, this case control study involved forty women who were clinically diagnosed with PCOS based on Rotterdam criteria10 (oligo- and/or anovulation or clinical and/or biochemical hyperandrogenemia or polycystic ovaries on ultrasonography) and twenty apparently healthy women served as a control group.

Anthropometric measurements were calculated including height and weight, and body mass index (BMI). Case history and all relevant information were taken by a questionnaire. Upon their approval, five milliliters of venous blood was collected from each participant for necessary laboratory investigations.

Hormonal assays including follicular stimulating hormone (FSH) and luteinizing hormone (LH) were measured using enzyme immunoassay technique (Biomerieux manufacturer, France). Serum levels of high sensitivity C-reactive protein were assayed using ELISA (Monobind Inc., USA Kit). Quantitative measurement of Malondialdehyde (MDA, nmol/ml) was determined in serum samples using thiobarbituric acid method[11]. Serum levels of gamma glutamyl transferase (GGT) were measured by spectrophotometric method (Biolab Manufacturer, France).

SPSS version 18 (Chicago, USA) was used for statistical analysis of study values. All variables were expressed as mean ± standard deviation (SD). The independent t-test was used to determine the statistical significance of difference in mean between study groups, p values of 0.05 or less were considered statistically significant.

RESULTS:

Both study groups had a mean age of 29 years while PCOS subjects had an average infertility duration of 3 years. Among PCOS patients, 90% were registered married versus 10% virgins. Study results showed a highly statistically significantly

increased BMI (p=0.005) in PCOS women compared to control (28.14 vs. 22.9). Follicular stimulating hormone (FSH) displayed a statistically significant decrease in PCOS women compared to control (p=0.04). Luteinizing hormone (LH) showed a statistically significant elevation (p=0.01) in women with PCOS versus controls (Table1).

Table 1: Basic characteristics of PCOS patients and control subjects

Parameters	PCOS	Control	p value
Age (years)	29.1 ± 4.71	29.7 ± 3.88	0.91
Duration of infertility (years)	3.34 ± 2.57	NA	NA
Body Mass Index (BMI)	28.14 ± 3.12	22.9 ± 2.05	0.005
% and number of married vs. virgin	90% vs. 10% (36 vs. 4)	NA	NA
FSH	6.31 ± 2.44	10.59 ± 2.63	0.04
LH	13.23 ± 2.18	5.84 ± 1.95	0.01

Serum levels of high sensitivity C-reactive protein (hs-CRP) were statistically significantly elevated in PCOS women as compared to controls (p<0.05). Moreover, both serum gamma glutamyl transferase (GGT) and malondialdehyde (MDA) displayed a significant increase in women with PCOS compared to control (p=0.04 and p=0.05 respectively). (Table 2)

Table 2: Inflammatory and oxidative stress markers among study groups

Parameters	PCOS (No. 40)	Control (No. 20)	p value
hs-CRP (mg / dL)	3.74 ± 1.85	1.38 ± 4.38	< 0.05
GGT (IU / L)	38.97 ± 3.07	23.09 ± 5.62	0.04
MDA (nmol / ml)	3.11 ± 1.98	0.82 ± 4.27	0.05

The women with POCS were further classified based on body mass index in to two groups; obese (n=20, BMI> 30) and lean (no=20, BMI<25). Results indicated a highly statistically significant differences in hs-CRP between study groups (p=0.003). There were statistically significant differences in both GGT and MDA between study groups (p=0.001 and p=0.023 respectively),
(Table 3).

Table 3: Comparison in parameters between patients subgroups vs. control

Parameters	Lean PCOS (No. 20)	Obese (No. 20)	p value
hs-CRP (mg/dL)	2.77± 1.49	4.71±2.21	0.003
GGT (IU/L)	35.32 ± 2.31	42.62 ± 3.84	0.001
MDA (nmol/ml)	2.93 ± 2.4	3.28 ± 1.56	0.023

Pearson's correlation coefficient was used to determine the correlation between variables. There was a significant correlation between hs-CRP and GGT

(p=0.05) whereas both correlations hs-CRP-MDA and GGT-MDA were not significant (p=0.85 and p=0.91) respectively.

Table 4: Pearson's correlation coefficient among variables.

Variables	R value	P value
hs-CRP - GGT	**0.352**	0.05
hs-CRP - MDA	**0.12**	0.85
GGT - MDA	**0.16**	0.91

DISCUSSION:

The majority of previous studies reported an association between obesity and hyperandrogenemia in PCOS women[12]. Results of the present study confirmed the same idea represented by significant elevation in BMI (p =0.005). Although lack of androgen levels could be one of the possible limitation of this study but alternatively patients were clinically examined for presence or absence of hirsutism which is the consequence of excessive androgen levels. Hormonal profile of PCOS women displayed a significant reduction in FSH accompanied by a significant elevation in LH although both hormones were within their normal values. This is consistent with other studies concluding that dysfunction in hypothalamic pituitary adrenal axis represented by rapid short pulses in GnRH secretion may result in altering LH/FSH ratio which eventually leads to FSH deficiency compared to LH and subsequently preventing follicular maturation during follicular phase of the menstrual cycle[13,14]. The existence of low grade chronic inflammation in the pathogenesis of PCOS and other diseases is well established in previous studies. Our results are consistent with previous literature concluding that there is a significant elevation in inflammatory markers mainly hs-CRP which is also regarded as a risk factor for a variety of diseases mainly cardiovascular disorders and diabetes[15,16].

A variety of research have been focusing on the classical functions of GGT as a marker for excessive alcohol consumption as well as its contribution with cardiovascular, metabolic and liver diseases. It is indicated that GGT may be considered as a risk factor for cardiovascular disorders owing to its elevation and its association with other cardiovascular and metabolic disturbances[17,18,19]. Others reported that mild elevation of serum GGT is associated with incidence of diabetes and hypertension, these associations are consistent with a role for oxidative stress in risk for diabetes and hypertension20. Elevated fatty liver index (hypertriglyceridemia, elevated AST, ALT and GGT) is a commonly observed in

obese PCOS women, whereas normal weight PCOS showed no evidence for elevated FLI[21,22].

Although the association between oxidative stress and PCOS is well documented in previous literature, there is conflicting results regarding evaluation of γ-glutamyl transferase as a marker for oxidative stress. Our study results are consistent with studies concluding that GGT could represent an early marker of sub-clinical inflammation and oxidative stress in obese PCOS patients[23,24]. Even though there is lack of evidence regarding the precise involvement of GGT in oxidative damage, there are few theories and explanations based on previous research. Recent experimental studies concluded that GGT may play an important role in generation of reactive oxygen species (ROS). In addition, the oxidative damage effects of GGT exacerbate in the presence of iron[25,26,27]. The possible mechanism underlying GGT capability of generating ROS could be due to cysteinylglycine, which has a strong ability to reduce Fe3 to Fe2 and subsequently promoting generation of free radical species. Moreover, GGT-mediated oxidative stress has been reported to be capable of inducing oxidation of lipids, thiol protein, alterations of the normal protein phosphorylation patterns in addition to biological effects represented by activation of transcription factors[28,29,30].

The second mechanism could be due to inverse relation between antioxidants and GGT. Studies examining on associations between dietary intake and serum GGT reported an inverse association between fruit intake and serum GGT in a dose–response manner. More specifically, dietary antioxidants such as vitamin C and beta-carotene showed inverse associations with serum GGT level, whereas dietary iron was positively related to serum GGT levels[31,32,33]. Our results also showed a significant correlation between hs-CRP and GGT which illustrates the role of both inflammation and oxidative stress in orchestrating PCOS pathogenesis[34].

In conclusion, our results suggest that a mild elevation in GGT is indicated in the sera of women with PCOS particularly among obese. These findings may have clinical implications due to increased risk of oxidative stress. For that reason, targeting oxidative stress should be considered when treatment strategies are applied to PCOS patients.

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پوختە

ئەنزیما کاما کلوتامیل ترانسفیراس و پەیوەندیا وێ ب کارێ هێکدانێ ڤە لجەم نەساخێن کیسبونا هێکدانێ

پێشەکی و ئارمانج: کیسکبونا هێلکەدانێ ئێکە ژنەخوشییێن بەربەلاڤ لجەم ژنا و تا نوکە ئەگەرێن وێ ددیار نینن, ژنا نەساخ بڤێ نەخوشیێ دەورا وێ یا هەیڤانە گیرو دبیت و هێك دروست نا چێبیت. ئارمانج ژڤێ ڤەکولینێ دیارکرنا رولی ئەنزیما کاما کلوتامیل ترانسفیراس و پەیوەندیا وێ ب کارێ هێکدانێ ڤە لجەم نەساخێن کیسبونا هێکدانێ.

ڕێکێن ڤەکولینێ: ئەڤ ڤەکولینە هاتە ئەنجامدان ل کولپژا پزیشکی بەشێ فسیولوجی و پشکدار هاتنە دابەش کرن لسەر دوو گروپا: گروپێ ئیکێ نەساخ و ژمارا وان ٤٠ کەس بون و گروپێ دووێ ژنێن نورمال بون و ژمارا وان ٢٠ کەس بون. تاقیکرنێن لابورێ یێن پێدڤی هاتنە ئەنجامدان و هەرهوسا پێزانینێن کلینیکی بڕێکا فورمەکا تایبەت هاتنە وەرگرتن.

ئەنجام: ئەنجامێن ڤەکولینێ دیارکرن کو خوینا نەساخێ کیسکبونا هێلکەدانێ لیڤەلێن پتر ژ نورمال یێن ئەنزیما کاما کلوتامیل ترانسفیراس هەیە و بتایبەت لجەم نەساخێن کێشا وان زێدە وهەرهوسا هەردو کەرەستەیێن مالون دایئەلدیهاید و سی ریئەکتڤ پروتین و ئەڤ چەندە کاریگەریەکا نەرێنی لسەر کارێ هێکدانێ دکەت.

دەرئەنجام: زێدەبونا لیڤەلێ ئەنزیما کاما کلوتامیل ترانسفیراس پەیوەندیەکا ئێکسەر ب ئوکسیدەتڤ ستریس ڤە هەیە و یا پێدڤیە ئەڤ چەندە پتر بێتە رون و ئاشکەرا کرن د ڤەکولینێن بهێت دا.

الخلاصة

كاما كلوتاميل ترانسفيراس لدى المرضى المصابات بمتلازمة تكييس المباييض: علاقتها بالاجهاد التأكسدي

الخلفية والاهداف: متلازمة تكييس المبايض هو خلل افرازي أيضي غير معروف السبب يتميز بعدم الاباضة و زيادة في مستوى الاندروجين في الدم وأحيانا خلل في افراز الانسولين. الهدف من هذه الدراسة هو قياس مستويات أنزيم كاما كلوتاميل ترانسفيراس لدى المرضى وبيان علاقتها بالاجهاد التأكسدي.

طرق البحث: تضمنت هذه الدراسة تسعون مشاركات و قد تم تقسيمهن الى مجموعتين, المجموعة الاولى تألفت من اربعون مريضا مشخصاً كلينيكيا بمتلازمة تكييس المبايض أما المجموعة الثانية تضمنت عشرون اشخاصا أصحاء كمجموعة ضابطة. تم اجراء جميع التحليلات المختبرية في مختبر الفسلجة بكلية الطب والحصول على المعلومات الاكلينيكية الاضافية حول حالات المرضى من خلال أستبيان. تم تحليل المعلومات و اجراء الاحصاء الطبي باستعمال البرامج المختصة.

النتائج: أضهرت نتائج الدراسة وجود ازدياد ملحوض في مستويات أنزيم كاما كلوتاميل ترانسفيراس في دم المرضى مقارنة بالمجموعة الضابطة اضافة الى وجود ازدياد ملحوض في المادة الموكسدة (مالون دايألديهايد) وسي ريأكتف بروتين في دم المرضى المصابين بمتلازمة تكييس المبايض.

الاستنتاج: تلخصت الدراسة بأن هناك ازدياد ملحوض في مستويات أنزيم كاما كلوتاميل ترانسفيراس في دم المرضى المصابين بمتلازمة تكييس المباييض و خاصة المرصى اللواتي يعانون من السمنة. أضافة الى أن الانزيم المذكور لها علاقة مباشرة بالاجهاد التأكسدي والتي يجب الانتباه الى النقطة المذكورة وتحديد دورها في الابحاث القادمة.

A STUDY OF SODIUM CONCENTRATION IN DIFFERENT BREAD CONSUMED IN DUHOK CITY –KURDISTAN REGION –IRAQ

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ABSTRACT

Background: Cardiovascular disease is the main cause of death and disability worldwide. Hypertension is among the highly important major risk factors and up to 62% of cerebrovascular accidents and 49% of coronary heart disease are credited to raised Blood Pressure. There are strong evidences that present human consumption of salt is the major factor increasing Blood Pressure and thereby Cardiovascular diseases. Since bread is the main part in people diet, particularly in our country, the determination of sodium content of bread is of highest priority and needs further researches.

Methods: (120) samples of six types of bread were collected from (120) different bakeries in Duhok city and thereafter assessed for sodium content in the laboratories of the Institute of Nutrition Researches in Baghdad

Results: This study showed that 35% of bread's samples has sodium concentration overrides the standard level and the residual 65% is within the usual range. Average proportion of bread's sodium concentration was as 248.149 mg / 100g.

Conclusions: The sodium contents of one third of studied bread samples are higher than is acceptable limit and may be contributing to adverse health outcomes. Therefore, an urgent public health intervention is highly advisable

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Keywords: Sodium, bread, Duhok city.

The daily salt consumption of human ancestors was less than 0.25g. But this rate increased when the Chinese discovered that salt could be used to preserve food (about 5000 years ago).[1]

After World War II, refrigeration and deep freezing began to displace salt from being the main food preservative. In spite of that, salt consumption has increased in the past decades due to consumption of highly salted processed foods. About 75% of salt intake is estimated to come from processed food.[2]

The sodium content of processed foods is higher if compared with their natural counterparts. For example, chick peas, sweet corn and peas naturally have a very low sodium content, while processing them increases the sodium content by 10–100-fold; and foods such as corned beef, bran flakes or smoked salmon, have sodium intakes of 1–2%, equivalent to, or more than, the sodium concentration of Atlantic seawater.[3]

Sodium content is high in processed foods, such as bread (approximately 250

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mg/100g), processed meats (approximately 1500mg/100g), snack foods such as pretzels, cheese puffs and popcorn (approximately 1500 mg/100g), as well as in condiments such as soy sauce (approximately 7000mg/100g), and bouillon or stock cubes (approximately 20000mg/100g).[4]

Current data on sodium intake reveal that people all over the world are consuming much more sodium than their physiological needs (184-230mg/day).[5] Most individuals consume an excessive amount of salt-on average 9–12 grams per day,[6] or around double the advised upper limit of sodium intake by World Health Organization (WHO) for adults, which is less than two grams' sodium/day (equal to five grams' salt/day).[7]

Cardiovascular diseases (CVD) is the leading cause of mortality and morbidity globally. Elevated blood pressure is among the most significant major risk factors, and up to 62% of strokes and 49% of coronary heart disease are attributed to raised BP There are strong evidences that existing human intake of salt is the major factor increasing BP and thereby CVD.1,8,9 Hypertension is responsible for at least 45% of deaths due to heart disease and 51% of deaths due to stroke.[4] According to the Iraqi national survey for non-communicable diseases risk factors in 2006, 40.4% of Iraqi population are hyper tensive.[10]

Bread, in its various forms, is the most widely consumed food in the world. It is the staple food and essential diet in many countries including Iraq and, because it is consumed so frequently, it is also the single biggest contributor of salt to our diet.[11] Recent findings from multiple studies conducted in several countries suggest that bread in Ireland provides 25.9% of total salt intake, with corresponding values of 25.5% for Turkey, 24.8% for Belgium, 24.2% for France, 19.1% for Spain, 19% for the UK, 26% for Lebanon, and 28.5% for Kuwait.[12-14]

Over the different eras the salt content of bread has grown gradually. The greatest increase occurred with the industrialization of bread making in the 20th century, when quick bulk manufacture techniques required salt to regulate the process and the resulting product, thereby lessening bread's lack of flavor and reaching values as high as 2%.[15]

This study assesses the concentration of sodium in samples of bread produced and consumed in Duhok city, Kurdistan Region, Iraq; the probable contributions of bread in population level exposure to salt; and draws attention to the need to develop effective strategies to ensure that reduction in salt consumption is achieved as the

bread provides up to one quarter of daily sodium intake.

MATERIALS AND METHODS

This is a cross sectional study designed to determine the sodium (salt) content of bread samples taken from 120 bakeries in different districts of Duhok city. For administrative purposes, Duhok city was divided into four districts and there are (268) bakeries at time of the study in Duhok city. Thirty samples from each district were collected in one day by 8 trained teams; each team was composed of two staff. The amount of bread that was collected from each bakery was more than 150grams and each sample of bread or Samoon saved in labelled air free plastic bag. Considering the numbers of bakeries in every district, samples were collected from six different types of bread. These are called flat bread (Naan) (Figure. 1a), Saj bread (Figure. 1b), Turkish flat bread (Figure. 1c), Samoon (Figure. 1d), Samoon hajari (Iraqi bread made on stone) (Figure. 1e) and Turkish pita samoon (Figure. 1f). Samples were sent to the Nutrition Research Institute laboratories in Baghdad for assessment of their sodium content. The technique utilized for measuring breads' sodium is Dry Ashing. The main objective of Dry Ashing procedure is to combust all of the organic material and to prepare the sample for subsequent treatment using fusion techniques.[16]

As to the a lot of pastry shops, gathered examples of every sort of bread was different. By using proportionate stratified sampling procedure, the largest samples were flat bread (Naan) and Samoon, while the smallest were Turkish pita Samoon (Table 1).

Due to the lack of any limitation of the highest permissible level of sodium in bread within the Iraqi standard specifications of the Bread No. (677), So Nutrition Researches Institution are relying on the Kuwaiti standard specifications of the Bread, which defines the 262.640mg/100g as a maximum permitted level of sodium in the bread.

a 

b 

c 

d 

e 

f 

Figure 1. Different kinds of bread. flat bread (Naan) (Fig. 1a), Saj bread (Fig. 1b), Turkish flat bread (Fig. 1c), Samoon (Fig. 1d), Samoon hajari (Iraqi bread made on stone) (Fig.1e) and Turkish pita samoon (Fig. 1f).

Table 1: Bread Samples by Type

Type of bread	No. of available bakeries	No. of selected samples	%
Flat bread (Naan)	120	54	45.0
Saj bread	9	4	3.3
Turkish flat bread	9	4	3.3
Samoon	109	49	40.8
Samoon Hajari	16	7	5.8
Turkish pita samoon	5	2	1.7
Total	268	120	100.0

Statistical analysis

Chi square test was done for statistical analysis of the data by practicing SPSS soft- ware version 23. P value $\leq$ 0.05was considered significant.

RESULTS

This study showed that 35% (42) of the samples has sodium content higher than 262.640 mg /100g and the rest 65% (78) of the samples has sodium content less than 262.640 mg /100 g.

Up to 50% (28) of samples of flat bread (Naan) type and Turkish pita samoon showed higher sodium contents than standard level, in reducing order was found in Sammon, Saj bread, Turkish flat bread, Samoon and Samoon hajari Table 2. ($p<0.05$)

Table 2: Bread Samples by Type and Sodium contents

Type of Bread	Sodium Content No. (%)		Total
	>262.64 mg / 100 g.	< 262.64 mg / 100 g.	
Flat bread (Naan)	28 (51.9)	26 (48.1)	54 (100)
Saj bread	1 (25)	3 (75)	4 (100)
Turkish flat bread	1 (25)	3 (75)	4 (100)
Samoon	10 (20.4)	39 (79.6)	49 (100)
Samoon hajari	1 (14.2)	6 (85.8)	7 (100)
Turkish pita samoon	1 (50)	1 (50)	2 (100)
Total	42 (35)	78 (65)	120 (100)

The mean sodium content of whole samples was 248.149g. The average mean sodium content in the samples of district IV was the highest (282.7mg/100g) while in the district I, samples were the lowest in sodium (216.5mg/ 100g). Table 3

Table 3: Sodium Contents of Bread by Districts and Number of Bakeries

Districts	Mean	No. of bakeries with Sodium content > 262.64 mg / 100 g.	No. of bakeries with Sodium content < 262.64 mg / 100 g.	Total
District I	216.5	6 (20)	24 (80)	30 (100)
District II	248.5	12 (40)	18 (60)	30 (100)
District III	241.9	12 (40)	18 (60)	30 (100)
District IV	282.7	12 (40)	18 (60)	30 (100)
	248.14	42 (35)	78 (65)	120 (100)

DISCUSSION

Non -communicable diseases (NCDs) are the main contributor to mortality and morbidity globally[17,18] and interventions to reduce the burden of NCDs are highly cost-effective.19 Elevated sodium intake has been associated with a number of NCDs (including hypertension, cardiovascular diseases and stroke), Hence lowering sodium intake may reduce blood pressure and the risk of developing related NCDs.[20] Recent data on sodium intake show that populations around the world are consuming much more sodium than the physiological requirement. The estimated sodium intake in Jordan is up to 7623

mg/day,[21] while the estimated sodium intake in Turkey is 5905mg/ day[22], On other hand, there is no available data on estimation of sodium intake in Iraq.

Bread is the unique processed food that is available, and consumed daily by, both low and high income people. Moreover, it is the largest sodium contributor to the Iraqi diet. Due to the fact that excess sodium consumption contributes to premature death and disability, therefore any reduction in the level of salt in bread would have a major impact on public health but unfortunately, there are no regulations or public laws in Iraq that regulate the salt or sodium contents in processed foods specially bread. This study which assumed to be the first of its kind in Kurdistan Region was conducted to determine sodium (salt) content in the bread.

The mean sodium content of whole samples was 248.149mg/100g which is lower than that obtained in a similar study conducted in Bagdad city in 2014 (293.812mg/100g).[16] The present study showed that (35%) or 42 samples out of 120 have sodium contents above permissible level. Meanwhile in Baghdad study, the sodium content exceeded the permissible level in (61%) or 92 out of 150 of bread samples.[22] A similar study done in Nigeria showed that the mean sodium content of two brands of bread was very high (660-716.7mg/100g) and 70% of the studied samples had considerably more sodium than the recommended limit in Nigeria which is 440mg/100g.[23] Silva and her colleagues did a study in Maputo, Mozambique, and they found that the mean sodium content of bread was 450.3mg/100g, with no significant differences between bakeries and traditional markets.[24] In Montero-Campos Mde study in Costa Rica, 99 samples of bread showed that sodium concentration was between 496 and 744mg/100g ,and 80% reported greater amount than found by direct analysis.[25]

The results of similar studies on salt levels of bread in Iran carried out from 1994 to 2009 indicated that the amount of salt in bread was higher than the standard level in Shiraz, Mashhad, Sanandaj and Isfahan[26-28]

The current study showed that there is a wide variation in bread sodium content among bakeries from 31,725mg/100g to 948mg/100g. This may be due to the absence of unified standards, and in turn it will lead to disparity in the amount of daily- consumed salt in bread and other foods, As if a person eating four average slices of bread twice daily from two different bakers. First consumer may take 60mg sodium if they bought their bread from the craft baker with the lowest sodium levels compared with other one take 1820mg sodium from the craft baker

with the highest sodium level. There are also differences in bread sodium content among districts inside the same city

The sodium content of bread could be gradually decreased over 4-6 weeks without affecting consumer's palatability or acceptability of sensory characteristics, including overall liking, appearance, aroma, flavor, sweetness, salt level and texture, or purchase intent.[29] Bolhuis et al, found that salt reduction of up to 50% in bread does not decrease bread consumption.[30]

It seems that most bakers either do not have enough knowledge about the standard level of salt used for the production of bread, or they have some other reasons for using salt below or above the standard (e.g. type of flour) or some other factors which are needed to be investigated in further studies.

Finally, there should be a strict supervision and effective measures by relevant local authorities for bakeries to control the amount of salt in bread.

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پوختە

ڤەکولینا ئاستێ صودیومی لناف جورێن نانی ئەوین دهینە بکارئینان ل باژیری دهوکێ

پێشەکی وئارمانج: ئێشێن دلی ولولێن خوینی ئەگەرێن سەرەکینە بۆ مرنێ وپەکفتنێ ل جهانێ. نیزیکە ٦٢٪ ل جەلتێن مێشیکی و ٤٩٪ ل ئێشێن دەمارێن خوینی یا دلی دهینە رویدان ژئەگەرێ زێدەبونا فیشارا خوینی. وبەلگێن بەهێز هەنە دیار دکەن کو بکارئینانا مروڤی بۆ خویی خارنی ب رێژا نوکە، ئەگەرەکی سەرەکیە بۆ زێدەبونا فیشارا خوینی ول ئەنجامدا زێدەبونا ئێشێن دلی ولولێن خوینی. ژبەر کو نان بەشەکی سەرەکی یە ل خارنی گەلێ مە یا روژانە , دیارکرنا ئاستی صودیومی (خویی) گەلەك گرنگە و پیدڤی هەیە بۆ ڤەکولینێن زێدەتر.

رێکێن ڤەکولینێ: (١٢٠) نمونێن ل شەش جورێن نانی لـ(١٢٠) نانپێژا وسەمونخا ل باژیری دهوکی هاتنە وەرگرتن وئاستی صودیومی هاتنە پشکنین ل تاقیگەهێن پەیمانگەها خوڕاکێ ل بەغدا.

ئەنجام: ئەڤ ڤەکولینا دیارکر کو ئاستی صودیومی لـ٣٥٪ ل نمونێن نانی زێدەترە ل ئاستی ستاندەرد و٦٥٪ نورمال بوون، و رێژا خویی ل هەمی نموونا ٢٤٨.١٤٩ ملیگرام/ ١٠٠ گرام.

دەرئەنجام: وەك دەرئەنجام رێژا صودیومی ل سێ یەکا نموونا نانی بلندترە ل ئاستی ستاندەرد ودێ ئەنجامێن نەرینی هەبیت ل سەر ساخلەمیا گشتی ژبەر ڤی ئەگەری, پیدڤیە پێنگاڤێن بلەز بهینە هاڤێتن ژلایی دەزگەهێن پیوەندیدار.

الخلاصة

دراسة تركيز الصوديوم في عينات من مختلف انواع الخبز المستهلك في مدينة دهوك –أقليم كوردستان العراق

الخلفية والاهداف: أمراض القلب والأوعية الدموية هي السبب الرئيسي للوفاة والعجز في جميع أنحاء العالم. ارتفاع ضغط الدم هو من بين أهم عوامل الخطورة الرئيسية والهامة جداً، إن حوالي ٦٢٪ من الجلطات الوعائية الدماغية و٤٩٪ من أمراض القلب التاجية تعزى إلى ارتفاع ضغط الدم. وهناك أدلة قوية على أن الاستهلاك الحالي للإنسان من الملح هو العامل الرئيسي لزيادة ارتفاع ضغط الدم وبالتالي زيادة الإصابة بأمراض القلب والأوعية الدموية. وحيث أن استهلاك الخبز هو جزء رئيسي في الوجبات الغذائية اليومية للناس ولاسيما في بلادنا، لذا فإن تحديد محتوى الصوديوم وبالتالي (الملح) في الخبز يعتبر من الأولويات القصوى ويحتاج إلى مزيد من الأبحاث.

طرق البحث: تم جمع (١٢٠) عينة من ستة أنواع مختلفة من الخبز من (١٢٠) مخبزا مختلفاً في مدينة دهوك وتم بعد ذلك دراسة تركيز (محتوى) الصوديوم في مختبرات معهد بحوث التغذية في بغداد.

النتائج: أظهرت الدراسة أن ٣٥٪ من عينات الخبز تحتوى على تركيز الصوديوم تتجاوز المستوى القياسي المسموح بها في العراق وبينما كانت النسبة المتبقية ٦٥٪ ضمن النسب المسموحة. وكان متوسط نسبة تركيز الصوديوم في جميع عينات الخبز ١٤٩،٢٤٨ ملغ/ ١٠٠ غرام.

الاستنتاجات: تركيز الصوديوم في ثلث عينات الخبز المفحوصة كانت أعلى من الحد المقبول ويمكن أن تؤدي إلى نتائج صحية سلبية. ولذا فإن تدخل الجهات المسؤولة عن الصحة العامة يعتبر في غاية الأهمية.

VITAMIN D STATUS AMONG APPARENTLY HEALTHY POPULATION IN DUHOK, KURDISTAN REGION, IRAQ

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ABSTRACT

Background: Vitamin D deficiency and insufficiency are a commonly reported health problem throughout the world. This cross sectional survey was conducted in Duhok governorate with an aim to assess vitamin D status in a sample of apparently healthy population.

Methods: Serum 25-hydroxyvitamin D was determined for all enrolled subjects (n=1270), including newborn babies and infants (n=24), primary school children (n=53), adolescents (n=85), adults (n=1086) and elderly (n=22).

Results: There was a statistically significant difference in mean 25-hydroxyvitamin D levels between different age groups (p= 0.02) and different gender (P= 0.001). Overall 731(57.6%) subjects were with low 25-hydroxyvitamin D < 30ng/ml, of these, 651(51.3%) subjects were vitamin D insufficient (10-29.9 ng/ml), while 80(6.3%) subjects had severe vitamin D deficiency (< 10 ng/ml), with a significant difference among age groups (p= 0.003).

Conclusion: A low vitamin D status is present in 57.6% of the study population in Duhok. This finding may have clinical implications due to the increased risk of future metabolic diseases.

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Keywords: Vitamin D, Apparently healthy population, Duhok governorate

Much interest has recently arisen in the function and metabolism of vitamin D .This is because it has been reported to be essential nutrient for maintaining good health and play an important role in the pathogenesis of various diseases[1,2,3]. Worldwide, the prevalence of vitamin D insufficiency is high and rising[4,5]. The third National Health and Nutrition Examination Survey (NHANES III) reported the prevalence of vitamin D deficiency in the USA to be between 25% and 57% of adults[6]. In developing countries, the deficiencies of important nutrients such as vitamin D, iron and zinc are major public health problems and have significant adverse health impacts. For example the prevalence of vitamin D deficiency in patients with type 1 diabetes mellitus was 15%to 90.6%[7,8].

The main marker of vitamin D status is the metabolite 25(OH) D, which is synthesized in the liver[9,10]. Serum 25(OH) D concentrations are largely determined by

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environmental factors, mainly through vitamin D intake and ultraviolet exposure. Measurement of serum 25(OH) D levels may be considered medically necessary in general population and might be used as a marker of metabolic bone disease with other bone disease detection markers. Little is known, however, about the level and the prevalence of vitamin D deficiency among the population of Duhok governorate. The present study was designed to determine vitamin D status among different age and sex groups.

METHODS

Subjects and Study design

This cross-sectional study was conducted at the Department of Chemistry and Clinical Biochemistry, College of Medicine, University of Duhok, Kurdistan Region, Iraq from May 2015 to January 2016. One thousand and two hundred seventy apparently healthy subjects were included in this study. Among these 24 were newborns babies and infants who were brought for vaccination at the vaccination unit of primary care centers in Duhok city. Fifty three samples from primary school children were obtained from previously collected samples[11], while 85 samples were drawn from adolescents attending intermediate and secondary schools in different areas of Duhok governorate. Adults (n=1086) were recruited by personal request from the staff and blood bank donors of Azadi Teaching Hospital and Duhok Blood Bank. The rest of the sample comprised 22 elderly people chosen from the relatives of patients attending Duhok Emergency Teaching Hospital.

The inclusion criteria were the absence of recent infections, chronic and endocrine diseases. Subjects on drug therapy including steroids, calcium or vitamin D supplementation were excluded from the study. Subjects with sunlight exposure less than 15 minutes in summer and 30 minutes in winter were also excluded from the study. Formal consent was obtained from the parents of children and adults after the nature of the study had been explained to them. The board of postgraduate committee of the Duhok University, medical branch approved the study protocol.

Data collection

An especially-designed questionnaire was used to obtain information from the participants about age, sex, past medical history including (hypertension, diabetes mellitus, thyroid and parathyroid disease, liver and renal disease). Blood samples were collected for serum 25(OH) D and blood glucose measurement. The serum levels of 25(OH) D and glucose were measured by cobas 6000 using electrochemiluminescence immunoassay principle and glucose oxidase principle,

respectively. Serum 25(OH) D levels were defined as: Severe deficiency (<10 ng/ml), insufficiency (10-29.9 ng/ml), and sufficiency (30-150 ng/ml)[12]. Diagnosis of asymptomatic hyperglycemia based on World Health Organization criteria 2006[13].

RESULTS

The main characteristics of the study sample are presented in (Table 1). There was a significant difference in mean 25(OH) D levels between the age groups (Table 2) that showed 25(OH) D levels of 21.98, 25.20, 28 19, 31.32 and 38.31 ng/ml (p= 0.02). There was a significant difference in mean 25(OH) D levels among adult males and females (p= 0.001). There was also a significant difference in mean 25(OH) D levels among adolescent males and females (p= 0.01).Overall, mean 25(OH) D levels were significantly lower in females (p= 0.001) as compared to males (Table3). Overall 731(57.6%) subjects were with low 25(OH) D (< 30 ng/ml), of these, 651(51.3%) subjects were vitamin D insufficient (10-29.9 ng/ml), while 80(6.3%) subjects had severe vitamin D deficiency (< 10 ng/ml), with a significant difference (p= 0.003) among age groups (Table 4). Comparison of the present study results with that reported elsewhere is demonstrated in Table[5].

Table 1 Characteristics of the different Study Groups

Characteristics	Infants	Children	Adolescents	Adults	Elderly
Study group n (%)	24(1.9)	53(4.2)	85(6.7)	1086(85.5)	22(1.7)
Age (years)	<1.0	2-12	13-19	20-60	>60
Male sex n (%)	13(54.2)	28(52.8)	28(32.9)	344(31.7)	9(40.9)
FSG>100 mg/dl n (%)	0.0	2(3.8)	2(2.4)	137(12.6)	5(22.7)
Pregnant women n (%)	0.0	0.0	0.0	101(13.6)	0.0

Table 2 Mean Serum 25(OH) D (ng/ml) by Age Group

Population	Number	Mean ±SD	Range
Infants	24	38.31±15.28	16.0 - 70.0
Children	53	31.32±12.44	9.8 - 63.0
Adolescents	85	21.98±10.42	7.9 - 58.3
Adults	1087	28.19±13.70	5.1 - 71.0
Elderly	22	25.20±16.30	9.44 - 68.45
Total	1270	28.04±13.26	5.1 - 71.0

Table 3 Mean Serum 25(OH) D (ng/ml) by Age Group and Gender

	Males Number	Mean ± SD	Females Number	Mean ± SD	*P* value*
Infants	13	38.73±18.07	11	37.81±12.03	0.88
Children	28	32.68±11.31	25	29.86±13.85	0.42
Adolescents	28	26.39±13.67	57	20.17±8.27	0.01
Adults	344	33.10±19.8	742	19.63±7.70	0.001
Elderly	9	26.02±13.23	13	24.73±15.33	0.839
Total	422	32.64±18.63	848	20.28±8.09	0.001

Table 4 Vitamin D Status by Age Groups

Age Group	Number	Vitamin D status 25(OH) D (ng/ml)		
		<10 n (%)	≥10-29.9 n (%)	≥30-150 n (%)
Infants	24	0(0.0)	6(25.0)	18(75.0)
Children	53	1(1.8)	18(34.0	34(64.2)
Adolescents	85	6(7.1)	55(64.7)	24(28.2)
Adults	1086	72(6.6)	560(51.6)	454(41.8)
Elderly	22	1 (4.6)	12(54.5)	9(40.9)
Total	1270	80(6.3)	651(51.3)	539 (42.4)
Chi squared test	P value	0.0003		

Table 5 Vitamin D Status in Duhok Compared to Other Countries

Country	Mean±SD	Vitamin D (ng/ml)	
		Deficient (%)	Insufficiency (%)
Duhok	28.04±13.26	6.3	51.3
Israel[14]	22.9±10.1	27	51
Turkey[15]	16.9±13.09	74.9	13.8
Saudi Arabia[16]	26.6±9.8	28.3	39.4
Kuwait[17]	13.3±6.5	58.8	24.5
Egypt[18]	32.2±7.6	23.7	13.6
Germany[19]	18±4.2	30.2	61.6

DISCUSSION

There are no enough data about vitamin D status of age and sex groups in Duhok province, Kurdistan region, Iraq. Thus, vitamin D status was assessed in this cross-sectional study by measurement of serum 25 (OH) D levels. This study revealed that 57.6% of the apparently healthy subjects living in Duhok have suboptimal serum vitamin D levels, and 6.3% are vitamin D deficient. The mean 25(OH) D level for the entire study population (28.04+13.26 ng/ml) was found to be in the range considered to be

insufficient (<30ng/ml). The insufficiency status in the present study was somewhat milder among infants and children when compared with that of older individuals. In our study population, mean 25(OH) D levels in females were significantly lower than in males. The results of this study are consistent with the findings reported by others, but, in contrast with other reported values[14,15,16,17,18,19]. This discrepancy of our results from other studies may be related to the cutoff point for identifying vitamin D status. Most of the studies selected serum 25 (OH) D levels less than 20 ng/ml, cutoff point for identifying vitamin D deficiency[20,21], whereas in our study a cutoff point of < 10 ng/ml was used for identifying severe vitamin D deficiency. However, such a high prevalence of suboptimal vitamin D status in our population is especially noteworthy, because several factors are known to impact negatively on vitamin D status. Of these, nutrient status, malabsorption, drug therapy, dressing style and exposure to sunlight are the most marked negative effect on vitamin D level 22. In addition, low vitamin D status has been reported in patients with diabetes and during the course of pregnancy[23,24]. The present study showed a high number of subjects with asymptomatic hyperglycemia as well as pregnancy. However, the dietary intake of vitamin D was not determined, which is a limitation of this study. A second limitation was the variation in sample size among the different age groups, i.e. the majority of the subjects were adults in comparison to infants, children, adolescents and elderly. Although low vitamin D status may be caused by a number of factors, including insufficient synthesis in the skin, due to limited sunlight exposure and inadequate intake or absorption of vitamin D, further studies are needed to determine if improving 25(OH) D levels from deficiency to sufficiency improves vitamin D status in general population and reduce the risk of metabolic diseases..

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پوختە

ئاستێ ڤیتامین د ل دەف تاکئن کومەلگەهێ ییں ساخلەم ل پارێزگەها دهوکێ، هەرێما کوردستانا عیراقێ

پێشەکی و ئارمانج: کێمبون و نەبەسییا ڤیتامین د دهێتە هەژمارتن ژ ئاریشێن ساخلەمیێ یێن بەرچاڤ سەرانسەری جیهانێ. ئەڤ ڤەکولینە هاتە ئەنجامدان ژبو هەلسەنگاندنا ئاستێ ڤیتامین د دنمونەکا تاکین کومەلگەهێدا یێ ساخلەم.

رێکێن ڤەکولینێ: ئاستێ ڤیتامین د هاتە سنورکرن دخوینا ١٢٧٠ کەسێن بسەرڤە ساخلەم، دگەل ژێێن دناڤبەرا (کێمتر ژ ١ سال تا پتر ژ ٦٠ سال). ژوانا ییێن نیبوی وڤرنیك (٢٤ کەس)، زاروکێن قوناغا سەرەتایی (٥٣ کەس)، سنێل (٨٥ کەس)، مەزن (١٠٨٦ کەس) ئو یێن پیر (٢٢ کەس). رێژا بەربەلاڤبونا کێمبون و نەبەسییا ڤیتامین د هاتە سنورکرن.

ئەنجام: ب شێوەکێ بەرچاڤ نەوەکەهڤی هاتە دیتن د ئاستێ ڤیتامین د دا دناڤ بەرا ژێین جیاواز (P=0.02)، هەروەسا نەوەکەهڤی ب شێوەکێ بەرچاڤ هاتە دیتن د ئاستێ ڤیتامین د دا دناڤ بەرا هەردوو رەگەزاندا. ب گشتی ل دەف ٧٣١ کەسان (٥٧.٦٪) ئاستێ ڤیتامین د دناف خوینێدا یێ کیمبو (کیمتر ژ 30 ng/ml) ژوانا ٦٥١ کەسان (٥١.٣٪) ئاستێ ڤیتامین د پیجەك یێ کیمبو (10-29.9ng/ml)، بەلێ ل دەف ٨٠ کەسان (٦.٣٪) ئاستێ ڤیتامین د گەلەك یێ کیمبو (کیمتر ژ 10 ng/ml) دگەل نەوەکەهڤیەکا ب شێوەکێ بەرچاڤ دناڤ بەرا ژێێن جیاوازدا (p=0.003).

دەرئەنجام: کێمبونا ئاستێ ڤیتامین د هاتە دیتن ب ریژەیا (٥٧.٦٪) ل دەف کەسێن ب خوڤەگرتی دڤێ ڤەکولینێدا ل دهوکێ. دبیت ئەڤێ دیتنێ کارتێکرنێن کلینیکی هەبن ژ ئەگەرێ بەرزبونا مەترسیێن ئیشین میتابولزمی دپاشەرۆژێ دا.

الخلاصة

حالة الفيتامين د لدى افراد المجتمع الاصحاء ظاهريا في محافظة دهوك اقليم كوردستان العراق

الخلفية والاهداف: إن نقص وعدم كفاية فيتامين د من المشاكل الصحية الشائعة حول العالم. تم اجراء هذه الدراسة المقطعية في محافظة دهوك لغرض تقييم حالة الفيتامين د لدى عينة من افراد المجتمع الاصحاء ظاهريا.

طرق البحث: تم قياس مستوى فيتامين د 25(OH) D في مصل الدم لـ١٢٧٠ شخص من الاصحاء ظاهرياً، شملت العينة مختلف الاعمار وضمت حديثي الولادة والرضع (عدد ٢٤)، أطفال من المرحلة الابتدائية (عدد ٥٣)، المراهقين (عدد ٨٥)، البالغين (عدد ١٠٨٦) والمسنين (عدد ٢٢).

النتائج: اظهرت النتائج اختلافا في معدل مستويات الفيتامين د بين مجاميع الاعمار وكذلك بين الجنسين بمستوى احصائي معنوي. عموماً ٧٣١ (٥٧.٦%) شخص كان لديهم مستوى فيتامين د أقل من(30 ng/ml)، من هولاء ٦٥١(٥١.٣%) شخص كان لديهم عدم كفاية (10–29.9 ng/ml)، بينما ٨٠ (٦.٣%) شخص كان لديهم نقص فيتامين د (أقل من 10 ng/ml).

الاستنتاج: أظهرت الدراسة ان حالة نقص الفيتامين د موجودة لدى ٥٧.٦% من الافراد المشمولين في هذه الدراسة في دهوك. قد يكون لهذا الاستنتاج آثار سريرية مهمه ويرجع ذلك إلى زيادة اختطارالاصابة بأمراض التمثيل الغذائي في المستقبل.

CAN PERIODONTAL THERAPY REDUCES THE SEVERITY OF ACTIVE RHEUMATOID ARTHRITIS?

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ABSTRACT

Background: A significant association between periodontitis and Rheumatoid Arthritis (RA) has been reported.

Aim: This study was done to determine the effect of periodontal treatment on severity of RA.

Patients and Methods: This study was done on 60 patients, age 30-60 years, who were randomly selected from patients attending Duhok Center for Rheumatic Diseases and Medical Rehabilitation. The patients were classified into two groups: Group 1: patients with diagnosis of RA and periodontal disease who received Non-Surgical Periodontal Treatment (NSPT) during the study and group 2: patients with diagnosis of RA and periodontal disease who were monitored during the study but did not receive periodontal treatment. At the initial visit, periodontal health status of the patients based on clinical attachment loss and probing pocket depth score, and disease activity score were determined. After six month, the periodontal status and severity of rheumatoid arthritis were rescored and reassessed for both groups following the same procedure.

Results: Initially, there were no significant difference in periodontal status and severity of RA for both groups. After 6 months period, there was significant difference in intra-group analysis for both groups regarding periodontal status and severity of RA but there was no significant difference in inter-group analysis of periodontal status and disease activity score.

Conclusion: There is no significant difference in improvement of severity of RA and periodontal disease in patients with RA treated with NSPT, compared to control cases with RA.

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Keywords: Periodontitis, Rheumatoid arthritis, Non-surgical periodontal treatment

Rheumatoid arthritis (RA) is characterized by systemic inflammation of wrist and hand joints, leading to permanent deformity. RA and periodontitis share the same pathogenic and clinical features.[1]

Recent studies suggest association between periodontitis and RA.[2-5] In addition, two clinical trials studies suggested that management of periodontal disease could have a significant effect on severity of RA.[4] Similarly, a significantly increased periodontal attachment loss was observed in RA patients compared to controls.[5]

Few studies have shown that periodontal management could induce a significant decrease in Disease Activity Scores (DAS28) and Erythrocyte Sedimentation Rate (ESR).[6-9] More studies are needed to determine whether full therapy of

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periodontitis in RA patients leads to improvement of clinical outcomes. The goal of this study is to demonstrate the effect of periodontal therapy on the severity of RA.

PATIENTS AND METHODS

This flow-up study was conducted during March 2013 to April 2015. The study population consist of 60 male and female patients, aged 30-60 years, who attended Duhok Center for Rheumatic Disease and Medical Rehabilitation. All patients were informed about the nature of the study and verbal consent was obtained from each one. The study protocol was approved by the ethical Committee of the General Directorate of Health in Duhok. All RA patients have already been diagnosed by rheumatologists according to revised American College of Rheumatology/ European League Against Rheumatism classification criteria.[10]

Patients were assigned into two groups: Group 1 were patients diagnosed with RA and Periodontal Disease (PD) who received Non-surgical Periodontal Treatment (NSPT) during the study, while Group 2 were patients diagnosed with RA and PD who were monitored during the study but did not receive periodontal treatment (they were treated after the end of the study). The two groups were followed up for 6 months. The Probing Pocket Depth (PPD), Clinical Attachment Level (CAL), RA Disease Activity Score[28] (DAS28) were measured at baseline and six months later.

Exclusion criteria

1. Systemic disease, e.g. diabetes, hypertension.
2. Smoking, pregnancy.
3. Antibiotic coverage for dental or medical reasons during the 3 months before the study.
4. Patients with RA without periodontal disease.

Rheumatoid Arthritis Severity Measurement

Disease activity was assessed using the Disease Activity Score derivative for 28 joints [DAS28].[11]

Periodontal measurement

In the Dental Health Polyclinic, assessment of periodontal disease was done using disposable gloves and mask, disposable dental mirror and periodontal probe (William) probe. CAL was assessed by measuring the distance from cement-enamel junction (CEJ) to base of the pocket in millimeters. The PPD was assessed from gingival margin to base of the pocket.[12]

Periodontal therapy (Scaling and Root planning)

For removal of supra-gingival and sub-gingival plaque and calculus, Scaling and Root Planning (SRP) were performed using both hand instruments and an

ultrasonic system, under local anesthetic if necessary (in case of pain or on patient's request).

Statistical analysis

Collection and analysis of data were done using SPSS version 23. Quantitative data were analyzed with independent or paired t-tests and categoral data with chi-square, McNemar-Bowker and Fisher's exact tests. A p–value less than 0.05 was considered significant.

RESULTS

The distribution of the baseline variables (age, gender, RA severity and periodontal status) of the study groups is shown in Table 1. There was a significant difference in the age of the participant: the mean age of patients in case group and control was 51.77± 1.56 and 45.90 ± 1.83 respectively, p-value <0.018. There was no significant difference in gender distribution between the case and the control groups. In addition, there was no significant difference in periodontal status and severity of rheumatoid arthritis for both groups.

Table 1: Baseline characteristics of the two study groups

		Cases (n = 30)		Controls (n = 30)		
		No. (%)	Mean ± SE	No. (%)	Mean ± SE	P
Sex	**Male**	**12 (40)**		**15 (50)**		**0.604***
	Female	**18 (60)**		**15 (50)**		
Age			**51. ٧٧± 1.56**		**45.9 ٠± 1.83**	**0.018****
DAS at baseline			**2.0 ٣± 0.15**		**1. ٨٧± 0.17**	**0.464****
Severity of periodontal disease at baseline	**Mild**	**8 (26.7)**		**9 (30)**		**0.725***
	Moderate	**15 (50)**		**12 (40)**		
	Severe	**7 (23.3)**		**9 (30)**		

* Based on Chi square test.

** Based on independent t-test.

SE = standard error

Table 2 shows comparison in periodontal and RA parameters at baseline and after 6 months for the case group. There was a highly significant difference in periodontal status and rheumatoid arthritis severity at baseline and after 6 months (p= 0.003 and < 0.001, respectively).

Table 2: Comparison of the cases (n = 30) at baseline and after 6 months of periodontal treatment

		At baseline		After 6 months		
		No. (%)	Mean ± SE	No. (%)	Mean ± SE	P
DAS			2.0 ٣± 0.15		1.0 ± 0.17	< 0.001*
Severity of periodontal disease	Mild	8 (26.7)		18 (60)		
	Moderate	15 (50)		9 (30)		0.003**
	Severe	7 (23.3)		3 (10)		

* Based on paired t-test.

** Based on McNemar-Bowker test.

SE = standard error.

Table 3 shows comparison in periodontal and RA parameters at baseline and after 6 months for the control group. Again there was a highly significant difference in rheumatoid arthritis severity (p <0.001); the difference was also significant for the periodontal status (p= 0.014).

Table 3: Comparison of the controls (n = 30) at baseline and after 6 months

		At baseline		After 6 months		
		No. (%)	Mean ± SE	No. (%)	Mean ± SE	P
DAS			1. ٨٧± 0.17		1.0 ± 0.19	< 0.001*
Severity of periodontal disease	Mild	9 (30)		19 (63.3)		
	Moderate	12 (40)		9 (30)		0.014**
	Severe	9 (30)		2 (6.7)		

* Based on paired t-test.

** Based on McNemar-Bowker test.

SE = standard error.

Table 4 presents the differences in periodontal and RA parameters after six months for the case and the control groups. There was no significant difference in improvement between the two groups.

Table 4: Comparison of the two study groups after six months

		Cases (n = 30)		Controls (n = 30)		
		No. (%)	Mean ± SE	No. (%)	Mean ± SE	P
DAS after 6 months			1.00 ± 0.17		1.00 ± 0.19	1.0*
Severity of disease after 6 month	Mild	18 (60.0)		19 (63.3)		
	Moderate	9 (30.0)		9 (30.0)		1.0**
	Severe	3 (10.0)		2 (6.7)		

* Based on independent t-test.

** Based on Fisher's exact test.

SE = standard error.

DISCUSSION

An association between RA and PD has been suggested since 1820, when the management by extraction was the most commonly executed. Epidemiological studies found that the prevalence of PD and RA is the same: about 5% of the population greater than 50 years old of age are affected. PD and RA are chronic diseases that may be influenced by immunologic, genetic and environmental factors, resulting in destruction of bone and tissue during periods of outbreaks of periodontal disease.[13] Patients with RA can have greater difficulties with dental hygiene due to limitations in the movements of the hands and pain in the temporomandibular joint.[14]

The pathobiology of rheumatoid arthritis and periodontal disease is the same; both are chronic inflammatory diseases, with releasing of cytokines, production of other inflammatory cell products and activation of complement.[15,16]

In the present study, lack of significant deference between cases and controls may be due to small sample size and equal number of patients. There is a significant difference in age between two groups, which may be because it often occurs later in life or family history increase the rate of happing of RA.

Intra-group analysis of case group at baseline and after six month showed a highly significant difference in Disease Activity Score for severity of the RA. The severity of PD significantly decreased after six months, thus systemic inflammatory products decreased by periodontal treatment and this agree with other studies done.[17,18] The improvement in RA after periodontal treatment could be related to decrease in these markers. Other explanation is that removing of periodontal pathogens by periodontal treatment could decrease exposure of the joints to bacteria and their toxins, leading to improved RA conditions.[19]

In Table 3, intra-group analysis of the control group at baseline and after six month showed a high significant difference in disease activity score of the rheumatoid arthritis and severity of periodontal diseases significantly decreased after six months, which may be due to taking their drugs, or after oral examination, they become more aware about their oral hygiene.

In Table 4, inter-group analysis of the case and the control groups at baseline and after six month showed no significant difference in disease activity score of the RA and severity of PD.

CONCLUSION

There was no significant difference in improvement of severity of rheumatoid arthritis and periodontal diseases in patients with rheumatoid arthritis, so

control of periodontal infection and inflammation by means of scaling and root planning or taking drugs of rheumatoid arthritis in patients with periodontal disease and rheumatoid arthritis might contribute to a reduction in signs and symptoms of active RA.

RECOMMENDATION

Larger studies are needed to explore the effect of non-surgical periodontal therapy on clinical indicators of RA, using more rigorous clinical outcome and biochemical measures as well as giving attention to confounding factors of co-morbidity.

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پوختە

کارتێکرنا چارەسەرکرنا پدیێ ل سەر دژواریا ئیشین گەها

ئارمانج: پەیوەندیا مەعنەوی دناڤبەرا ئێشێت پدیێ و ئێشێت گەها هاتە دەست نیشان کرن. ئارمانج ژڤی ڤەکولینێ دیارکرنا کارتێکرنا چارەسەریا پدیێ ل سەر کێمکرنا دژواریا ئێشێت گەها.

ڕێکێن ڤەکولینێ: ڤەکولینەکا چاڤدێری کری ل سەر (٦٠) نەخوشا هاتە کرن ئەڤێت ژیێ وان دناڤ بەرا (٣٠–٦٠) سالی دا ئەوێن هاتینە ژێگرتن بشیوەکێ گوترە یێ ل نەخوشخانا گەهان ل دهوکێ ونەخوش هاتنە دابەشکرن بو دوو گروپا.

گروپێ ئێکێ: ئەو نەخوشێن ئێشێن پدیێ و ئێشێن گەها هەین و چارەسەریا ئێشێن پدیێ وەرگرتین د دەمێ ڤەکولینێ دا.

گروپێ دوویێ: ئەو نەخوشێن ئێشێن پدیێ و ئێشێن گەها هەین وچ چارەسەریا ئێشێن پدیێ وەرنەگرتینە د دەمێ ڤەکولینێ دا.

ئەنجام: دەستپێکێ چ جیاوازییێن دیار دناڤبەرا ئێشێن پدیێ و دژواریا ئێشێن گەهان نەبو. پشتی شەش هەیڤا جیاوازی دناڤبەرا گروپاندا هەبو، دناڤبەرا گروپێ ئێکێ و گروپێ دوویێ بو ئێشێت پدیێ و ئێشێن گەهان.

دەرئەنجام: دەستپێکێ چ جیاوازییێن دیار دناڤ بەرا ئێشێن پدیێ و دژواریا ئێشێن گەهان نەبو. پشتی شەش هەیڤا جیاوازی دناڤبەرا پروپاندا هەبو.

الخلاصة

تأثير علاج امراض اللثة على شدة التهاب المفاصل

الهدف: علاقة معنوية بين التهاب اللثة و التهاب المفاصل تم طرحها. الهدف من الدراسة لايجاد مدى تاثير علاج امراض اللثة على التقليل من شدة التهاب المفاصل.

طريقة البحث: دراسة تتابعية اجريت على ٦٠ مريض الذين اعمارهم تتراوح بين ال(٣٠-٦٠) سنة و الذين اختيروا عشوائيا من المرضى الذين يراجعون مركز الروماتيزم والتهاب المفاصل في دهوك . تم تصنيف المرضى الى مجموعتين

المجموعة الاولى: المرضى الذين لديهم التهاب المفاصل و التهاب اللثة والذين استلمواعلاج امراض اللثة خلال الدراسة.

المجموعة الثانية: المرضى الذين لديهم التهاب المفاصل و التهاب اللثة والذين لا يستلمون اي علاج للثة خلال الدراسة.

في البداية صحة اللثة و الانسجة الداعمة يعتمد على قياس جيوب اللثة و قياس مدى فقدان الانسجة الداعمة و قياس شدة المرض بعد ستة اشهر لمعرفة تاثير علاج اللثة على شدة المرض.

النتائج: في البداية لم يلاحظ اي فرق معنوي بين اللثة و شدة المرض. بعد ستة اشهر هناك فرق معنوي ملحوض داخل المجاميع للمجموعتين الاولى والثانيه بالنسبه لحالة اللثة و شدة التهاب المفاصل .

الاستنتاجات: في البداية لم يلاحظ اي فرق معنوي بين اللثة و شدة المرض. بعد ستة اشهر هناك فرق معنوي ملحوض داخل المجاميع .

VITAMIN D STATUS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is a common endocrinopathy affecting women in their reproductive age characterized by anovulation. This heterogeneous disorder is usually accompanied by hormonal and metabolic disturbances mainly FSH-LH imbalance, insulin resistance, dyslipidemia and hirsutism. A variety of previous studies emphasized on the evaluation of dihydroxy vitamin D 25(OH)D in sera of PCOS patients. Its concluded that PCOS patients are more likely to have vitamin D deficiency and or insufficiency. The aim of the present study is to evaluate the role of vitamin D in PCOS pathogenesis and its association with metabolic disturbances.

Methods: This case control study involved forty clinically diagnosed PCOS patients according to Rotterdam criteria with twenty apparently healthy women as a control group. Physical examination was done as well as case history was taken by a questionnaire. Laboratory examinations were performed by automated method using Cobas 6000 analyzer.

Results: Total serum vitamin D levels showed a highly significantly statistically decrease in PCOS women compared to control ($p < 0.005$). Among patients, 75% were considered deficient, 15% insufficient and 10% with normal levels respectively. Moreover, there was a significant correlation between vitamin D deficiency and body mass index (BMI).

Conclusion: Vitamin D deficiency may have a role in the pathogenesis of PCOS through initiating metabolic disturbances mainly insulin resistance and increased BMI which may have an influence on the ovarian functions.

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Keywords: Polycystic ovary syndrome, vitamin D and lipid profile.

Polycystic ovary syndrome (PCOS) is a common endocrinopathy affecting around 6-10% of women in their reproductive age characterized by anovulation. This heterogeneous disorder is usually accompanied by hormonal and metabolic disturbances mainly FSH-LH imbalance, insulin resistance, dyslipidemia and hirsutism.[1,2,3] Until 2003, there was no concise and universally accepted clinical definition for PCOS, but The Rotterdam ESHRE/ ASRM- sponsored PCOS consensus workshop group managed to establish a set of criteria enabling clinicians to diagnose PCOS in a precise manner.[4,5] It was concluded that no single diagnostic criterion was sufficient for clinical diagnosis of PCOS, therefore, two out of three criteria have to be exist; chronic anovulation, clinical and/or biochemical hyperandrogenism and polycystic ovaries.[6]

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However, vitamin D traditionally plays an important role in bone metabolism as well as calcium-phosphorus homeostasis.[7] Moreover, recently new functions have been revealed such as its crucial role in mediating immune cells functions.8 Reduced vitamin D levels have been linked with a variety of conditions mainly cardiovascular diseases, diabetes, metabolic diseases and cancer.[9,10] Even though the variety of research have been conducted regarding the association of PCOS with various conditions, negligible studies have focused on the role of vitamin D and its contribution to the pathogenesis of PCOS. The aim of this study is to evaluate the role of vitamin D and its possible association with variable manifestations in women having PCOS.

METHODS:

This case control study was conducted at Department of Physiology, College of Medicine, University of Duhok from November 2015 to February 2016 . Participants involved forty clinically diagnosed PCOS patients according to Rotterdam criteria (oligo- and/or anovulation or clinical and/or biochemical hyperandrogenism or polycystic ovaries on ultrasound) with twenty apparently healthy women as a control group. Following clinical diagnosis, physical examination was done including height, weight and body mass index as well as case history was taken by a questionnaire. Five milliliters of venous blood were collected from each participant for laboratory investigations.

Lipid profile including total serum cholesterol (Tch), triglyceride (TG), high density lipoprotein (HDL) were measured manually (BioLab, France) whereas low density lipoprotein (LDL) and very low density lipoprotein (VLDL) were calculated using Friedewald formula. Total serum vitamin D levels were assayed by automated method using Cobas 6000 (Roche Diagnostics, USA). Hormonal assays including follicular stimulating hormone (FSH) and luteinizing hormone (LH) were performed using enzyme immunoassay technique (Biomerieux manufacturer, France).

Statistical analysis was done using SPSS version 18 (Chicago, USA). All variables were expressed as mean ± standard deviation (SD) and the independent t-test used to determine the statistical significance of difference in mean between two groups. p values of 0.05 or less were considered statistically significant.

RESULTS:

The mean age of participants in this study (both patients and controls) was 29 years. PCOS patients who were clinically diagnosed had infertility of about 3.34 years. Body mass index (BMI) was statistically significantly higher in PCOS

patients (28.14 vs. 22.9) compared to control (p= 0.005). Follicular stimulating hormone (FSH) of PCOS group was significantly lower compared to control (p=0.04) whereas luteinizing hormone (LH) was significantly higher in patients vs. control (p= 0.01) (Table 1).

Table 1: Basic characteristics of PCOS patients and control subjects

Parameters	PCOS	Control	p value
Body Mass Index (BMI)	28.14 ± 3.12	22.9 ± 2.05	0.005
Duration of infertility (years)	3.34 ± 2.57	NA	NA
Age (years)	29.1 ± 4.71	29.7 ± 3.88	0.91
FSH	6.31 ± 2.44	10.59 ± 2.63	0.04
LH	13.23 ± 2.18	5.84 ± 1.95	0.01

Fasting blood glucose levels of PCOS patients was significantly higher compared to control (p= 0.001). Concerning lipid profile, total serum cholesterol and low density lipoprotein were significantly higher (p = 0.001) in PCOS patients compared to control. Furthermore, high density lipoprotein (HDL) was significantly lower in PCOS compared to control subjects (p =0.005). However, both triglyceride and VLDL did not show significant differences between study groups (Table 2).

Table 2: Lipid profile and D 25(OH)D among study groups.

Parameters	PCOS (N = 40)	Control (N = 20)	p value
Fasting Glucose	111.7 ± 2.65	92.3 ± 3.75	0.001
Total Cholesterol	170.12 ± 4.52	136.8 ± 3.03	0.001
Triglyceride	94.2 ± 4.02	92.7 ± 3.53	0.77
HDL	38.57 ± 1.16	47.11 ± 0.92	0.005
LDL	108.7 ± 4.68	71.9 ± 3.16	0.001
VLDL	18.7 ± 0.88	17.6 ± 0.67	0.32
Total 25 hydroxy vitamin D (ng / ml)	16.25 ± 2.31	43.2 ± 1.16	< 0.005

Total serum 25(OH)D levels showed a highly statistically significant decrease in PCOS women compared to control (p < 0.005) (table 3). Among patients, 75% were considered deficient, 15% insufficient and 10% with normal levels respectively. 90% of control subjects had normal vitamin D levels with 10% of insufficient (Table 4).

Table 3: Number and percentage of deficient and insufficient patients and controls.

Parameters	Deficiency (< 20 ng/ml)	Insufficiency (20-30 ng/ml)	Normal levels (30-100 ng/ml)
PCOS patients (No. = 40)	30 (75 %)	6 (15%)	4 (10%)
Controls (No. = 20)	0 (0 %)	2 (10 %)	18 (90%)

Pearson's correlation coefficient between vitamin D and body mass index (BMI) displayed a significant negative correlation (p=0.05) with a negligible and non significant values with HDL, FSH and LH respectively.

Table 4: Pearson's correlation coefficient between variables.

Parameters	r value	p value
Vitamin D - BMI	- 0.254	0.05
Vitamin D - HDL	- 0.16	0.1
Vitamin D - FSH	- 0.08	0.31
Vitamin D - LH	- 0.05	0.38

DISCUSSION:

This study aimed to demonstrate the association between vitamin D deficiency and PCOS pathogenesis as well as the possible mechanisms underlying that. PCOS women had significantly increased BMI (p=0.005) which was significantly correlated with vitamin D deficiency (table 5). This is indicated in previous literature concluding that this may be due to existence of obesity and excess androgen levels which subsequently resulting in insulin resistance.[11,12,13] Metabolic and endocrine disturbances in PCOS are well expressed in our study represented by elevated fasting glucose and low HDL levels (Table 2) as well as hormonal disturbances including disturbances in FSH and LH values (Table 1). Previous studies indicated that altered FSH/LH ratio in PCOS patients have adverse effects on ovulation represented by failure in maturation of ovum during menstrual cycle and subsequently unovulation.[14,15] In addition, present results are in concordance with previous literature indicating that borderline hyperglycemia, hyperinsulinemia and hyperlipidemia may be regarded as the main inducer of insulin resistance in PCOS women.[16,17]

This study showed a highly statistically significant decrease in total 1,25 hydroxyvitamin D levels in PCOS women compared to control (p<0.005) as well as the majority of patients (75%) were considered to have hypovitaminosis D. Although the exact mechanisms of vitamin D deficiency in PCOS are not well understood, these results are supported by previous studies concluding that polymorphisms in vitamin D receptor (VDR) gene and deficiency in VDR expression on target cells might be associated with metabolic and endocrine disturbances in PCOS.[18,19] Moreover, studies suggested that there is association between vitamin D and insulin resistance. Vitamin D potentiates insulin action by stimulating insulin receptors expression and thereby enhancing insulin responsiveness for glucose.[20,21] Furthermore, transcription of insulin gene is activated by 1,[25] (OH) D2.[22,23] Vitamin

D regulates both intracellular and extracellular calcium that is important in insulin-mediated intracellular processes in insulin responsive tissues such as adipose tissues.[24,25,26]

Although absence of androgen measurement could be one of the possible limitations of the present study, this is managed by diagnosing study participants according to Rotterdam criteria based on the presence or absence of hirsutism. Moreover, the sample size of the present study may be low for such a common women health problem. Despite the researcher's attempts for including more participants, the study was conducted based on availability of participants. In conclusion, this study suggest that vitamin D deficiency may have a role in the pathogenesis of PCOS through initiating metabolic disturbances mainly insulin resistance and increased BMI which may have an influence on the ovarian functions. Therefore, its recommended that vitamin D should be prescribed to PCOS patients having vitamin D deficiency as an ancillary treatment to improve metabolic disturbances mainly insulin resistance. Future studies should pay further attention to the relationship between vitamin D and metabolic disturbances to clarify the association between insulin resistance and hypovitaminosis D.

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پوختە

فیتامین دی ل جەم نەساخێن کیسبونا هێکلدانێ

پێشەکی و ئارمانج: کیسکبونا هێلکەدانێ ئێکە ژنەخوشییێن بەربەلاڤ لجەم ژنا و تا نوکە ئەگەرێن وێ ددیار نینن, ژنا نەساخ بڤێ نەخوشیێ دەورا وێ یا هەیڤانە گیرو دبیت و هێك دروست نا چێبیت. ئارمانج ژڤێ ڤەکولینێ دیارکرنا رولێ فیتامین دی یە دیارکرنا کاریگەریا وێ لسەر کارێ هیلکەدانێ.

رێکێن ڤەکولینێ: ئەڤ ڤەکولینە هاتە ئەنجامدان ل کولپژا پزیشکی بەشێ فسیولوجی و پشکدار هاتنە دابەش کرن لسەر دوو گروپا: گروپێ ئیکێ نەساخ و ژمارا وان ٤٠ کەس بون و گروپێ دووێ ژنێن نورمال بون و ژمارا وان ٢٠ کەس بون. تاقیکرنێن لابورێ یێن پێدڤی هاتنە ئەنجامدان و هەرهوسا پێزانینێن کلینیکی بریکا فورمەکا تایبەت هاتنە وەرگرتن.

ئەنجام: ئەنجامین ڤەکولینێ دیارکرن کو خوینا نەساخێ کیسکبونا هێلکەدانێ کێمیا فیتامین دی هەنە و ئەڤ چەندە کاریگەریەکا نەرێنی لسەر کارێ هێکلدانێ دکەت.

دەرئەنجام: کێمبونا فیتامین دی کاریگەریەکا خراب لسەر کارێ هێکلدانێ هەیە و دبیتە فاکتەرەکێ سەرەکی ژبو کارکرنا وێ بشێوەکێ نە نورمال.

الخلاصة

تقييم دور الفيتامين دي لدى النساء المصابات بمتلازمة تكييس المبايض

خلفية وأهداف البحث: متلازمة تكييس المبايض هو خلل افرازي أيضي غير معروف السبب يتميز بعدم الاباضة و زيادة في مستوى الاندروجين في الدم و احيانا تترافق مع اعراض اخرى مثل خلل في افراز الانسولين. الهدف من هذه الدراسة هو تحديد دور الفيتامين دي لدى النساء المصابات بمتلازمة تكييس المباييض.

طرق البحث: تضمنت هذه الدراسة ستون مشاركات و قد تم تقسيمهن الى مجموعتين, المجموعة الاولى تألفت من أربعون مريضا مشخصا كلينيكيا بمتلازمة تكييس المبايض اما المجموعة الثانية تضمنت عشرون اشخاصا اصحاء كمجموعة ضابطة. تم اجراء جميع التحليلات المختبرية في مختبر الفسلجة بكلية الطب و الحصول على المعلومات الاكلينيكية الاضافية حول حالات المرضى من خلال أستبيان. تم تحليل المعلومات و اجراء الاحصاء الطبي باستعمال البرامج المختصة.

النتائج: أضهرت نتائج الدراسة وجود نقصان ملحوض في مستوى الفيتامين دي في دم المرضى مقارنة بالمجموعة الضابطة.

الاستنتاج: تلخصت الدراسة بأن نقص الفيتامين دي في دم المرضى المصابين بمتلازمة تكييس المباييض من المرجح ان يكون لها دورا فعالا و تأثيرا مباشرا على وضائف المبايض. لذلك ينصح بأعطاء الفيتامين دي كجزء من العلاج للمرضى الواتي عندهن نقص بالفيتامين المذكور.

ACNE VULGARIS: THE PREVALENCE, SEVERITY AND THE ASSOCIATED FACTORS AMONG SECONDARY SCHOOL STUDENTS IN A DISTRICT OF KURDISTAN REGION /IRAQ

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ABSTRACT

Background and objectives: Acne vulgaris is a common dermatological disorder among secondary school students. It is frequently complained by students in our locality without being properly studied. This study aimed to measure the prevalence and severity of acne vulgaris and factors affecting them among secondary school students in a district of Kurdistan Region, Iraq.

Methods: A cross sectional design was performed. A multistage random sample of 575 secondary school students of both genders selected from 6988 students in Amedi district/ Duhok Governorate. All Students were clinically examined and interviewed for data collection regarding socio- demographic variables of age, gender, ethnicity, residence and family income. Also information was collected regarding parental history of acne, self excoriative behavior and make up use among females. Their nutritional status was measured by the body mass index. The severity of acne was assessed by using Global Acne Grading system. Data were collected and analyzed by using the statistical package for social sciences (SPSS version 22).

Results: The results revealed prevalence rates of 71.7% and 87.8% by self–reporting and by clinical examination respectively. The mild, moderate and severe forms were found respectively in 90.8%, 9% and 0.2% of students diagnosed with acne vulgaris. Papules and comedones were the most prominent acne lesions. No statistically significant associations were detected between prevalence or severity of acne vulgaris and socio demographic factors of age, gender, ethnicity, residence and body mass index. Family history of acne vulgaris was significantly associated with severity ($p < 0.05$) but not with the prevalence ($p > 0.5$).

Conclusions: The study demonstrated a high prevalence of acne vulgaris with substantial genetic role in the severity of the disease.

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Keywords: Acne Vulgaris, Prevalence, Severity. Kurdistan region

Acne vulgaris (AV) is a common dermatological health problem among secondary school students with greatest frequency at the ages of 15-18 in both sexes.[1-3] A prevalence rate of 70-80% has been reported, with a wide variation in different countries.[4-8] The disease is mainly encountered on the face, chest and back. Factors like excessive sebum excretion, hormonal stimulation, poral

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occlusion and bacterial colonization play a role in etiology. Also several other factors have been incriminated in the etiology and severity of the disease like age, gender, ethnicity, nutritional status and family history.[1-3]

SUBJECTS AND METHODS

A cross sectional study was conducted on a random sample of secondary school students in Amedi district during the period from January to April, 2015. Amedi district is one of the seven districts comprising Duhok governorate in Kurdistan Region, Iraq. Two ethnic groups share living in the area Kurds who are the majority and Assyrians Christians as a minority. After obtaining a formal approval from the scientific committee of the Kurdistan Board for Medical specializations, a multistage random sampling method was used for obtaining a sample size of 575 students. In the first stage 12 secondary schools were selected at random out of 25 present in Amedi District with total number of (6988) students. In the second stage each school was stratified into 6 strata, three for males and three for females of 10th, 11th and 12th classes, and a systematic random sampling method was used to take equal percentages of students from each stratum and 615 students were recruited for the study.

Each selected student was then seen in a private room by one of the researchers who has a 10 years practice in dermatology. A questionnaire was filled up regarding socio demographic characteristics of age, gender, ethnicity, residence, family income. Moreover data were also collected regarding make up use among females, self excoriative behavior and parental history of AV. After that each student was examined for dominant types of acne lesions (comedones, papules, pustules, nodules or no lesion) in all six locations of body (forehead, right cheek, left cheek, nose, chin, chest /upper back). The severity of AV was measured using Global Acne Grading System (GAGS). The six locations were first graded according to severity (4 for nodules, 3 for pustules, 2 for papules, 1 for comedones and zero for no lesion). The severity of AV was then calculated as the sum of multiplying the location factor by the grade of its dominant lesion of all six locations as follow[9]:

Type of acne lesion and it is grade	Location of Acne lesion							
		Forehead*2F	Right cheek*2F	Left cheek *2F	Nose*1F	Chin*1F	Chest and upper back*3F	Total
	Comedones (G=1)							
	Papules (G=2)							
	Pustules (G=3)							
	Nodules (G=4)							
	Grand Total							
	F: Location Factor, G: Grade of acne lesion, Local Score = F*G, Total Score =Sum of local sores . Mild acne =1-18, Moderate acne 19-30, Severe acne =31-38, Very severe acne =39 and more							

Weight and height were measured for estimation of body mass index which was classified into three categories according to WHO growth reference chart for 5-19 years.[10] Obese or overweight (>one SD), normal weight (1SD to -2SD) and thinness or severe thinness (<-2SD). Family income was divided into 3 categories: good (owning a house, car and have constant salary), sufficient (having one of the three) and insufficient (having none of the three). Statistical package for social sciences (SPSS, version 22) was used for data entry and analysis. P value at ≤ 0.05 was considered statistically significant. Chi-square ($\chi 2$) test was used for comparing proportions of different characteristics. Non parametric tests like Mann-whitney and Kruskal Wallis tests were used for comparing continuous variables of different categories.

RESULTS

A total of 575 students completed the survey successfully with a mean age ± SD of 17.27 ±1.08 years. The sample comprised 304 (52.9%) females and 271(47.1%) males. Table 1 shows that the prevalence of AV was 87.8%; with 86% for males and 89.5% for females. Table 1 also shows that the self reporting prevalence was significantly lower than actual one estimated by clinical examination.

Table 1: The prevalence of AV and Reliability of self-reporting by gender

	No.	Prevalence of AV by Examiners %	Prevalence of AV by student's self-reporting %	Total agreement %	Kappa	P value
Males	271	86.0	67.5	77.1	0.39	<0.001
Females	304	89.5	75.3	83.2	0.44	<0.001
All	575	87.8	71.7	80.3	0.42	<0.001

Table 2 shows the six prone areas for AV. Forehead area was less times free of acne lesions especially in males. Papules were more frequently dominant in all acne prone areas except the nose in which the comedones were more frequently observed

Table 2. Frequency distribution according to dominant acne lesions in six acne prone areas of the body

	Dominat type of acne lesion					
	Clear N (%)	Comedones N (%)	Papule N (%)	Pustules N (%)	Nodule N (%)	Total N (%)
Forehead						
All	188 (37.2)	85 (16.8)	225(44.6)	6 (1.2)	1(0.2)	505(100)
M	104 (44.6)	31(13.3)	94(40.3)	3(1.3)	1(0.4)	233(100)
F	84 (30.9)	54(19.9)	131(48.2)	3(1.1)	0(0)	272(100)
Right cheek						
All	255(50.5)	52(10.3)	184(36.4)	11(2.2)	3(0.6)	505(100)
M	110(47.2)	30(12.9)	83(35.6)	8(3.4)	2(0.9)	233(100)
F	145(53.3)	22(8.1)	101(37.1)	3(1.1)	1(0.4)	272(100)
Left cheek						
All	303(60.0)	36(7.1)	152(30.1)	10(2.0)	4(0.8)	505(100)
M	132(56.7)	21(9.0)	71(30.5)	7(3.0)	2(0.9)	233(100)
F	171(62.9)	15(5.5)	81(29.8)	3(1.1)	2(0.7)	272(100)
Chin						
All	288(57.0)	50(9.9)	156(30.9)	9(1.8)	2(0.4)	505(100)
M	144(61.8)	14(6.0)	67(28.8)	6(2.6)	2(0.9)	233(100)
F	144(52.9)	36(13.2)	89(32.7)	3(1.1)	0(0.0)	272(100)
Nose						
All	243(48.1)	234(46.3)	26(5.1)	1(0.2)	1(0.2)	505(100)
M	120(51.5)	96(41.2)	15(6.4)	1(0.4)	1(0.4)	233(100)
F	123(45.2)	138(50.7)	11(4.0)	0(0.0)	0(0.0)	272(100)
Chest / upper back						
All	303(60.0)	3(0.6)	189(37.4)	7(1.4)	3(0.6)	505(100)
M	146(62.7)	2(0.9)	78(33.5)	4(1.7)	3(1.3)	233(100)
F	157(57.7)	1(0.4)	111(40.8)	3(1.1)	0(0.0)	272(100)

Table 3. Shows that age, gender, ethnicity, residence, family income, BMI and make up usage had no significant association with the prevalence of AV .

Table 3: Prevalence of acne vulgaris by socio-demographic variables

	N	%	P value
Age Group			
16	**175**	**83.4**	
17	**167**	**89.2**	**0.1**
18-19	**233**	**90.4**	
Total	**575**	**87.8**	
Gender			
Male	**271**	**85.6**	
Female	**304**	**89.8**	**0.1**
Total	**575**	**87.8**	
Ethnicity			
Kurdish	**505**	**88.3**	
Assyrian	**70**	**84.3**	**0.3**
Total	**575**	**87.8**	
Residence			
Urban	**298**	**86.6**	
Rural	**276**	**89.1**	**0.3**
Total	**574**	**87.8**	
Family Income			
Not sufficient	**71**	**94.4**	
Sufficient	**472**	**86.9**	**0.2**
Good	**32**	**87.5**	
Total	**575**	**87.8**	
BMI			
Normal	**340**	**88.2**	
Overweight a/ obese	**92**	**90.2**	**0.3**
Thin /severe thinness	**134**	**84.3**	
Total	**566**	**87.6**	
Females using make up			
YES	**185**	**90.7**	
No	**86**	**86.3**	**0.4**
Total	**304**	**89.1**	

Table 4 reveals that family history of AV has no significant effect on the prevalence of the disease among siblings. However, the association was higher when both parents and/or mothers had history of AV, but also did not reach a statistical significance. Similar non significant association was found with history of AV among sisters and/or brothers of students.

Table 4: Association between family history and prevalence of acne vulgaris

		N	Acne prevalence		P value
			NO.	%	
Parental history of acne vulgaris	**Father**	**113**	**97**	**85.8**	
	Mother	**93**	**86**	**92.5**	
	Both parents	**47**	**43**	**91.5**	**0.3**
	None of them	**322**	**279**	**86.6**	
	Total	**575**	**505**	**87.8**	
Sisters and/or brothers with acne vulgaris	**One or more**	**429**	**383**	**89.3**	
	No one	**146**	**122**	**83.6**	**0.06**
	Total	**575**	**505**	**87.8**	

Table 5 shows no significant association between the severity of AV and each one of the variables of age, gender, ethnicity, residence, family income, BMI and make up use by female students.

Table 5: The association between severity of acne vulgaris with variables; age, gender, ethnicity, residence, family income, BMI and make use by females.

	N	% mild	% moderate	P value
Age Group				
16	**145**	**25.2**	**3.6**	**0.2**
17	**149**	**28.0**	**1.6**	
18-19	**210**	**37.7**	**4.0**	
Total	**504**	**90.9**	**9.1**	
Gender				
Male	**231**	**41.1**	**4.8**	
Female	**273**	**49.8**	**4.4**	**0.4**
Total	**504**	**90.9**	**9.1**	
Ethnicity				
Kurdish	**445**	**81.0**	**7.3**	
Assyrian	**59**	**9.9**	**1.8**	**0.09**
Total	**504**	**90.9**	**9.1**	
Residence				
Urban	**257**	**45.9**	**5.2**	
Rural	**246**	**44.9**	**4.0**	**0.5**
Total	**503**	**90.9**	**9.1**	
Family income				
Not sufficient	**67**	**11.5**	**1.8**	
Sufficient	**410**	**74.1**	**6.9**	**0.5**
Good	**28**	**5.0**	**0.6**	
Total	**505**	**90.5**	**9.3**	
BMI				
Normal	**385**	**69.9**	**6.8**	**0.6**
Over weight and Obese	**91**	**16.1**	**2.0**	
Thinness and Severe thinness	**26**	**4.8**	**0.4**	
Total	**502**	**90.8**	**9.2**	
make up use by females				
Yes	**185**	**63.0**	**6.8**	
No	**80**	**28.7**	**1.5**	**0.2**
Total	**265**	**91.7**	**8.3**	

Table 6 reveals a significant association between the severity of AV and family history of the disease. A significantly higher scores of mean rank of AV severity scores were encountered when the affected students had parental history of AV of both parents and/or mother compared to those with no parental history and/or father history of AV(P=0.04). Similarly,

students who had sisters and/or brothers with AV experienced significantly more severe forms of the disease compared to those with no such history ($p<0.001$).

Finally the study found that the overall prevalence of self excoriative behavior was 64.7%.

Table 6: severity of acne vulgaris association with family history of acne vulgaris

		N	Mean Ranks of Acne severity scores	P value
Parental history of acne vulgaris	None of them	319	270.8	0.04
	Father	113	291.6	
	Mother	93	313.8	
	Both Parents	47	326.2	
	Total	572		
Sisters and /or brothers with acne vulgaris	Yes	429	245.4	<0.001
	No	146	302.5	
	Total	575		

DISCUSSION

Secondary school students are the most vulnerable ages for the disease and easily accessible. Despite that, however, this might limit generalizability of the findings as the disease might start earlier and clears at older ages[1-3]. The GAGS scale was selected for measuring the severity of AV as it is simple and quick method.[9]

The study showed an overall prevalence of 87.8%. Similarly, other studies reported high prevalence rates in Iran[4] (85.9%), Nigeria[5] (90.7%), and Brazil[6] (96.0%). However, much lower rates were reported in China[7] (38.0%) and Cameroon[8] (60.0%). This might be due to ethnic variation, using different diagnostic criteria or including younger age group.

In this study students underestimated their acne status in comparison to clinical examination. This finding was against that reported in a similar study in Norway,[11] where students had overestimated their acne status. This might be due to dissimilarities of psychosocial environment between the two populations. Female students in this study expressed better agreement than male students. This might be explained by the fact that the female are more linked with beauty and appearance and are more sensitive to changes in their body image than males. It was noted that papules and then comedones were the dominant acne .This is beneficial to health authorities to arrange for treatment modality which depends on the type of the lesion.[1,12]

Clinically more disfigured forms of acne scars were observed in about 3% of patients .This is an essential health problem due to the special treatment needed; with no guarantee of cure.[13] In

addition a high prevalence of self excoriative behavior (64.7%) was reported; which worsen the lesions and increases the probability of acne scars.

The study found no significant differences in the acne prevalence between males and females. Similar finding was observed in a study in Iran[4], however, a study in Greece found higher acne prevalence in females in ages of 11-14 years and in males in ages of 14-16 years.[14] In addition to that a study in Lithuania demonstrated a higher acne prevalence among female at ages 10-12 years which might be explained by earlier female maturation.[15]

The current study revealed no significant difference in the acne prevalence between the two ethnic groups of Kurds and Assyrians, which might be due to small number of the latter. Studies around the world found significant differences among different ethnic groups.[16,17]

The study found that previous history of AV among parents, sisters and/ or brothers had no significant effect on the acne prevalence among students. Contradictory results were reported in other studies; which might be due to variations in targeted ages and sample biases.[6]

A total of 90.7%, 9.1% and 0.2% were described as having mild, moderate and severe acne respectively. Similar findings were observed by other studies in different parts of the world such as in Iran[4], Nigeria[5], and Brazil[6].

In this study parental history of AV was significantly associated with the severity of the disease and the association remains significant with maternal history. This is consistent with the results of another study; indicating the role of mother's genetics in causing more severe forms of acne.[6] Similar significant association was found with sisters and/or brothers .This might be due to different types of genes from parents with variable ability to transmit to the next generation. On the other hand no significant association was found between the severity of AV and age group, gender, ethnicity, place of residence, nutritional status and using of makeup.

In conclusion AV is a highly prevalent skin disorder among the studied population with substantial genetic role in transmitting severe forms of acne vulgaris.

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پوختە

زیپکێت گەنجاتیێ: ڕێژەیا بەربەلاڤی و توندیا وێ و هوکارێن پەیوەندیدار

زەمینە و ئامانج: زیپکێت گەنجاتیێ دەردەکێ پیستی یێ بەلاڤە دناڤاخویندکارێن قوناغا ئامادەیی دا یا کو زوربەیا جاران خویندکارل کومەلگەها مە ل بەر دنالن بێی کو ئەوچەندە بباشی هاتبیتە لێکولینکرن. ئامانجا ڤێ ڤەکولینێ دەرئێخستنا بەربەلاڤیا زیپکێت گەنجاتیێو توندیا وێ و هوکارێن پەیوەندیدار دناڤا خویندکارێن ئامادەیی دا دناڤا یەك ژکەرتێن هەرێما کوردستانا عراقێ.

ڕێك: ئەڤ ڤەکولینە بشێوێ پانە برگەیی هاتە دارشتن, نمونەکا هەرەمەکی یا پێکهاتی ژ ٥٧٥ خویندکاران هاتە هەلبژارتن ژناڤا ٦٩٨٨ خویدکارێن ئامادەیی بێن سەر ب کەرتێ ئامێدیێ پارێزگەهادهوکێ ڤە. چاڤپێکەفتن دگەل هەمی خویندکارا هاتەکرن و پشکنینێن ناڤ جهی بو هاتنە کرن بو تومارکرنا پێزانینێن جڤاکی و دیموگرافی وەك ژی، رەگەز، نفش، داهاتێ خێزانێ، میژویا پرسکێت گەنجاتیێ ل دەف دایبابا، رەفتارا تیڤلکرنا بیستی و بکارئینانا میکیاژی ژلایێ خویندکارێن کچ ڤە. بارێ خوراکی یێ خویدکاران هاتە هەلسەنگاندن ب ریا نیشادەرێ بارمتا لەشی. پاشان پشکنین بو هەمیان هاتەکرن بو هەلسەنگاندنا توندیا زیپکێت گەنجاتیێ برێیا بکارئینانا سیستەما جیهانی یا پولینکرنا زیپکێت گەنجاتیێ دا بێن هاتنە کومکرن وشروڤەکرن ب ریا بەستەیا ئامارا یا زانستێن جڤاکی.

ئەنجام: ل دیف ئەنجامێن ڤێ لێکولینێ بەربەلاڤیا زیپکێت گەنجاتیێ ب ڕێژەیا ٧١.٧٪ و٨٧.٨٪ لگورەی دیتنا خویندکاران و پشکنینا نوژداری لدیف ئێك هاتە دەستنیشانکرن. ل ئەڤا دوماهیێ خویابو کو ٩٠.٨٪ ژ خویندکارێن زیپکەهەین ب سفکاتی توشببون ٩٪ ب ناڤنجی و بتنێ ٠.٢٪ ژ وانا ب گرانی توشی ڤێ نەخوشیێ ببون. زوربەیا حالەتێن پرسکێن گەنجاتیێ ژ جورێ پاپیول یان زیوان بو. چ پەیوەندیەکا بەرچاڤ دناڤبەرا بەربەلاڤیا زیپکێت گەنجاتیێ و توندیا وێ دگەل دگەل هوکارێن کومەلایەتی و دیموگرافی دا نەبون وەك ژی، رەگەز، نفش، خوجهی و نیشاندەرێ بارمتا لەشی. هەبونا میژویا خیزانێ یا پرسکێت گەنجاتیێ پەیوەندیەکا بەرچاڤ هەبو دگەل توندیا پرسکێت گەنجاتیێ ($p<0.5$) بەلێ نە دگە بەربەلاڤیا وێ ($p>0.5$).

دەرئەنجام: ڤێ لێکولینێ دیارکر کو ڕێژەیەکا زور یا خویندکارا توشی نەخوشیا پرسکێت گەنجاتیێ بوینە و رولێ بوماوەیی د توندیا پرسکێت گەنجاتیێ دا یا خویایە.

الخلاصة

حب الشباب: معدل الانتشاروالشدة والعوامل المقترنة بهما

الخلفية والاهداف: حب الشباب عبارة عن اعتلال جلدي شائع بين طلاب المرحلة الاعدادية والذي كثيرا ما يعاني منه الطلاب في مجتمعنا دون ان يدرس بشكل وافي. كان الهدف من هذه الدراسة احتساب معدل انتشار حب الشباب وشدته والعوامل التي توثر عليهما بين طلاب المرحلةالاعدادية في قاطع ضمن اقليم كردستان العراق.

طرق البحث: في هذه الدراسة التي اعتمد فيها التصميم المقطعي. تم اختيار عينة عشوائية مؤلفة من ٥٧٥ طالبا من كلا الجنسين من بين ٦٩٨٨طالبا في قاطع العمادية، محافظة دهوك. وقد تم مقابلة جميع الطلاب وفحصهم سريريا لغرض جمع البيانات المتعلقة بالخصائص الاجتماعية والديموغرافية مثل العمر، الجنس، العرق، دخل العائلة، التاريخ الابوي لحب الشباب، سلوك سلخ الجلد الذاتي، واستعمال المكياج من قبل الطالبات. تم قياس الحالة التغذوية للطلاب عن طريق احتساب مؤشر كتلة الجسم. وتم أيضاً تحديد شدة حب الشباب بالاعتمادعلى مقياس النظام العالمي لتصنيف حب الشباب وفي النهاية تم جمع البيانات و تحليلها باستعمال برنامج الحزمة الاحصائية للعلوم الاجتماعية.

النتائج: أظهرت الدراسة بان معدل انتشار حب الشباب بين الطلاب كان ٧١.٧% و٨٧.٨% اعتمادا على الابلاغ الذاتي والفحص السريري على التوالي. تبين من الاخير بان ٩٠.٨% من حالات حب الشباب كانت من النوع البسيط، ٩% من النوع المتوسط بينما ٠.٢% فقط من الطلاب وصفت حالتهم بالشديدة. ابرز اصابات حب الشباب كانت من النوع الحبيبي والزؤاني.

لم يجد علاقة ملحوظة بين معدل انتشار حب الشباب او شدته والعوامل الاجتماعية و الديموغرافية مثل العمر، الجنس، العرق، السكن ومؤشر كتلة الجسم. التاريخ العائلي لحب الشباب كانت ذا علاقة ملحوظة مع شدة حب الشباب ($p<0.5$) وليس بمعدل انتشارها ($p>0.5$).

الاستنتاجات: أظهرت الدراسة معدلاً عالياً لانتشار حب الشباب مع وجود دور ضمني (أساسي) للوراثة في شدة حب الشباب.

SPECTRUM OF BONE MARROW PATHOLOGY AT HEVI PEDIATRIC HOSPITAL: SIX YEARS EXPERIENCE

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ABSTRACT

Background: Hematological disorders are relatively frequent in children. The spectrum of hematological disorders in children is broad, ranging from very frequent conditions like iron deficiency anemia to relatively rare congenital disorders. Bone marrow examination is one of the common and relatively non- dangerous invasive procedures done regularly in pediatric units. The objective of the study is to determine the spectrum of hematological disorders at Hevi pediatric teaching hospital in Duhok province, Kurdistan, Iraq.

Methods: The study was a retrospective one. All children who underwent bone marrow examination reported by the hematology department, at Hevi hospital over a period of six years from 2009-2014, were reviewed and re-examined. The clinical data, clinical examination and the indication for the marrow test on the request form as well as the marrow end result were all recorded and analyzed to know the relative frequencies.

Results: A total 814 cases of bone marrow examination results were considered from patients the age ranged from 20 days to 15 years. The median age of the cases was 4 years and male to female ratio (M:F) was 1.1:1. Out of the 569 de novo patients, 455 (80%) were non-malignant, while the remaining 114 (20%) patients were of malignant hematological disorders. The most common non-malignant hematological disorder was peripheral consumption of platelets (idiopathic thrombocytopenia purpura ITP) accounting for 28.4%, followed by megaloblastic anemia (12.8%), hypersplenism (12.1%), aplastic anemia (4.4%), marrow erythroid hyperplasia (4.2%), storage disorders (2.8%), while in 148 (32.5%) cases there were no pathological marrow disorder detected. Among the malignant hematological disorders, ALL constituted (70%), while AML cases were (21%), less common cases included mature B-cell leukemia (Burkitt's Lymphoma/leukemia) (4.4%) and mixed lineage acute leukemia (1.7%). Inadequate or diluted samples were encountered in 45 cases (5.5%), while in 200 (24%) cases bone marrow done for follow up and 188 (94%) of them were of known cases of acute leukemia.

Conclusion: The most common non-malignant hematological disorders in the pediatric Hevi hospital are peripheral consumption of platelet (ITP). The most common amongst the malignant hematological disorders is ALL followed by AML.

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Keywords: ....bon marrow aspiration and biopsy, bon marrow pathology, a plastic anemia

Hematological disorders are relatively frequent in children. Unlike adults the spectrum of hematological disorders in children is broad, ranging from very frequent conditions like iron deficiency anemia to relatively rare congenital disorders like Fanconi's anemia, thrombocytopenia with absent radius (TAR syndrome) and Blackfan Diamond syndrome. Similarly the spectrum of

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hematological disorders is somewhat different in the developing world than the industrial countries[1].

Bone marrow examination is one of the common and relatively safe invasive procedures done regularly in pediatric units. Though an invasive, process, it can be performed without any problems, even in the presence of severe thrombocytopenia with slight or no danger of bleeding.

The cellular elements of the blood produced by bone marrow; include whole formed blood cells (platelets, red cells and leucocytes). While a lot of information can be gathered by testing the peripheral blood itself, it is sometimes necessary to examine the source of the blood cells in the bone marrow to find more about the nature of hematopoiesis; this is done essentially by bone marrow study (aspiration and biopsy)[2].

Bone marrow aspiration and trephine biopsy are vital to prepare the marrow sample 2. The aspirate yields bone marrow which can be examined under a microscope by a hematopathologist and sometime used to perform more requested tests including flow cytometry, cytogenetic and molecular studies.

Examination of bone marrow is helpful in the diagnosis of both hematological and some non-hematological disorders. Malignant hematological diagnosis, staging, and therapeutic monitoring are essential indications of the marrow study. Also, estimation of peripheral blood cytopenia, thrombocytosis, leukocytosis, different types of anemia can be done[3]; this is also an important tool in the diagnosis of some non-hematological disorders like storage diseases, leishmaniasis, metastatic carcinoma, pyrexia of unknown origin, and disseminated infection in immunocompromised hosts[4].

MATERIAL AND METHODS

In this retrospective study all children who underwent bone marrow examination reported by the hematology department, Hevi pediatric teaching hospital, Duhok-Kurdistan region - Iraq over a period of six years from 2009-2014, were reviewed and re-examined. The clinical data including age, gender, clinical examination records and the indication for the marrow test on the request form as well as the marrow end result were all documented.

Bone marrow examination results were also recorded. Data was analyzed to know the relative frequencies in our pediatric patients.

Inclusion criteria:

All cases coming for bone marrow examination. Indications were unexplained anemia, cytopenia (mono–di and pancytopenia,), fever, organomegaly,

lymphadenopathy, and /or bleeding manifestations.

Insufficient or dry tap samples were excluded from the study.

The study was approved by ethical committee.

at the College of Medicine – University of Duhok (Kurdistan region).

RESULTS

A total of 814 cases that had undergone bone marrow examination were reviewed. The age of patients ranged from 20 days to 15 years. Inadequate or diluted samples were 45 (5.5%) and were excluded from the study, follow up cases was 200 (24.5%), leaving a total of 569 (70%) cases that were de novo cases. The median age of the latter group was 4 years and included 306 (52.8 %) males and 263 (47.2%) females. The male to female ratio (M:F) was 1.1:1 of the de novo cases, 455 (80%) patients were found to have non-malignant conditions (table 1), while the remaining 114 (20%) patients were having malignant hematological disorders (table 2).

As seen in (table 1) peripheral consumption of the platelets (idiopathic thrombocytopenia purpura ITP) was the most common, accounting for 28.4% amongst the non-malignant group. Megaloblastic anemia ranked as the second most frequent non-malignant condition 12.8%. Hypersplenism leading to consumption of two or more blood elements was presumed to be the diagnosis in another 12.1%. Other important diagnoses were less frequent and included aplastic anemia in 4.4% (this was mostly non-severe as shown in table 2), marrow erythroid hyperplasia in 4.2%, storage disorders in 2.8%; other cases were sporadic as shown in table I. In 148 (32.5%) cases there were no significant marrow pathology disorder made.

Table 1- Variety of non-malignant hematological disorders

Disorders	No. of cases	%	Median age (years)	Male	Female
No significant marrow pathology	**148**	**32.5**	**4.3**	**80**	**68**
Peripheral consumption of platelets (ITP)	**129**	**28.4**	**3.5**	**73**	**56**
Megaloblastic anemia	**58**	**12.8**	**1**	**26**	**32**
Peripheral consumption of blood elements	**55**	**12.1**	**5**	**30**	**25**
Aplastic anemia	**20**	**4.4**	**7**	**10**	**10**
Marrow erythroid hyperplasia	**19**	**4.2**	**5**	**11**	**8**
Iron deficiency anemia	**7**	**1.5**	**2.2**	**4**	**3**
Guacher disease	**7**	**1.5**	**3.8**	**5**	**2**
Niemann-Pick disease	**6**	**1.3**	**1.4**	**3**	**3**
Visceral leishmaniasis	**2**	**0.4**	**8;16 months**	**0**	**2**

Disorders	No. of cases	%	Median age (years)	Male	Female
Pure red cell aplasia (PRCA)	1	0.22	6 months	0	1
Chediac-Higashi syndrome	1	0.22	3	1	0
Absent megakaryocytes	1	0.22	18 months	1	0
TAR syndrome	1	0.22	3 months	1	0
Total	455			245	210

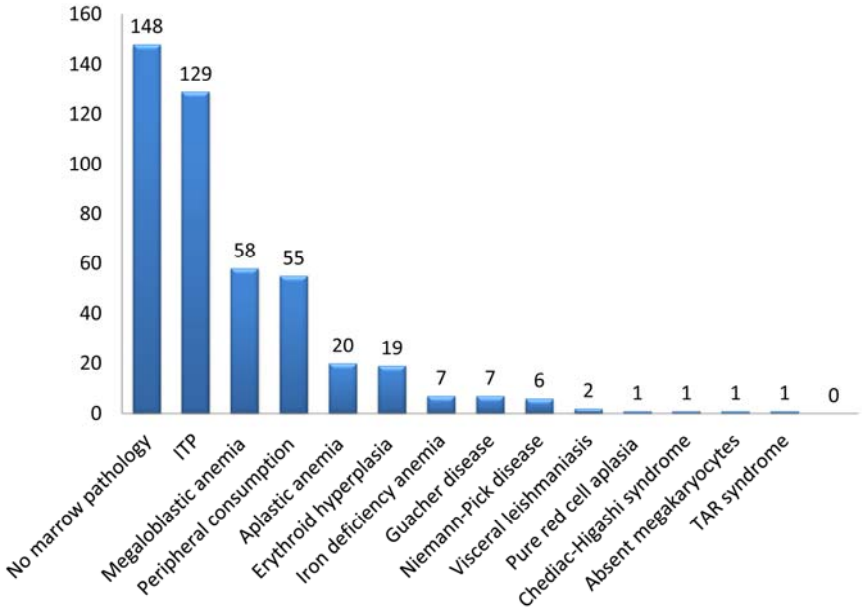

Figure (1) Variety of non malignant hematological disorder

Table 2- Classification of disease severity in aplastic anemia (AA), *classified according to Hoffbrand et al*

Prognostic classification of aplastic anemia	No	%
Non- severe AA	16	85 %
Severe AA	3	15 %
Very-severe AA	1	5 %

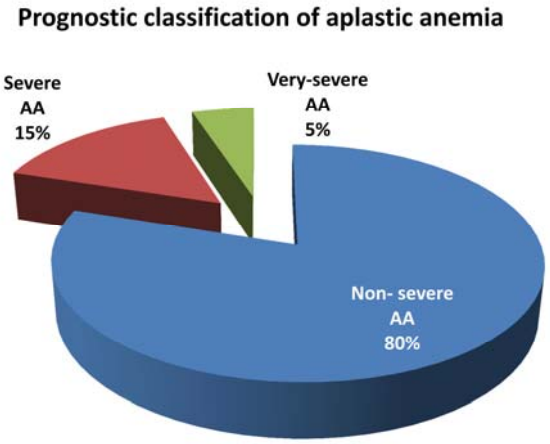

Figure (2) Classification of disease severity in aplastic anemia

During the period of the study a total of 114 malignant hematological disorders were diagnosed by bone marrow examination (table 3), the most common (70%) were acute lymphoblastic leukemia (ALL), the second frequency was acute myeloid leukemia (AML), less common were mature B-cell leukemia (Burkitt Lymphoma/leukemia) and mixed lineage acute leukemia, other malignant cases were sporadic as shown in (table 3)

Table 3 - Variety of hematological and non-hematological malignant disorders

Disease	No. of cases	%	Median age (years)	Male	Female
Acute lymphoblastic leukemia B-type	70	61.3	4.5	36	34
Acute lymphoblastic leukemia T-type	10	8.8	7	5	5
Acute myeloid leukemia	24	21.1	4	11	13
Mature B-cell ALL (Burkitt leukemia)	5	4.4	7.5	4	1
Mixed lineage acute leukemia	2	1.7	5	0	2
Chronic myeloid leukemia	1	0.9	6	1	
Small solid tumor (neuroblatoma)	1	0.9	4		1
B.M. with secondary malignancy	1	0.9	7		1
Total	114	100		57	57

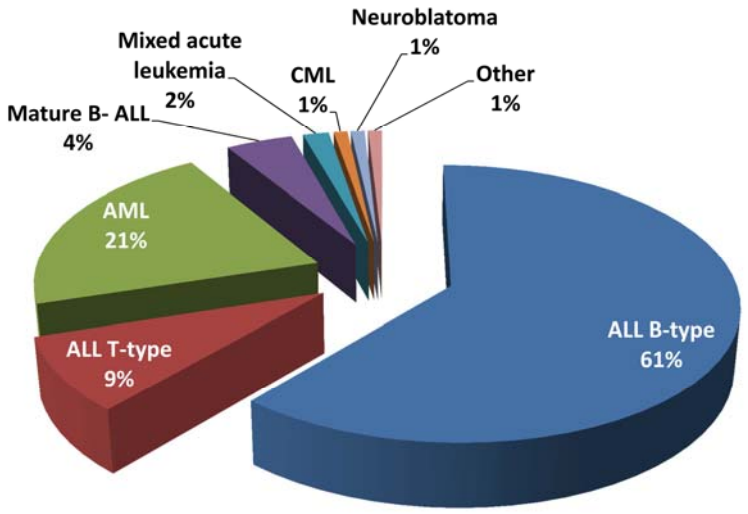

Figure (3): Frequency of hematological malignant disorder

The follow up subgroup included 200 cases out of which 94% were follow up case of acute leukemia. The bone marrows were in complete remission in about three quarter of the cases, while they were in relapse state in 9%, while other bone marrow states are outlined in table 4.

Table 4 - Variety of followed known cases of hematological and non-hematological malignancy.

Followed cases of leukemia and malignant	No. of cases	%
Complete remission	151	75.5
Failure of remission or partial remission	19	9.5
Relapsed	18	9
Cases non-hematological follow up	12	6
Total	200	
No of cases followed by two times BME	31	
No of cases followed by three or more times BME	18	

DISCUSSION

The spectrum of hematological disorders in children is very broad and bone marrow examination may offer a definitive diagnosis in a good number of cases. It is a relatively harmless and straightforward procedure in experienced hands. Infection, extreme bleeding or embolism was seldom reported complications during or after bone marrow examination[2].

The two important nutritional anemias in namely: megaloblastic and iron deficiency anemia constitute about 9.3% of non-malignant diagnoses in this study, which is lower in relationship to other studies where its frequencies ranged from as low as 24% to as high as 68%[5]; the cause of this lower frequency is that the majority of these nutritional anemias can diagnosed based on peripheral blood counts and film and supplementary serum/red cell testing rather than bone marrow, like iron study, serum vitamin B12 and folate estimation and thereafter can be confirmed by response to appropriate by therapy.

It was noted that the most frequent causes of referral to the hospital for marrow examination in the above subgroup of patients were anemia, pallor, or failure to thrive, which are common problems in developing countries much less frequent cause of

referral in the latter category is blood counts abnormalities as cytopenia (pancytopenia, dicytopenia) or macrocytic anemia. It is quite unlikely that megaloblastic anemia presents with thrombocytopenia or leucopenia only[6]. Determination the causes of megaloblastic anemia could not be ascertained because of the retrospective nature of the current study, but it is well known that folate deficit is more frequent in children, while B12 deficiency is more frequent in adults, the usual presentation age of megaloblastic anemia in the industrial world is in early life[5]. While it can occur at any age in developing countries like ours, in this study megaloblastic anemia occurred in earlier age and median age of

one year. Amongst other nutritional anemias was iron deficiency accounting for only 1% of bone marrow diagnoses which is unlike the study Fazlur Rahim et al[7] from Iran, where anemia of iron deficiency cause accounted for 5% of bone marrow diagnoses. This percentage is lower than expected as an expected 60-80% of the world residents are affected by iron deficiency anemia[8]. The likely reason is as we stated earlier, is that iron deficiency is generally diagnosed by non-invasive investigations without the need for bone marrow.

Idiopathic thrombocytopenia purpura (ITP) was the most frequent bone marrow diagnosis found in this study and accounted a third of the non-malignant cases. Mucocutaneous bleeding in pediatrics is mostly caused by ITP[9]. Its incidence on testing bone marrow varies from 32% to 48%[5] in different studies. ITP incidence in the current study is higher than 4.62 % reported by AL-Ghazaly[10] and the 9.43% by Fazlur Raheem et al[7] from Yemen and Iran respectively. The cause of this high incidence of ITP is likely due to the practice of referring almost all cases of thrombocytopenia for bone marrow examination even if they do not show any atypical features, despite the American Society of Hematology (ASH) recommendations are stated that BM examination should be restricted to those with the atypical features. A study of Hevi pediatric hospital in 2011, bone marrow examination in isolated childhood thrombocytopenia without any atypical features, did not show any to be leukemias or aplastic anemia11 thus questioning the need for a bone marrow aspiration in children with suspected idiopathic thrombocytopenic purpura[12]. Physician and parental concern about the possibility of a diagnosis of leukemia frequently underlies the justification for the performance of this procedure. The limitations of the current study includes: data being collected retrospectively, drug history could not be ascertained from the records of every case and the lack of availability of immunological tests related to ITP.

Aplastic anemia (AA) was the third most common found in the study and constituted 4.4% of the cases. In this study, AA was seen to affect equally both males and females and the median age was 7 years because the most frequent cause of hypoplastic marrow was Inherited AA (Fanconi anemia) which is recessively inherited and clinically usually presents between the ages of 3-10 years[13], while the remaining cases were due to chemotherapy induced marrow suppression in known cases of malignancy managed in Hevi pediatric hospital. Pallor (anemia), failure to thrive, mucocutaneous hemorrhage,

dysmorphism, and skeletal abnormality like polydactyl and small face and eyes were the cause of child's parents or family doctors seeking medical attention, in cases thereafter diagnosed as Fanconi Anemia. The latter diagnosis was generally presumptive in our practice, since chromosomal breakage studies were not available.

Aplastic anemia epidemiologically has an unusual geographical distribution compared to that of acute leukemias, with higher frequency in the developing world than in the industrial countries[1,14]. Its exact prevalence in Iraq is unknown due to lack of dependable population based studies. European studies have implicated certain drugs in the etiology of marrow failure. Unexpectedly, drugs play little role in etiology of the disease in Thailand, where it is mostly idiopathic[15]. Prognosis of AA is directly correlated to the decrease in peripheral blood cell counts, mainly the neutrophil amount: <200GRA/μL and platelets <20,000/μL defines very severe aplastic anemia. Repeated bacterial sepsis or fungal infections resulting from refractory neutropenia are common causes of death[16].

Malignant hematological disorders in this study were 114 cases (14.8%), and acute lymphoblastic leukemia (ALL) constituted the majority (70%) followed by AML in 21% while the rest were cases of lymphoma and one case each of chronic myeloid leukemia and neuroblastoma. The high incidence of ALL in children in this study is similar to that reported from other developing countries like Kenya and Pakistan[17,18].

Follow up bone marrow constituted 24.5% of all bone marrows performed during the study period. The cause of such large number of cases is due to the fact that Hevi pediatric teaching hospital is the only oncology center in the province

About 22% of the requested marrow examinations turned out to be normal marrows with well represented marrow elements and the clinical diagnoses were not hematological, therefore some time marrow examination had been done to exclude other causes of anemia, fever and especially in cases of pyrexia of unknown origin.

We found 13 cases of metabolic storage disorders; 7 cases of Gaucher's disease and 6 cases of Niemann-Pick disease. These rare disorders which are autosomal recessive disorders tend to be more likely to occur in populations with high consanguinity rates, as it is the case in Duhok where consangueous marriages constitute 27% of all marriages[19].

Among parasitic afflictions that maybe diagnosed by marrow examination, two cases of Leishmaniasis were diagnosed during the study period, a finding shared

by earlier studies from Yemen and Iran (Fuzlar et al[7] and AL-Ghazaly[9]). The latter studies also reported malaria, which we did not find in the current study, most likely to earlier successful mosquito eradication programs.

Marrow erythoid hyperplasia constituted 19 (4.2%) cases in the study due to high frequency of inherited hemolytic anemia that can influence the marrow's capacity to produce an enough number of blood cell types and liberate them into the circulation[20].

CONCLUSIONS

Bone marrow examination is an essential step in verifying the diagnosis of many hematological disorders. The most common disorder among the non-malignant hematological conditions was peripheral consumption of platelets (ITP) in this study. The second most common condition was megaloblastic anemia while iron deficiency anemia was the least common disorder. Aplastic anemia ranked as the third most serious nonmalignant disorder found in this study. The most common amongst the malignant hematological disorders is ALL followed by AML.

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پوختە

جورێن نەخوشیێن مەژیێ هەستی ل نەخوشخانا هیڤی یا زاروکان: دیڤچوونا ٦ سالا

پێشەکی و ئارمانج: تێکچوونێن خوینێ زورن ل دەڤ زاروکان، جورێن ڤان تێکچوونێن خوینێ بەرفرەهن ژ جورێ بەربەلاف وەك کیموونا خوێنێ ژ کیماتیا ئاسنی بو جورێن کەلەکێن کێم ئەڤێن ئەگەرێن تێکچوونا زکماکی. تێستا مەژیێ هەستی ئیك تێستێن زورە و کێم مەترسیە دهێتە کرن ل یەکەیێن زاروکان بشێوەکێ بەردەوام. ئارمانجا ڤێ ڤەکولینی ئەوە بو نیشانکرنا جورێن درست ژ تێکچوونێن خوینێ ل نەخوشخانا هیڤی ڤێرکرنێ یا زاروکا، ل پارێزگەها دهوکێ، کوردستانا عیراقێ.

ڕێگێن ڤەکولینێ: ئەڤ ڤەکولینە یا دیڤ چوونی بوو، دیڤ چوونا ٨١٤ کەیسێن دیفیکرا ئەڤێن تێستا مەژیێ هەستی بو هاتیە کرن و نڤێسین ل بەشێ نەخوشییێن خوینێ ل نەخوشخانا هیڤی دەمێ ٦ سالا ژ ٢٠٠٩–٢٠١٤. هەمێ پێزانین ڤان نەخوشا و ئەگەری چێکرنا ئەڤێ تیستێ و ئەنجامێ تێستێ هاتینە نڤێسین.

ئەنجام: کوژمێ ٨١٤ کەیسێن تێستا مەژیێ هەستی بو هاتیە کرن ئەنجامێن وان هاتینە وەرکرتن ژیێ وان ژ ٢٠ روژی تاکو ١٥ سال بوون و ناڤنجیا سالێن وان ٤ سالیە و ڕێژا نێر بو مێ 1:1.1 . ئەڤێن ژێکرتی ٤٥٥ (٨٠٪) نەخوش ئەنجامێن وان تێکچوونا خوێنی نە پەنجەشیری بوو و ئەڤێن مایین ١١٤(٢٠٪) نەخوش ئەنجامێ تێکچوونا وان خوینێ پەنجەشیری بوون.

پێترپا تێکچوونا خوینێ نەیا پەنجەشێری ئەوژی کێمبوونا پلێتین خوینێ بریکا شکاندنا دەرفەی مەژی هەستی یا بی ئەگەر (٢٨.٤٪), کێمبوونا خوینێ Megaloblastic anemia (١٢.٨٪), پیچبوونا تەپگێن خوینێ ژ ئەگەرێ مەزنبوونا تحێلێ (١٢.١٪), کێمبوونا خوینێ Aplastic anemia (٤.٤٪), کێمخووینا یا زکماکێ ژ ئەگەرێ شگاندنێ تەپکێن خوینێ (٤.٢٪), تێکچوونا کومکرنێ (٢.٨٪), و ١٤٨(٣٢.٥٪) کەیس چ ئەگەر نەبوون و نەهاتنە دەست نیشانکرن.

ناڤ تێکچوونێن خوینێ یێن پەنجەشێری جورێ ALL (٧٠٪)، جورێ AML (٢١٪)، بشتی وان جورا لیوکیمیا گەهشتی B (لیوکیما و لیمفوما Burkitt) (٤.٤٪)، و لیوکیمیا لەز جورێ تێکهل (١.٧٪). ئەڤ کەیسێن سامپلێن وان کێم و رون ٤٥ (٥٠.٥٪) بوون، ئو ٢٠٠ (٢٤٪) کەیسا تێستا مەژیێ هەستی بو هاتە کرن ژ بەر دیڤچوونا نەخوشییێن وان یێن گەڤن ئەڤێن بەری نوکە هاتینە دەست نیشانکرن و (٩٤٪) ژوان پەنجەشێرا لیوکیمیا لەز بوون.

دەرئەنجام: تێستا مەژیێ هەستی ئیك ژ ڕێکێن گرنگە بو دەست نیشانکرنا گەلەك نەخوشیێن خوینێ. پێترین تێکچوونا خوینێ نەیا پەنجەشیری لڤێ ڤەکولینێ ئەوە کێمبوونا پلێتین خوینێ بریکا شکاندنا دەرفەی مەژی هەستی. یا دوویێ کێمبونا خوینا کێم خوارنا ئەوژی کێمبوونا خوینێ جوری Megaloblastic anemia و کێمبوونا خوینێ ژئەگەرێ کێمبوونا ئاسنی کێمتر بوو. پشتی وان یا سێ تێکچوونا نە پەنجەشێری ئەوژی کێمبوونا خوینێ ژ Aplastic anemia. ئو ژ تێکچوونێن پەنجەشیرێ یا هەمیا پتر جورێ ALL پاش جورێ AML.

الخلاصة

طيف من أمراض نخاع العظم في مستشفى هيفي لاطفال: تجربة ٦ سنوات

الخلفية وأهداف البحث: الاضطرابات الدموية متكررة نسبيا في الاطفال. وطيف الاضطرابات الدموية في الاطفال واسع تتكون من الحالات الشائعة مثل فقر الدم الحديدي الى حالات النادرة من الاضطرابات الخلقية. ويعتبر فحص نخاع العظم من إحدى الفحوصات الشائعة وليست خطيرة نسبياً من حيث التعامل تجرى بشكل متكرر في مختبرات مستشفيات الاطفال. والهدف من الدراسة هو لتحديد الاطياف الدقيقة للاضطربات الدموية في مستشفى هيفي التعليمي للاطفال في محافظة دهوك، كوردستان العراق.

طرق البحث: تعتبر من الدراسة الاستعادية. راجعنا ٨١٤ حالات متتالية من تقارير فحوصات نخاع العظم التي أجريت من قبلي في وحدة أمراض الدم مختبر مستشفى هيفي لاطفال للسنوات ٢٠٠٩-٢٠١٤. وتدون لكل حالة المعلومات السريرية منها الفحص السريري للمريض و الهدف من اجراء الفحص مع نتيجة تقرير الفحص.

النتائج: مجموع نتائج فحوصات نخاع العظم ٨١٤ حالة، العمر تتراوح بين ٢٠ يوم الى ١٥ سنة والمعدل العمري كانت ٤ سنوات ونسبة الذكور الى الاناث هو ١.١: ١. ونتائج ٤٥٥ (٨٠%) مريض من الحالات المختارة كانت ليست سرطانية، بينما ١١٤ (٢٠%) مريض اضطراباتهم الدموية كانت سرطانية. وأكثر الحالات الغير السرطانية هو فرفرية نقص أقراص الدم المجهولة السبب وكانت (٢٨.٤%)، فقر الدم الضخم الارومات (١٢.٨%)، نقص الخلايا الدم الناتج من فرط نشاط الطحال (١٢.١%)، فقر الدم من عدم التنسج (٤.٤%)، فقر الدم الانحلالي الخلقي (٤.٢%)، اضطرابات التخزين (٢.٨%) ونتائج ١٤٨ (٣٢.٥%) حالة كانت طبيعية ولم تكن هناك اي اضطراب دموي في نخاع العظم.

وبالنسبة لحالات السرطانية نوع ALL (٧٠%)، AML (٢١%) وأقل حالات المسجلة كانت ليوكيميا حادة من نوع B الناضج (٤.٤%) وليوكيميا حادة مختلطة النسب (١.٧%)

والنماذج القليلة والغير كافية للدراسة كانت ٤٥ (٥.٥%)، بينما ٢٠٠ (٢٤%) حالة أجريت الفحص من أجل متابعة حالاتهم المرضية المشخصة و١٨٨ (٩٤%) من الحالات المشخصة كانت ليوكيميا الحادة.

الاستنتاجات: تعتبر فحص نخاع العظم من الخطوات المهمة لتوصيح تشخيص معظم حالات الاضطرابات الدموية. ومعظم حالات الغير السرطانية كانت فرفرية نقص أقراص الدم المجهولة السبب و ثاني حالات شيوعاً من فقر الدم التغذية كانت فقر الدم الضخم الارومات ونقص فقر الدم الحديدي من الاسباب القليلة والاخير فقر الدم من عدم التنسج من الحالات المهمة الغير السرطانية. وأما بالنسبة لحالات اضطربات الدم السرطانية هو ALL ثم تأتي AML.

ZINC DEFICIENCY AMONG WOMEN DURING CHILD BEARING AGE

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ABSTRACT

Background: Zinc deficiency appears to be an important public health problem throughout the world. The objective was to assess zinc status among randomly selected women of child bearing age.

Methods: Women of child bearing age (15-45 years) from 3 urban and 3 rural areas in Duhok governorate, Kurdistan region were included in the study. Collection of data was carried out during the period from August 2015 until the end of January 2016. Serum zinc level and zinc status was determined.

Results: Overall 121 (30.3%) women were zinc deficient (≤70µg/dl) .Of these, 51(12.8%) had severe zinc deficiency (<50µg/dl) and 70(17.5%) had marginal zinc deficiency (50-70µg/dl).Mean serum zinc level was significantly lower in women of older age group, pregnant and those with > 6 number of children.

Conclusion: Moderate Zinc deficiency was found among women during child bearing age with a high prevalence in older age group, married, pregnant and those with > 6 number of children.

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Keywords: Serum Zinc, Child bearing age women.

Zinc is a trace metal required in modest amounts to maintain health and optimal physiological functions. It plays an important role in growth and reproduction[1]. Approximately 300 enzymes are known to require zinc for their activities. Zinc is required for DNA synthesis, cell division and protein synthesis[2]. Zinc deficiency therefore results in adverse consequences on the body, although severe deficiency is now considered rare, mild to moderate zinc deficiency may be relatively common throughout the world[3,4], and appears to be an important public health problem in many developing countries, including Iraq[5].

To date, attempts to assess zinc status in vulnerable groups to zinc depletion and low plasma zinc concentration have been few[6,7]. Therefore , this preliminary study aimed to assess zinc status as hypnotized in the most vulnerable sector of our population i.e. the women of child bearing age and to ascertain the relationship between zinc and some other factors

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which could be relevant in the low status of zinc in women, such as age, marital status, parity, pregnancy status , residency and socioeconomic status.

METHODS

Design

This cross-sectional study included 400 apparently healthy females of child bearing age province of Duhok Governorate, Kurdistan region Iraq. Selection of the participants was done through simple random sampling method. They were chosen from the relatives of patients attending Health Care Centers in villages (Zaweta, Mangesh and Batofa) and in Duhok city center (Malta, Bahdenan and Tanahe). Characteristics among females included age, socioeconomic, educational and marital status. Height, weight and blood pressure recorded by using standard methods. Data on the number of house hold and number of rooms of the house, crowding index is an indicator for socioeconomic status was calculated by dividing the number of household by the number of rooms.

Measures

Blood samples were collected after overnight fasting for 12-14 hours for later measurement of serum zinc level. Serum zinc was analyzed by flame atomic absorption spectrophotometer (Perkin Elmer) using a standard procedure.

Women Zinc deficiency was defined as "concordant" by age if they were no more than 45 years apart, by pregnancy if either pregnant or non-pregnant by self report, by parity if they self-reported as the number of children one or more, and by area if they were no far from the defined urban or rural areas. Women with serum zinc level 50-70 µg/dl considered with marginal zinc deficiency, and severe zinc deficiency for levels < 50 µg/dl8.

Ethical clearance for the study was taken from the General Directorate of Health in Duhok Governorate. Informed consent was obtained from the respondents after explaining the objective of the study.

STATISTICAL ANALYSIS

All data were analyzed using the Statistical Package for Social Sciences SPSS. Unpaired students t-test was calculated to assess differences in serum zinc among study groups. Significance of association between various variable was assessed using chi-square test.

RESULTS

The General characteristics of the study females have been described in Table 1.The mean of age was 26.6(±6.8) years, height 159.6(±5.9)cm, weight 57.2(±9.7)kg and mean BMI was 22.3(±3.0). The mean serum zinc level was 86.1(+21.4), it was higher for urban women compared to rural women, but the difference was not significant. Higher

percentages (75.0) of women were married. Mean age at marriage was 20.2 years. of the 300 married women 126(42.0%) were pregnant. 79(19.8%) of women were belong to good families and 263(65.0%) were belong to medium and 58(14.5%) were belong to poor families. About 232(58.0%) of females were illiterate. No statistically significant difference was found using a P value of <0.05 for general characteristics in rural and urban women.

The sample population was distributed in different age groups as <20, 20-30, 31-40 and >40 years and their zinc levels analyzed. It was found that mean zinc level was higher in age group (<20) as compared to other age groups(20-30 and 31-40) then starts decreasing significantly up to 40 years(Fig.1).

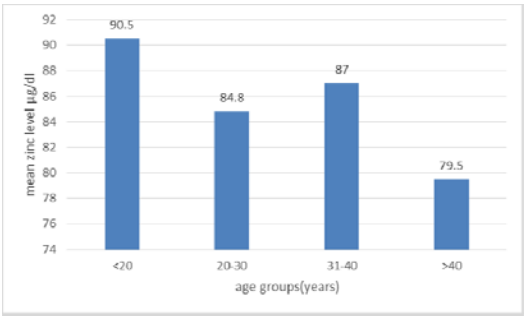

Fig 1 Comparison of mean serum Zinc level among women of different age groups.

Table 1 Main characteristic of women of childbearing age.

Characteristic	All (n=400) Mean±SD	Rural (n=181)* Mean±SD	Urban (n=219) Mean±SD	p-value
Age(years)	26.6±6.8	26.2±7.0	26.2±7.0	0.2
Height(cm)	159.6±5.9	159.4±6.1	159.4±6.1	0.5
Weight(kg)	57.2±9.7	57.1±9.9	57.1±9.9	0.7
BMI(kg/m^2)	22.3±3.0	22.3±3.0	22.3±3.0	0.9
Systolic blood pressure (mmHg)	112.4±14.4	112.7±13.2	112.7±13.2	0.6
Diastolic blood pressure (mmHg)	75.8±9.9	76.1±9.5	76.1±9.5	0.8
S. Zinc	86.1±21.4	87.1±21.03	84.9±21.9	0.3
Family size	7.5±3.9	7.3±4.0	7.7±3.8	0.4
	n(%)	n(%)	n(%)	
Married	300(75.0%)	138(76.2%)	162(74.0%)	
unmarried	100(25.0%)	43(23.8%)	57(26.0%)	
Marriage age	300			
Pregnant women	126(42.0%)	55(39.9%)	71(43.8%)	
Non pregnant	174(58.0%)	83(60.1%)	91(56.2%)	
Literate	168(42.0%)	70(38.7%)	98(44.7%)	
Illiterate	232(58.0%)	111(61.3%)	121(55.3%)	
Family size				
SES:				
Good	79(19.8%)	23(12.7%)	56(25.6%)	
Medium	263(65.0%)	121(66.9%)	142(64.8%)	
poor	58(14.5%)	37(20.45)	21(9.6%)	

* Rural women Vs. Urban women

Of the four hundred women, 121(30.2%) were zinc deficient. Severe zinc deficiency <50 µg/dl was found in 51(12.7%) women. Out of 51 women with severe zinc deficiency, 33(64.7%) were pregnant (Table 2).

Table 2 Frequency of zinc deficiency in women of childbearing age

Serum zinc (ug/dl)	Overall (n=400) n (%)	Pregnant (n=126) n (%)	non-pregnant (n=174) n (%)
<50	51(12.7)	33(64.7)	18(35.2)
50-70	70(17.5)	27(38.5)	22(31.4)
>70	279(69.7)	66(23.6)	134(48.0)

The mean and SD of serum zinc level in pregnant and non-pregnant women is demonstrated in Table 3. Statistically significant difference was found in the mean value of serum zinc in second (unadjusted OR (95% CI) 5.86(2.65-12.9), P<0.0001) and third trimester (unadjusted OR (95% CI) 3.05(1.53-6.09), p=0.001) when compared with the non-pregnant women.

Table 3 Frequency and mean+SD serum Zinc level in pregnant and non-pregnant women

	n	Mean±SD	Serum zinc ≤70n(%)	level (ug/dl)>70	Unadjusted OR(95%CI)	p-value
Non-pregnant	(174)	89.9±21.0	40(23.0%)	134(77.0%)		
Pregnant	(126)					
1st trimester	(49)	82.6±23.2	18(36.7%)	31(63.3%)	1.94(0.98-3.83)	0.05
2nd trimester	(33)	71.5±21.8	21(63.6%)	12(36.4%)	5.86(2.65-12.9)	<0.0001
3rd trimester	(44)	78.8±26.1	21(47.7%)	23(52.3%)	3.05(1.53-6.09)	0.001

The mean serum zinc level with respect to parity is demonstrated in Table 4. Significantly higher level of serum zinc was found (p=0.03) in women having no children versus women with ≥6 number of children.

Table 4 Association between serum Zinc levels and number of children

(Children) n	(mothers) N	Mean±SD	Serum zinc ≤70 n (%)	level (ug/dl) >70 n (%)	Unadjusted OR(95%CI)	p-value
0	78	92.9±23.7	32(41.0%)	46(59.0%)		
1-2	102	85.7±21.9	33(32.4%)	69(67.6%)	1.45(0.78-2.68)	0.23
3-5	92	86.3±22.3	32(34.8%)	60(65.2%)	1.30(0.69-2.43)	0.40
≥6	28	78.6±21.2	5(17.0%)	23(82.1%)	3.20(1.10-9.30)	0.03

The association between serum zinc level and the different variables were analyzed (Table 5). A significance association has been found in married and un- married women (P=0.02).

Table 5 Association between different variables with serum Zinc levels among rural and urban women

Variables	S. Zinc ≤70µg/dl n (%)	S. Zinc >70µg/dl n (%)	Unadjusted OR(95%CI)	P-value
Age:				
<20 yrs.	**22(32.4%)**	**46(67.6%)**	**1.12(0.64-1.97)**	**0.67**
≥20 yrs.	**99(29.8%)**	**233(70.2%)**		
Married	**100(33.3%)**	**200(66.7%)**	**1.88(1.09-3.22)**	**0.02**
Un-married	**21(21.0%)**	**79(79.0%)**		
Age at marriage:				
<17 yrs.	**20(32.2%)**	**42(67.8%)**	**0.94(0.51-1.70)**	**0.84**
≥17 yrs.	**80(33.6%)**	**158(66.4%)**		
Children:				
Yes	**68(30.6%)**	**154(69.4%)**	**0.63(0.37-1.08)**	**0.09**
No	**32(41.0%)**	**46(59.0%)**		
BMI:				
<23 kg/m^2	**71(31.3%)**	**156(68.7%)**	**1.11(0.72-1.72)**	**0.60**
≥23 kg/m^2	**50(28.9%)**	**123(71.1%)**		
Literate	**51(30.4%)**	**117(69.6%)**	**1.00(0.65-1.55)**	**0.96**
Illiterate	**70(30.2%)**	**162(69.8%)**		
Urban	**60(27.4%)**	**159(72.6%)**	**0.74(0.48-1.13)**	**0.17**
Rural	**61(33.7%)**	**120(66.3%)**		

DISCUSION

Zinc deficiency appears to be an important public health problem in many developing countries, including Iraq9, 10. In our sample of women included, the overall prevalence of zinc deficiency was 30.2%, of whom 12.7% women were severe zinc deficient. It is therefore, such a high prevalence of low zinc status in the women during child bearing age is especially noteworthy because several factors are known to impact negatively on zinc status. Of these, can be insufficient intake of dietary zinc and physiological stress by pregnancy[11,12] Mild to moderate zinc deficiency is common in several developing countries, because the commonly consumed staple food have low zinc contents and are rich in phytates. The phytate contents of cereal proteins is known to decrease the availability of zinc , thus the prevalence of zinc deficiency is likely to be high in a population consuming large quantities of cereal proteins. Therefore, the zinc status in population reported here appears to be associated, at least in part, with low intakes of poorly available dietary zinc[13]. But in fact, we noticed that this low zinc status (<70 ug/dl) is highly associated with course of pregnancy in women. Zinc deficiency appears to be highly prevalent in the pregnant women 60/126(47.6%) compared to 40/176(23.0%) non-pregnant. Similar decline in serum zinc levels during pregnancy is reported by others[14],

Considering the differences in risk factors across countries, rural women during child bearing age have significantly lower mean serum zinc levels compared to urban

women[15]. But, in our study, the mean serum zinc level was nearly similar in rural and urban women, which confirmed the data presented are likely to be a representative of the general population actual data, although, zinc bioavailability based on zinc intake and availability factor (percentage of available dietary zinc) has not been determined, which is a limitation of this study. However, it is likely that the changes in serum zinc level were caused solely by other factors. i.e. a vast majority of females studied were married with an age >20 years, multi parity, illiterate, medium-poor socioeconomic status and in the second and third trimesters of pregnancy, all these factors may collectively affected serum zinc level and zinc status in women during child bearing age.

In conclusion, a low zinc status is present in 30.2% of women during child bearing age. This finding suggests that greater priority should be given to the correction of abnormal zinc status in susceptible women.

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پوختە

کێمبوونا تۆخمێ توتیایێ ل دەڤ ئافرەتان دماوێ ژیێ ئینانا زاروکاندا

پاشین و ئارمانج: کێمبوونا تۆخمێ توتیایێ دناڤلەشێ مرۆڤی ئێکە ژ ئاریشەیێن ساخلەمیێ بێن هەرە بەربەلاڤ و گرنگ ل سەرانسەری جیهانی. مەرەم ژ ئەنجامدانا ڤێ ڤەکۆلینێ ئەوە داکو ئاستێ تۆخمێ توتیایێ د ماوێ ژیێ ئینانا زاروکاندا بهێتە پیڤان ل دەڤ وان ئافرەتان بێن کو ب شێوەیەکی هەرەمەکی ل باژێرێ دهۆکێ بۆ ڤێ ڤەکۆلینێ هاتینە هەلبژارتن.

کەرەستە: ژبۆ ئەنجامدانا ڤێ ڤەکۆلینێ، نموونە بێن هەرەمەکی ژ ٤٠٠ ئافرەتان هاتنە وەرگرتن کو ژیێ وان دناڤبەرا ١٥–٤٥ سالان دابوو. ژ سەرجەمێ ڤان ئافرەتان، ٢١٩ (٥٤.٧٪) ئاکنجیێن باژێری بوون و ١٨١ (٤٥.٣٪) ئاکنجیێن گوندان بوون. ئەڤ نموونە دماوێ دناڤبەرا هەیڤا تەباخا سالا ٢٠١٥ هەتا دوماهیا کانونا ئێکێ یا سالا ٢٠١٦ هاتنە کومکرن و ل دویڤدا ئاستێ توخمێ توتیایێ ل دەڤ وان هاتە پیڤان.

ئەنجام: ژ سەرجەمێ ٤٠٠ ئافرەتێن نموونە ژێ هاتینە وەرگرتن، ١٢١ (٣٠.٣٪) ئافرەتان ئاریشەیا کێمیا تۆخمێ توتیایێ هەبوو ب تێکرایێ (٧٠ مکگ\دل)، ٥١ (١٢.٨٪) ئافرەتان ئاریشەیا کیمیا توتیایێ یا توند هەبوو ب تێکرایێ (٥٠ مکگ\دل)، هەردیسان ٧٠ (١٧.٥٪) ئافرەتان ژی ئاریشەیا کێمیا توتیایێ یا پەڕاوێزی هەبوو ب تێکرایێ (٥٠–٧٠ مکگ\دل). تێکرایێ ئاستێ توخمێ توتیایێ ل ب شێوەیەکێ بەرچاڤ ل دەڤ ئافرەتێن ژیێ وان مەزن، خێزاندار، دووگیان و ئاکنجیێن گوندان بلندتربوو.

دەرئەنجام: پشتی ئەنجامدانا ڤێ ڤەکۆلینێ، ئەنجامان هوسا بۆمە دا دیارکرن کو کێمیا تۆخمێ توتیایێ یا ناڤنجی ل دەڤ ئافرەتان هەبوو د ماوێ ژیێ ئینانا زاروکاندا و ئەڤ ئاریشە ل دەڤ ئافرەتێن دووگیان پتر یا بەربەلاڤ بوو.

الخلاصة

نقص الخارصين لدى النساء خلال سن الانجاب

الخلفية والاهداف: يبدو أن نقص الخارصين تكون مشكلة صحية عامة ومهمة في جميع أنحاء العالم، والهدف من هذه الدراسة هو تقييم حالة الخارصين بين النساء في سن الانجاب.

طرق البحث: شملت الدراسة ٤٠٠ امرأة وكانت أعمارهن ما بين ١٥-٤٥ عاماً، منهم ٢١٩(٥٤.٧%) من المناطق الحضرية، و١٨١(٤٥.٣%) من المناطق الريفية. جمع البيانات كانت خلال الفترة ما بين آب ٢٠١٥ وحتى نهاية كانون الأول ٢٠١٦، وتم تحديد مستوى الخارصين في مصل الدم.

النتائج: كانت ١٢١(٣٠.٠%) من النساء تعاني من نقص الخارصين (٧٠≥ مايكروكرام/ ديسيليتر)، منهن ٥١(١٢.٨%) لديهن نقص شديد في الخارصين (٥٠≥ مايكروكرام/ ديسيليتر) و٧٠(١٧.٥%) من النساء لديهن نقص هامشي في الخارصين (٥٠-٧٠ مايكروكرام/ ديسيليتر).

الاستنتاج: أظهرت الدراسة نقص معدل الخارصين بين النساء خلال سن الانجاب مع انتشار عالية في النساء الحوامل.

IS FINE NEEDLE ASPIRATION CYTOLOGY A VALID DIAGNOSTIC TOOL IN NODULAR GOITER?

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ABSTRACT

Background: Fine needle aspiration cytology (FNAC) is commonly used tests for diagnosis of thyroid nodules. Is available procedure and provides specific diagnosis rapidly with minimal complications.

Aim: To assess the validity of FNAC in the evaluation of thyroid nodules performed at our institution and to compare our results with other studies elsewhere.

Patients and methods: This study was conducted on 51 consecutive patients who underwent FNAC for diagnosis during the period from Feb 2012-Feb 2015. The final histopathological diagnosis was considered the gold standard.

Results: The sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of FNAC for the diagnosis of neoplastic thyroid nodules were 84.6%, 97.3%, 94.1%, 91.6%, 94.8% respectively. Papillary carcinoma was the common type in neoplastic group (53.8%).

Conclusion: Our study suggest that FNAC is a sensitive , specific and accurate initial diagnostic test for the preoperative evaluation of patients with thyroid nodules. Our results are comparable with current published articles and the clinician should be encouraged to use FNAC as the initial modality in assessment of thyroid nodules.

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Keywords: Thyroid nodule, Fine needle aspiration cytology, Accuracy.

Nodular goiter remains a problem of enormous magnitude all over the world. The problem in clinical practice is to distinguish reliably the few malignant tumors from the many harmless nodules. Thyroid nodules have a reported prevalence of 4–7% of adult population and fewer than 5% of adult thyroid nodules are malignant[1]

There are a variety of tests giving anatomical and functional information (as isotope scan and ultrasound) about the thyroid gland but fine needle aspiration cytology (FNAC) gives direct morphological information and has supplanted most other tests for preoperative evaluation of thyroid nodules. Histological examination of the removed thyroid swelling is the most accurate way to determine the pathology.

FNAC is established as a first line diagnostic test for assessment of nodular goiter and give a significant increase in the diagnosis of malignant lesion of

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thyroid[2,3]. FNAC is therefore used as the key investigation in combination with imaging investigations in many recognized centers to diagnose or exclude malignancy in nodular goiter. Several studies have reported a high degree of specificity, sensitivity, positive and negative predictive values of FNAC for thyroid lesion[3,4].

FNAC is, however, not without limitations; accuracy is lower in suspicious cytology and in follicular neoplasms. The main aim of FNAC is to identify nodules that require surgery and those benign nodules that can be observed clinically and decrease the overall thyroidectomy rate in patients with benign diseases.

This study is aimed at determining the diagnostic accuracy of FNAC of thyroid nodules performed at our institution and to compare our results with other studies elsewhere.

MATERIALS AND METHODS

A cross sectional study was conducted on fifty one patients with goiter (multiple and solitary thyroid nodules) during the period Feb.2012–Feb.2015 in Duhok private hospitals. All patients underwent complete history taking, physical examination, otolayrngeal assessment, hormonal assay (serum T3, T4 and TSH), ultrasound examination and chest x-ray. Isotope thyroid scan was not performed because it is not available. Patients showing either solitary or multiple nodules were included in the study. Informed consent was obtained from all participants included in the study. FNAC was performed on all solitary nodules and dominant nodules of multinodular goiter. Fine needle aspiration was done by pathologist using a 22- or 23-gauge needle attached to a 20 cc air tight disposable syringe without Ultrasound guide. Samples were smeared onto glass slides and fixed in 95% methanol, along with one or two air-dried smears for May Grunwald Giemsa (MGG) stain. In cystic lesions, after aspiration of fluids, the lesion was again aspirated. The fluid was centrifuged and smears are made from sediment. Wet-fixed smears were stained with Hematoxylin and Eosin and Papanicolaou stains, while air-dried smears were stained with MGG stain.

Type of surgical operation performed depend on the pathology of the gland and surgical specimen was sent for histopathology in all operated cases. The main outcome measures were to correlate the preoperative diagnostic workup with FNAC along the clinical findings with that of postoperative pathological findings.

Inclusion criteria include those patients presenting with thyroid swelling who underwent FNAC, thyroid surgery and histopathological examination. Exclusion criteria was those patients having FNAC

done but did not had thyroid surgery and patients with unsatisfactory aspirate.

The sensitivity, specificity, diagnostic accuracy , positive and negative predictive values of FNAC in diagnosing thyroid lesions relative to the final histological diagnoses were analyzed by SPSS software, according to the following equation:

Sensitivity = True positive/ True positive + False negative Specificity = True negative/ True negative + False positive Positive predictive value = True positive/ True positive + False positive Negative predictive value = True negative/ True negative + False negative Diagnostic accuracy = True positive + True negative / Total number of patients

Statistical analysis was done using SPSS software.

RESULTS

This study consist of 51 cases, there were 44 females and 7 males F/M 6.3/1. Age range was 19–70 years, mean age and standard deviation was 44.8 ± 15.43.

All patients presented with swelling in the front of the neck (100%), other complaint was pain in the neck (3.9%), pressure effect mainly shortness of breath (13.7%). Multinodular goiter in (70.5%) and solitary nodule in (29.4%) as in Table 1.

Table 1 Study Sample by Demographic and Clinical Characteristics

Characteristic		Total Cases	
		No.	%
Age	< 20 year	2	3.9%
	20 - 30	9	17.6%
	31 - 40	13	25.4%
	41 - 50	14	27.4%
	> 50	13	25.4%
Sex	Male	7	13.7%
	Female	44	86.2%
Presenting complaint	Swelling	51	100%
	Pain	2	3.9%
	Pressure effect	7	13.7%
Duration	1 – 5 months	15	29.4%
	6 – 12 months	20	39.2%
	> 1 year	16	31.3%
Site of swelling	Right lobe	8	15.6%
	Left lobe	7	13.7%
	Both lobes	36	70.5%

FNAC was categorized into neoplastic and non-neoplastic groups (no intermediate group recorded in current study) and results were compared with the corresponding histopathological diagnosis shown in Table 2. We identified one false positive result from neoplastic group and two false negative results from benign group as in Table 3 and histopathological diagnosis was shown in Table 4.

Table 2 Type of Lesion by FNAC and Histopathology

Type of lesion		FNAC	Histopat-hology
Non-neoplastic	Solitary nodular goiter	6	5
	Multinodular goiter	31	24
	Hashimoto,s thyroiditis	2	9
Neoplastic	Follicular adenoma	3	3
	Follicular carcinoma	0	1
	Papillary carcinoma	8	7
	Medullary carcinoma	0	1
	Anaplastic carcinoma	1	1
Total		51	51

Table 3 False FNAC Yield by Histopathological Diagnosis

False Results	No.	FNAC Yield	Histopathological Diagnosis
False positive	1	Follicular adenoma	Hashimoto,s thyroiditis
False negative	1	Nodular goiter	Papillary carcinoma
	1	Nodular goiter	Follicular adenoma

Table 4 Study Sample by Histopathological Diagnosis

Hisopathological Diagnosis	Number (%)
Multinodular goiter	24 (47)
Solitary nodulear goiter	5 (9.8)
Hashimoto,s thyroiditis	9 (17.6)
Follicular adenoma	3 (5.8)
Follicular carcinoma	1 (1.9)
Papillary carcinoma	7 (13.7)
Medullary carcinoma	1 (1.9)
Anaplastic carcinoma	1 (1.9)

Analysis of the FNAC results obtained were compared with the histological findings in order to rule out malignancy. The analysis yielded a sensitivity of 84.6%, specificity 97.3%, positive predictive value of 91.6%, negative predictive value of 94.8% and test accuracy of 94.1% as in Table 5.

Table 5 Validity of FNAC Test

Specificity	97.3%
Sensitivity	84.6%
Positive Predictive Value	91.6%
Negative Predictive Value	94.8%
Accuracy	94.1%

DISCUSSION

Early diagnosis of thyroid cancer still maintains its importance for higher life expectancy due to the low malignant potential of thyroid nodule.

FNAC of the thyroid gland has radically changed the management of patients with thyroid disease. It is an efficient method of differentiating benign from malignant thyroid nodules and is widely accepted as the most specific diagnostic test in the preoperative assessment of thyroid nodules[5,6,7].

In the present study, the age of patients ranged from 19-70 years with mean of 44.8 years and majority of patients were in their 4th decade (27.4%). Females were more affected than males (F/M 6.3 :1) Our results were in agreement with other studies[8,9,10,11,12]. The commonest lesion was non-neoplastic condition and comprised 74.5% while neoplastic lesion 25.4%. Out of the neoplastic lesions, papillary neoplasms were the commonest 53.8% (seven out of thirteen patients) which is similar to other studies[8,10]. The sensitivity and specificity for FNAC in published series range between 65-98% for sensitivity and 73-100% for specificity[13,14,15,16]. In our study, the analysis of the data revealed sensitivity of 84.6% and specificity of 97.3%, which translates into a test accuracy of 94.1%. The results of our study are comparable with the published data from different parts of the world. Kumar et al. in their study on 89 patients with enlarged thyroid

gland reported a sensitivity of 77%, specificity of 100%, and test accuracy of 97.7%[16,17]. Similarly, a study conducted by Nggada et al. in a teaching hospital in Nigeria reported a sensitivity of 88.9%, specificity of 96.1%, and test accuracy of 94.2%[7]. The wide range of values for sensitivity and specificity reported by different studies may be attributed to differences in number of cases and the included diagnostic categories. Some authors categorize follicular lesions as histopathologically benign, while others categorize these lesions as malignant[13,14]. In our study, we evaluated the follicular lesions in the neoplastic category . Factors that may reduce the validity of FNAC include, inexperience of the cytopathologist, inadequate sampling and difficulties of differentiation of benign and malignant follicular lesions. Inadequate sampling often results from calcified nodules or nodules with cystic degeneration in larger areas. US guided sampling reduces the error in diagnostic test rates in such conditions[13,18,19].

Most common lesions that contribute to false-positive results, as in our study, are nodular lesion . The false positive rate in neoplastic group amounted 8.3%. In general, it may be difficult to establish a cytologic differentiation between follicular hyperplastic nodules which are diagnosed as suspicious for malignancy or some of the follicular adenomas and well differentiated follicular carcinomas. It is reported that such conditions may lead to false-positive results[20,21].

The false negative rate (FNR) is defined as the percentage of patients with benign cytology in whom neoplastic lesions are later confirmed after thyroidectomy. The false negative FNAC results may occur because of sampling error or misinterpretation of cytology and are of great concern because they indicate the potential to miss a malignant lesion[22]. However, it is difficult to calculate the true frequency of false negative results, because only a small percentage of patients with benign cytological findings undergo surgery. In the present study, false negative FNA has occurred in two out of thirty seven (5.4%) patients with benign diagnosis. This is consistent with reports in the literature that suggest a false negative rate of 2 - 7%[23,24].

Limitation of our study was small sample size, inconclusive (intermediate) group was not detected in our study which might be due to small sample size as well as the FNAC were performred without ultrasound guide.

In conclusion our study suggest that FNAC is a sensitive, specific and accurate initial diagnostic test for the preoperative evaluation of patients with thyroid nodules. Our results are comparable with

current published articles and the clinician should be encouraged to use FNAC as the initial modality in assessment of thyroid nodules.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper

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پوختە

ئەرێ وەرگرتنا نمونێن شانەیی بدەرزیکێ رێکەکا باشە بو دەستنیشانکرنا پەریزادەیا گرێکی؟

پێشەکی: وەرگرتنا نمونێن شانەیی بدەرزیکێ ئێکە ژ رێکێن مشە کو دهێتە بکارئینان بو دەستنیشانکرنا گرێگێن گلاندا تایروید. ئەرێ ئەڤ رێکە دەستنیشانکرنەکا دروست ددەت بلەز و بکێمترین ئالوزی؟

ئارمانج: دیارکرنا بکێرهاتنا رێکا وەرگرتنا نمونێن شانەیی بدەرزیکێ بو هەلسەنگاندنا گرێکێن تایرویدێ لدەف مە و بەراوەردکرن دگەل ڤەکولینێن جیهانی.

رێکێن ڤەکولینێ: ئەڤ ڤەکولینە هاتە ئەنجامدان لسەر ٥١ نەساخا کو تاقیکرنا وەرگرتنا نمونێن شانەیی بدەرزیکێ بو هاتییە کرن ژبو دەستنیشانکرنێ هەر ژ شواتا ٢٠١٢ێ هەتا شواتا ٢٠١٥ێ و ئەنجام دهاتنە بەراوەردکرن دگەل تاقیکرنا نەسیجی وەك ستاندەرد.

ئەنجام: ڤەکولینێ دیارکر کو رێژا هەستداری و رێژا تایبەتمەندی و رێژا دروستییا گشتی یا رێکا وەرگرتنا نمونێن شانەیی بو دەستنیشانکرنا گرێکێن پەنجەشێری بڤی شێوەی بوو: ٨٤.٦٪ ، ٩٧.٣٪ و ٩٤.١٪ لدویف ئێك.

دەرئەنجام: وەرگرتنا نمونێن شانەیی بدەرزیکێ رێکەکا هەستدار و تایبەتمەند و گەلەك دروستە بو دەستنیشانکرن وهەلسەنگاندنا دەستپێکێ بەری نشتەرگەریێ بو گرێگێن گلاندا تایروید. ئەنجامێن ڤەکولینێ دبەراوردن دگەل ڤەکولینێن نوی یێن بەلاڤکری و نوژدارێن مە دشێن ڤێ رێکێ بکاربینن بو هەلسەنگاندنا دەستپێکی.

الخلاصة

هل الرشف الابري الدقيق أداة تشخيصية صحيحة لأنسجة عقد الغدة الدرقية؟

الهدف: تقييم دورالتشخيص بواسطة الرشف الابري الدقيق لأنسجه عقد الغدة الدرقية ومقارنتها مع نتائج الفحص النسيجى للغده بعد إجراء العملية الجراحية.

الطريقة: هذه الدراسة شملت ٥١ حالة مرضية (٤٤ من الاناث و٧ من الذكور) يعانون من عقد الغدة الدرقية خلال الفترة من شباط ٢٠١٢ لغاية شباط ٢٠١٥. لكل مريض تم اخذ عينة الرشف الابري على شرائح زجاجية ومعالجتها بمادة الهيماتوكسلين والايوسين ودراسة النتائج ومقارنتها بالزرع النسيجى لنفس المريض.

النتائج : أظهرت الدراسة ان الرشف الابري الدقيق ذو فاعلية كبيرة في تشخيص الاورام الخبيثة للغدة الدرقية وكانت نسبة حساسية الفحص ٨٤.٦% وخصوصية فى التشخيص ٩٧.٣% والدقة التشخيصية ٩٤.١%.

الاستنتاج: اعتماداً على نتائج هذه الدراسة تبين أن فحص الرشف الابري الدقيق لعقد الغدة الدرقية هو حساس ومتخصص وذا دقة تشخيصية عالية فى حالات أورام الغدة الدرقية االسرطانية ومقاربة لدراسات أخرى مماثلة ومن المفضل استخدامها لتقييم حالات عقد الغدة الدرقية.

EVALUATION OF SERUM ZINC LEVEL IN LIVER CIRRHOSIS PATIENTS IN DUHOK GOVERNORATE

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ABSTRACT

Background: In chronic liver disease, cirrhosis is a consequence that is whereby fibrous scar replaces normal hepatic tissue which leads to progressive loss of liver function. It is mostly caused by alcohol consumption and viral hepatitis B or C. Low serum zinc level is prevalent in liver cirrhosis and appears to be due to decreased oral intake especially intake of animal products, increase in cytokines or hormones responsible for zinc breakdown, increases zinc loss from kidneys and decreased gastrointestinal absorption secondary to congestion caused by portal hypertension.

Aim of study: To measure serum zinc level in liver cirrhosis in Duhok Governorate.

Methods: This case control study was conducted on a population of 70 randomly selected sample of patients with liver cirrhosis from 1st of January 2015 to 30th of December 2015, who come for follow up in the center of Gastrointestinal and Hepatic Disease, Duhok governorate, Iraq and those who admitted in the medical ward at Azadi General Teaching Hospital and 70 of matched healthy individuals as control group. Patients were interviewed, examined, and their blood samples taken for zinc level and assessment of Child–Pugh score was done for them.

Results: The mean zinc level in cases group was 73.11µg/dl versus 81.24 in control group (P = 0.006). The number of participants, who were low for zinc level was 29 (41.4%) versus 14 (20%) in cases and control groups respectively (P = 0.006). As severity of liver cirrhosis increased, the zinc level decreased, it was 2 (14.3%) in class A, versus 19 (43.2%) in class B, versus 8 (66.7%) in class C of Child-Pugh score, the P value was significant at 0.024.

Conclusion: Hypozincemia is very common in patients with liver cirrhosis in Duhok. A routine measurement of serum zinc level in these patients is esssential in the management, which will decrease the progression of liver cirrhosis.

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Keywords: liver cirrhosis, Zinc.

Cirrhosis is a long term liver damage in which the healthy liver tissue replaced by fibrosis and this leads to liver failure.. The most common causes behind cirrhosis are alocholism and hepatitis B or C. The distribution of liver cirrhosis shows variations among genders, ethnic groups and geographical areas[1] .Majority of patients remain asymptomatic until they decompensate when disease is advanced. The clinical features of decompensated liver disease are accumulation of fluid in

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the abdominal cavity, bacterial infection of peritoneum, encephalopathy due to liver cirrhosis and bleeding from varices secondary to portal hypertension. The clinical examination may show different findings that needs hepatic or gastrointestinal evaluation to identify the underlying cause[2].

The zinc, is a metallic element in group twelve of the periodic table (Zn, also called spelter) and its atomic number is 30[3].

Zinc is important for maturity of immune system. As its essential for function of almost 300 enzymes of human body[4]. Zinc has important role against scar formation in liver tissue. It prevents cellular damage caused by oxidative stress. It is estimated that two billion people in the developing countries suffer from zinc deficiency like people living in Iran, whom their main diet is rice[5]. While zinc status studied in Iraqi population showed that the prevalence of severe zinc deficiency among the studied sample was 2.7%, and mild to moderate zinc deficiency was 55.7% of the study sample[6]. The daily required zinc for women is 8 mg/day and for men is 11 mg/day. Zinc is abundant in foods based on red meats, such as beef, lamb and liver[3].

The low serum zinc level found in patient with liver cirrhosis appears because of effects of loss appetite and low intake of animal protein, increase in cytokines or hormones responsible for zinc breakdown, increases zinc loss from kidneys and decreased gastrointestinal absorption secondary to congestion caused by portal hypertension[5].

The protein produced by liver decreased in cases of liver cirrhosis. The metallothionein (MT) is a protein formed by liver have an important role in zinc metabolism, when oxidants process occur zinc released by this protein, the released zinc is essential in prevention of liver damage (cirrhosis). so any defects in synthesis of this protein will lead to zinc[5].

It has been suggested that some of the clinical features of liver cirrhosis, such as testicular atrophy, loss of body hair, night blindness, poor wound healing, poor appetite, decreased taste and smell acuity, susceptibility to infections, enhanced sensitivity to drugs, and decreased neurocognitive performances, may be related to zinc deficiency[4].

The patients with liver cirrhosis need regular checkup of serum zinc level in order to reduce the worsening of the disease. In some cases zinc therapy improve clinical outcome of these patients. In addition zink therapy corrects the reduced serum zinc level and decreases blood ammonia concentration by activating muscle glutaminsynthetase, resulting in decreasing incidence of

encephalopathy in patients with liver cirrhosis[7].

PATIENTS AND METHODS:

The population of this case-control study consisted of a total 70 randomly selected patients diagnosed with liver cirrhosis from 1st January 2015 to 30th December 2015, who came for follow up in the center of gastrointestinal and hepatic disease and those who were admitted in the medical ward at Azadi General Teaching Hospital and 70 of healthy individuals as control group. The patients were interviewed and examined, and their blood samples taken for zinc level and assessment of Child–Pugh score as shown in table 1[8].

Table (1) Child Pugh Score

Measure	1 point	2 points	3 points
Total bilirubin, µmol/l (mg/dl)	<34 (<2)	34-50 (2-3)	>50 (>3)
Serum albumin, g/dl	>3.5	2.8-3.5	<2.8
PT INR	<1.7	1.71-2.30	> 2.30
Ascites	None	Mild	Moderate to Severe
Hepatic encephalopathy	None	Grade I-II (or suppressed with medication)	Grade III-IV (or refractory)

Points	Class	One year survival	Two year survival
5-6	A	100%	85%
7-9	B	81%	57%
10-15	C	45%	35%

Inclusion criteria include patients already diagnosed with liver cirrhosis. This includes clinical finding (when liver span is less than 8 cm with ascites and spleen enlargement), biochemical tests (prothrombin time more than 12 seconds and serum albumin less than 3.5g/dl), radiologically (increased echo pattern of liver, liver shrinkage to less than 8cm, diameter of portal vein more 1.3cm and size of spleen more than 13cm longitudinally) and previous histopathological report (diffuse fibrosis, obliteration of central vein and regenerating nodules)[4].

Meanwhile, patients who were on zinc supplementation therapy, or those on hormonal therapy or cancer chemotherapy were excluded from the study. Further exclusion criteria were pregnancy, acute or chronic diarrhoea, or patients with autoimmune or immunodeficiency disorder (CD4+ count <200 and granulocytopaenia <500/mm3)4.

Fasting serum zinc level were measured by Flame Atomic Absorption Spectrophotometry, Pye Unicam 2900. The reference ranges of serum zinc level were (73-127 µg/dl for male, 70-114 µg/dl for females)[9].

Patients' informed consents were taken. Appropriate communication about the study was undertaken with the patients/carers.[4]

Venous blood samples were drawn and used for determination of serum zinc level (Flame Atomic Absorption

Spectrophotometry, Pye Unicam 2900) according to the data published by Pye Unicam Ltd.(reference Pye WPJ. Unicam atomic absorption data book. 2nd ed. Pye Unicam Ltd; 1976

A specially-designed questionnaire was used to obtain information from participants. Information include gender, age, weight. Data on personal health including history of chronic illnesses and any other drugs patient currently receiving it. All participants underwent a routine medical history & physical examination as clinically relevant.

All data were analyzed using the Statistical Package for Social Science (SPSS v21, Chicago, IL); paired student t- test was calculated to assess differences in serum analyte among groups. Significance of association between various risk factors was assessed using Chi-square test. Level of statistical significance was set at < 0.05.

RESULTS

The age of majority of cases was ≥ 60 years (47.1%), while the age of majority of control group was between 30-40 years (50%) as shown in table 2.

Table (2) Age distribution of study participants

	20-30 yr	30-40 yr	40-50 yr	50-60 yr	≥ 60 yr	Total
Cases	No. 2 (2.9)	No. 2 (2.9)	No. 15 (21.4)	No. 18 (25.7)	No. 33 (47.1)	70 (100)
Controls	0 (0)	35 (50)	14 (20)	7 (10)	14 (20)	70 (100)

Females constituted 51.4% (N=) of the patients, while number of males and females were equal in control group as shown in table 3.

Table (3) Gender distribution of study participants

	Male No. (%)	Female No. (%)	Total
Cases	34 (48.6)	36 (51.4)	70 (100)
Controls	35 (50)	35 (50)	70 (100)

The mean of zinc level in cases group was 73.11 µg /dl versus 81.24 in control group and the P = 0.006 (Standard deviation in cases group 20.947 versus 12.702 µg /dl in control group) as shown in table 4.

Table (4) Difference between cases and control regarding zinc measurement

	Zinc measure		
	Mean (microgm/dl)	Standard deviation (microgram/dl	P value*
Cases	73.11	20.947	0.006**
Controls	81.24	12.702	

* Statistical test used: independent t-test

** the difference is statistically significant

The number of participants, who were low for zinc level was 29(41.4%) versus 14 (20%) in both cases and control groups respectively (P=0.006) as shown in table 5.

Table (5) Difference between cases and control regarding zinc level

	Zinc Level		
	Normal No. (%)	Low No. (%)	P value*
Cases	41 (58.6)	29 (41.4)	0.006**
Controls	56 (80)	14 (20)	

* Statistical test used: Chi squared test

** the difference is statistically significant

The difference in zinc level according to age and gender of participants, statistically were not significant as shown in table 6 and 7.

Table (6) Difference in zinc level according to age of participants

	Zinc Level		
Age groups (years)	Normal No. (%)	Low No. (%)	P valu*
20-30	2	0	Not signif icant **
30-40	30	7	
40-50	16	13	
50-60	19	6	
60 and more	30	17	

* Statistical test used: Chi squared test

** the difference is statistically not significant

Table (7) Difference in zinc level according to gender of participants

	Zinc Level		
Gender	Normal No. (%)	Low No. (%)	P value*
Male	51 (73.9)	18 (26.1)	Not significant**
Female	46 (64.8)	25 (35.2)	

* Statistical test used: Chi squared test

** the difference is statistically not significant

As severity of liver cirrhosis increased depending on Child Pugh score, the zinc level decreased; 2 (14.3%) in class A, versus 19 (43.2%) in class B, versus 8 (66.7%) in class C, (P = 0.024;table 8).

Table (8) Difference in zinc level according to child Pugh score of patients

	Zinc Level		
Child Pugh Score	Normal No. (%)	Low No. (%)	P value*
A	12 (85.7)	2 (14.3)	0.024 **
B	25 (56.8)	19 (43.2)	
C	4 (33.3)	8 (66.7)	

* Statistical test used: Chi squared test

** The difference is statistically significant

HBV constitute the majority of cases 39(27.9%) of liver cirrhosis followed by cryptogenic 19(13.6%) as shown in figure 1.

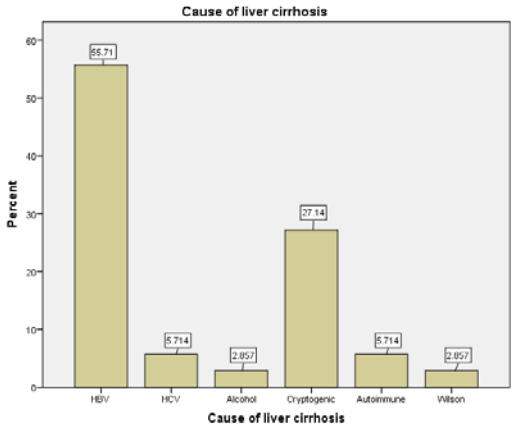

Figure (1) Causes of Liver Cirrhosis

Diabetes Mellitus (DM) was the most prevalent co morbidity among liver cirrhosis cases and was diagnosed in 18 (12.9%) patients followed by asthma 4 (2.9%) as shown in table 9.

Table (9) Co-morbidities

	Number	%
None	46	32.9
DM	18	12.9
Hypertension	2	1.4
Asthma	4	2.9
Total	70	100

DISCUSSION:

Elements in blood have important role in diagnosis and prognosis of many diseases[10]. Many studies done before and show strong relation between zinc deficiency and liver cirrhosis.

Pramoolsinsap et al. found that patients with chronic active hepatitis, hepatocellular carcinoma and liver cirrhosis have zinc deficiency[11]. In et al. have found Chinese patients with liver cirrhosis were suffering from zinc deficiency[12]. Zinc level is correlated with eating habit of each community. The developing countries suffer from zinc deficiency more such as people living in Iran, whom their main diet is rice[13]. The phytate and fiber, which present in cereals, are responsible for decreasing zinc absorption[14]. Malnutrition is prevalent in patients with liver cirrhosis secondary to hepatitis B and C, so measuring zinc level may be a good indicator of nutritional status in these patients[15]. Some studies found difference in zinc levels in human. Lopez et al. found that zinc level is higher in men than in women[16].

In the this study, as there is no significant difference between cases and controls regarding gender and age, the biases in interpretation of zinc level will decrease.

The results of our study showed the main cause of liver cirrhosis is viral hepatitis(HBV), which comprise the majority of cases of liver cirrhosis followed by cryptogenic type. There was significant difference between cases and control group regarding zinc status. These results are keeping with similar other studies (10, 11). The results of are of more importantance as there is role of zinc supplementation in treatment of viral hepatitis. Yuasa et al. found that Zinc replacement prevent replication of hepatitis C virus that is why zinc may play a important role in the development of future plans for treating intractable chronic hepatitis C[17]. Himoto et al. did a study on role of polaprezinc (complex of zinc and L-carnosine) on inflammation and fibrosis in patients with HCV. They found that polaprezinc have an anti-inflammatory effect on the liver in patients with chronic liver disease caused by HCV this by reducing iron level[18].

in the current study we found that zinc deficiency correlated with liver cirrhosis[19] and indicators of liver failure like total bilirubin, albumin, and cholesterol[11]. Low zinc is more common in liver cirrhosis secondary to alcohol consumption[20-25]. Indeed; the low level is more prevalent if the underlying cause of cirrhosis is alcohol in comparison with other causes[26]. Hepatic encephalopathy is related to low zinc level in liver cirrhosis[27,28]. Accordingly, zinc therapy improves psychometric performances in hepatic encephalopathy[29]. On the other hand, some data show no benefit of treatment of zinc deficiency in comparison to standard treatment[30,31]. Despite these mixed results, treatment of zinc deficiency is recommended for patients suffering from hepatic

encephalopathy who are reluctant to usual therapy[32,33].

In conclusion, hypozincemia is very common in patients suffering from liver cirrhosis. A regular evaluation of serum zinc in patients with liver cirrhosis will play a key role in managment of such patients and will prevent worsening of the underlying disease. We need more studies to evaluate the exact role of zinc replacement on clinical, pathological response of patients with cirrhosis in Duhok.

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پوختە

هەلسەنگاندنا ئاستێ زنکی دناڤ خوینێ دا لدەف نەخوشێن شەمابوونا جەرگی هەی لپارێزگەها دهوکێ

پێشەکی: شەمابوونا جەرگی ئێکە ژ دەرئەنجامێن نەخوشیێن دومدرێژێن جەرگی کو تێدا پێکهاتەیێ جەرگی دهێتە گوهارتن بتەخێن ئەلیافا و هێدی هێدی جەرگ کارێ خو ژدەست ددەت. پتریا جاران ژئەگەرێ نەخوشییێن ڤەخوارنێن کحولی یە لسەر جەرگی وهەروەسا کولبوونا جەرگی یا ڤایروسی ژ جورێ B و C. کێمییا کەرستێ زنک دناڤ خوینێ یا مشەیە لدەف نەخوشێن شەمابوونا جەرگی و ئەگەرێن وێ ژی دلنەچوونا خوارنێ، کێم خوارنا پروتینێ گیانەوەری، زێدەبوونا سایتوکاینا و هورمونێن لسەر زنکی کاردکەن، زێدە ژدەستدانا زنکی بریکا گولچیسکا و لاوازییا هەلمژتنا زنکی درویڤیکا دا.

ئارمانج: دەستنیشانکرنا ئاستێ زنکی لدەف نەخوشێن شەمابوونا جەرگی هەی لپارێزگەها دهوکێ.

ڕێکێن ڤەکولینێ: دڤێ ڤەکولینێ دا حەفتێ نەخوشێن شەمابوونا جەرگی بهەروەیی هاتنە هەلبژارتن ژناڤ ئەو نەخوشێن سەرەدانا سەنتەرێ نەخوشییێن جەرگی وکوئەندامێ هەرسکرنێ کری وهەروەسا ئەوێن هاتینە نڤاندن لنەخوشخانا ئازادی یا فێرکرنێ لپارێزگەها دهوکێ هەر ژ ئێکێ کانونا دووێ حەتا سیهێ کانونا ئێکێ، ٢٠١٥. دگەلدا ٧٠ کەسێن ساخلەم وەك گروپێ کونترول هاتنە وەرگرتن. ئەڤ نەخوشە هاتنە دیتن و نمونێن خوینێ ژێ هاتنە وەرگرتن بو دیارکرنا ئاستێ زنکی لدەف وان.

ئەنجام: تێکرایێ ئاستێ زنکی لدەف گروپێ نەخوشان ٧٣.١١ مکگم/دسیلیتەر ببەراوردی دگەل ٨١.٢٤ لدەف گروپێ کەسێن ساخلەم (قیمەتا P ٠.٠٠٦ بوو). ژمارا نەخوشێن کێماتییا زنکی هەی ٢٩ (٤١.٤٪) بوون بەرامبەر ١٤ (٢٠٪) ژ گروپێ ساخلەمان (قیمەتا P ٠.٠٠٦ بوو). دگەل زێدەبوونا دژواریا نەخوشییا شەمابوونا جەرگی کێمییا ئاستێ زنکی پتر بوو کو ئەوژی ٢ بوو (١٤.٣٪) ل پلەیا A و ١٩ (٤٣.٢٪) ل پلەیا B و ٨ (٦٦.٧٪) ل پلەیا C یا دژواریا نەخوشیێ و ئەڤ جیاوازییە یا ب بها بوو ژلایێ ئاماری ڤە (قیمەتا P ٠.٠٢٤ بوو).

دەرئەنجامێ دوماهیێ: کێماتییا زنکی گەلەکا مشەیە لدەف نەخوشێن شەمابوونا جەرگی هەی لدهوکێ. تاقیکرنا ئاستێ زنکی بو نەخوشێن شەمابوونا جەرگی بشێوەکی روتینی دێ پێنگاڤەکا گرنگ بیت بو چارەسەرکرنا ڤان نەخوشان یاکو بشیوەکێ بەرچاڤ پێشڤەچوونا نەخوشیێ کێم دکەت.

الخلاصة

تقييم مستوى الخارصين في مصل الدم لدى مرضى تشمع الكبد في محافظة دهوك

الخلفية: تليف الكبد هو نتيجة لأمراض الكبد المزمنة التي تتميز باستبدال نسيج الكبد بآخر ليفي مما يؤدي إلى الفقدان التدريجي لوظائف الكبد. والاسباب الأكثر شيوعا لتليف الكبد هي الإدمان على الكحول وكذلك التهاب الكبد الفايروسي نمط B أو C. انخفاض مستوى الخارصين في مصل الدم شائع لدى المرضى الذين يعانون من تليف الكبد ويبدو أن ذلك يعود إلى فقدان الشهية وقلة تناول البروتينات الحيوانية، وزيادة في السيتوكينات أو الهرمونات التي تشارك في عملية الأيض الغذائي للخارصين، زيادة فقدان الخارصين عن طريق الكلى وكذلك ضعف امتصاص العناصر الغذائية.

هدف الدراسة: تحديد مستوى الخارصين في مصل الدم لدى المرضى الذين يعانون من تليف الكبد في محافظة دهوك.

طريقة البحث: أجريت هذه الدراسة من نوع العينة والشاهد على ٧٠ من المرضى الذين يعانون من تليف الكبد تم اختيارهم عشوائيا من ١ كانون الثاني الى ٣٠ كانون الاول عام ٢٠١٥، ممن زاروا مركز أمراض الجهاز الهضمي والكبد ومستشفى آزادي التعليمي العام في محافظة دهوك، العراق، وكذلك ٧٠ من الأفراد الأصحاء كمجموعة الشاهد. أجريت المقابلة مع المرضى وتم فحصهم سريرياً ومن ثم أخذت عينات من دمهم لتحديد مستوى الخارصين لديهم.

النتائج: كان مستوى الخارصين لدى مجموعة المرضى ٧٣.١١ مكغم/ ديسيلتر مقابل ٨١.٢٤ في مجموعة الشاهد (P =٠.٠٠٠٦). وكان عدد المرضى الذين كانت لديهم نسب منخفضة من الخارصين ٢٩ (٤١.٤٪) مقارنةً ب ١٤ (٢٠٪) لدى الأصحاء (P = ٠.٠٠٠٦). كلما زادت شدة تليف الكبد، كلما ازداد انخفاض مستوى الخارصين، فكان ٢ (١٤.٣٪) في الفئة A، مقابل ١٩ (٤٣.٢٪) في الفئة B، مقابل ٨ (٦٦.٧٪) في الفئة C ، وكانت قيمة P ٠.٠٢٤ .

الاستنتاج: انخفاض مستوى الخارصين شائع جدا لدى مرضى تليف الكبد في دهوك. الفحص الروتيني لمستوى الخارصين في مصل الدم لمرضى تليف الكبد هو خطوة مهمة في علاج هؤلاء المرضى والتي تؤدي إلى الحد من تفاقم المرض لديهم.

پەربەندا ١٠ ژمارە ١
خــزیران ٢٠١٦

زانکویا دهوك
کولیژا پزیشکی

گوڤارا پزیشکی یا دهوکێ

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