

STATUS OF SERUM ZINC LEVELS IN FEMALES WITH THYROID DYSFUNCTION

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ABSTRACT

Background: Low serum zinc levels have been connected to thyroid function in more than one way, but to date there is still arguments about the association between zinc deficiency and thyroid disease, particularly in females. The aim of this study was to assess status of serum zinc levels in a sample of females with thyroid dysfunction in comparison with those of normal thyroid function and to ascertain its association with thyroid hormone levels.

Patients and Methods: A case control study was conducted on 225 females referred to the Endocrine Unit for definitive diagnosis of thyroid dysfunction and 100 females with normal thyroid function, serves as a control group.

Results: The results revealed that the serum zinc levels were significantly lower in Hypothyroid females ($62.2 \pm 16.3 \mu\text{g/dl}$) as compared to hyperthyroid ($80.5 \pm 13.9 \mu\text{g/dl}$) and controls ($86.2 \pm 13.2 \mu\text{g/dl}$) with $p=0.001$. The prevalence of severe zinc deficiency ($<50 \mu\text{g/dl}$) was found to be significantly higher in hypothyroid females (25.0%) as compared to hyperthyroid females (3.0%), p -value of 0.01, whereas none of the controls had severe zinc deficiency. In the hypothyroid group, positive correlations of zinc were observed with FreeT3 and FreeT4 ($p=0.007$, $p<0.001$, respectively) and a negative correlation was observed with thyroid stimulating hormone (TSH), $p<0.001$. In the overall studied subjects, negative correlation was also found for zinc with TSH ($p<0.001$). We did not observe a significant correlation of FT3, FT4 and TSH with zinc in controls or in hyperthyroid group.

Conclusions: Decreased serum zinc levels may lead to hypothyroidism in females. Efforts to increase zinc status in this group may help correct abnormal levels of thyroid hormones.

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Keywords: Zinc levels, Thyroid dysfunction, Serum of female.

Zinc is an essential element involved in many basic biochemical reactions in thyroid¹. It is an essential part of an enzyme 1, 5-deiodinase, which converts thyroxine (T4) into a functional triiodothyronine (T3). If zinc is low or missing from the body, T3 cannot be

made². Many studies have described a marked relationship between serum zinc levels and the thyroid hormones³. Moreover, zinc deficiency may be a risk factor for the hypothyroidism, a condition that is highly prevalent in the Iraqi women⁴. Nevertheless, the effect of zinc

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on thyroid hormone levels are still not clear and to date there is still arguments about the association between zinc deficiency and thyroid disease, particularly in females^{5,6}. Attempts to assess the relationship between status of serum zinc levels and thyroid dysfunction in our population are limited. We undertook this study to investigate serum zinc levels in females with hypothyroidism and hyperthyroidism and to ascertain its relationship with thyroid hormones.

MATERIALS AND METHODS

This study was conducted at Azadi Teaching Hospital, Duhok, Kurdistan Region (Iraq); during the period from February to November 2018. The study was formally approved by the research ethics committee; Directorate of Health of Duhok and the institutional Review Board of Duhok College of Medicine. The non-probability convenience sampling technique was used. It was a case control study, in which a group of females with thyroid dysfunction was compared with a control group of normal thyroid function females to find out the relationship between serum zinc levels and thyroid hormone profiles (FreeT3, FreeT4 and thyroid stimulating hormone, TSH).

Serum was obtained randomly from blood samples of 325 females; 225 with thyroid dysfunction (ages 25-70 years of age) and age matched normal thyroid females (n=100) referred to the Endocrine Unit of Azadi Teaching Hospital for definitive diagnosis of thyroid diseases. The diagnosis of hypothyroidism and hyperthyroidism were made first clinically and confirmed biochemically using FT3, FT4 and TSH. The hypothyroid group was

those with elevated TSH concentration (> 10 IU/L) in the presence of low concentration of FT4 and /or FT3, while the hyperthyroid group was with suppressed or undetectable TSH concentration (<0.05 IU/L) in the presence of elevated FT4 and/or FT3 concentration. Enrollees who had normal clinical examination as well as normal thyroid function test and with no history of thyroid illness were included as normal thyroid function females (control group).

Serum zinc measurement was obtained, and females with serum zinc level between 50 and 70 µg/dl considered with mild-moderate zinc deficiency, and severe deficiency for levels <50 µg/dl. Zinc levels were measured by flame atomic absorption spectrophotometer (Perkin Elmer) using a standard procedure. Serum FT3, FT4 and TSH were performed using commercially available standardized electro chemiluminescence immunoassay (ECLIA) method (Cobas 6000, Roche-Hitachi, Germany)).

All data were analyzed using the statistical package for Social Sciences (SPSS) version 21(USA). Independent t-test was used to assess differences in serum analyte among groups. Categorical variables were analyzed by Chi-square test. Pearson's correlation coefficient was used to describe the association between serum zinc and thyroid hormones. Power analysis was performed for zinc and thyroid hormones with values exceeding 0.90. P-value <0.05 was considered as statistically significant.

RESULTS

Table 1 illustrates the baseline characteristics of the studied females. Overall, hypothyroid females comprised 56.4% (n=127) and hyperthyroid females

43.5% (n=98). The mean serum zinc level was significantly lower in hypothyroid females compared to hyperthyroid and control females.

Table 1. Baseline Characteristics of the Studied Females

Parameters	Controls (n=100)		Cases (n=225)	
	Hypothyroid (n=127)	Hyperthyroid (n=98)	Mean±SD	p-value
Age (years)	38.2±13.5	36.7±15.0	36.3±11.6	0.57
TSH (IU/L)	2.09±4.1	29.8±35.3	0.02±0.04	< 0.001
FT3 (pmol/l)	4.5±0.6	4.2±1.4	12.1±10.8	0.001
FT4 (pmol/l)	14.8±2.5	10.1±4.9	36.1±24.4	<0.001
Zinc (µg/dl)	86.2±13.2	62.2±16.3	80.5±13.9	0.001

Table 2 illustrates the percentage of females with serum zinc levels. Of the three hundred-twenty five females, 35(10.5%) had severe zinc deficiency (<50 µg/dl). Of the severe zinc deficiency females, 32(25.2%) were with hypothyroidism, and hyperthyroidism comprise 3(3.0%). Sub-

clinical hypothyroidism was present in 48 of the females. The prevalence of females with sub-clinical hypothyroidism according to the current guidelines ranged from 10.4% of females with severe zinc deficiency to 39.6% with mild-moderate zinc deficiency (serum zinc between 50-70 µg/dl).

Table 2. Percentage of females with serum zinc levels.

Serum zinc (µg/dl)	Overall (n=325)	Control (n=100)	Hypothyroid (n=127)	Hyperthyroid (n=98)
<50, n (%)	35(10.8)	0(0.0)	32(25.0)	3(3.0)
50-70, n (%)	75(23.1)	13(13.0)	47(37.0)	15(15.3)
>70, n (%)	215(66.1)	87(87.0)	48(38.0)	80(81.7)

Table 3 illustrates the relationship between serum zinc and thyroid hormones in hypothyroid and hyperthyroid females. In the hypothyroid group, zinc correlated

positively with FT3 and FT4 ($p=0.007$; $p<0.001$, respectively) and a negative correlation was observed with TSH ($p<0.001$). In the overall studied subjects, negative correlation was also found for

Table 3. Correlation coefficient between serum zinc and free T3, free T4 and TSH

Thyroid Hormone	Overall		Control		Hypothyroid		Hyperthyroid	
	r	p	r	p	r	p	r	p
FT3	0.01	0.862	0.07	0.440	0.35	0.007	0.03	0.720
FT4	1.00	0.070	0.08	0.390	0.44	<0.001	0.11	0.280
TSH	-0.46	<0.001	-0.07	0.480	-0.56	<0.001	0.06	0.650

STATUS OF SERUM ZINC LEVELS IN FEMALES WITH THYROID

zinc with TSH ($p<0.001$). We did not observe a significant correlation of FT3, FT4 and TSH with zinc in controls or in hyperthyroid group.

Figures 1 and 2 shows a positive correlation between serum zinc levels and both free T3 and Free T4 in hypothyroid females ($r=0.35$ and $r=0.44$, respectively).

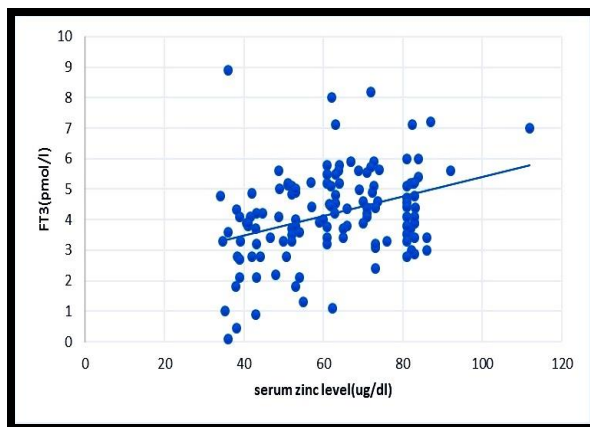


Figure1: Serum Zinc Relationship to FT3 in Hypothyroid Females. $r=0.35$, $p=0.007$

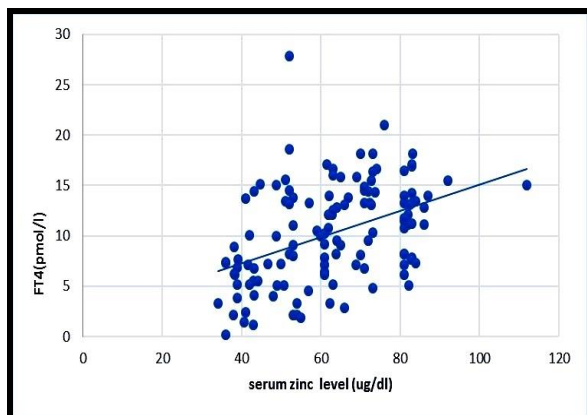


Figure2: Serum Zinc Relationship to FT4 in Hypothyroid Females. $r=0.44$, $p<0.001$

Figure 3 and figure 4 shows a negative correlation between serum zinc levels and TSH in hypothyroid females and in the overall studied females ($r=-0.56$ and $r=-0.46$, respectively).

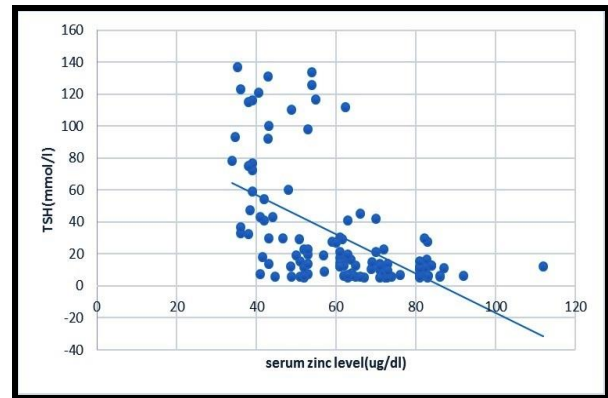


Figure 3: Serum Zinc Relationship to TSH in Hypothyroid Females. $r=-0.56$, $p<0.001$

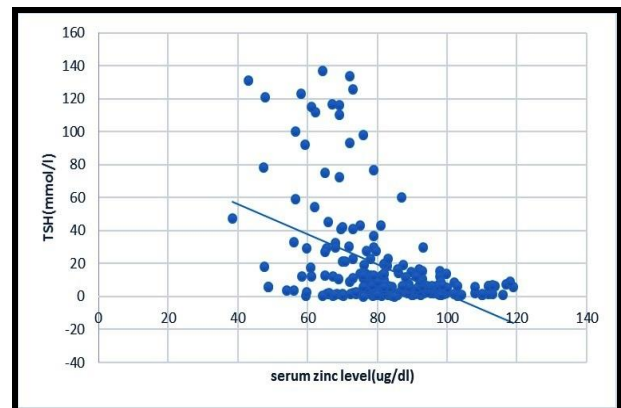


Figure 4: Serum Zinc Relationship to TSH in Overall Studied Females. $r=-0.46$, $p=0.001$

DISCUSSION

Zinc is one of the essential micronutrients that play a significant role in the metallo-enzyme process of the body⁷. Zinc is involved in protein and nucleic acid synthesis, as well as in various metabolic and cellular functions. Some Studies showed that zinc deficiency leads decrease in T3 level. In addition, a potential link between nutritional zinc deficiency and hypothyroidism has been suggested by de Lima *et al* and Baltaci *et al*^{8,9}. In our study we investigated females with and without thyroid dysfunction and we found a significant positive correlation between FT3 and FT4 with serum zinc levels in hypothyroid group, but no such correlations in the hyperthyroid and normal thyroid group. Moreover, there

were significant differences in the mean serum zinc levels among the groups. It was observed that, mean serum zinc was lower in hypothyroidism females than in hyperthyroidism and healthy control females. The same manner was observed for prevalence of zinc deficiency when compared among the three groups. The current results are in agreement with finding from previous study¹⁰, who found that T3 and T4 were significantly lower and TSH significantly higher in zinc deficiency patients and they demonstrated that T3 levels have been increased with zinc supplementation¹¹.

The present study also showed that zinc level correlated negatively with TSH in the hypothyroidism females. We found that 25% of females with hypothyroidism and that about 3% of the females with hyperthyroidism had severe zinc deficiency (<50 µg/dl). Such a high prevalence of low zinc status is worth mentioning. The potential link between zinc and thyroid metabolism is based on the hypothesis that T3 receptors, like other nuclear receptors, include nuclear zinc-binding proteins¹². Therefore, zinc is thought to be an integral part of nuclear receptor proteins, stabilizing them in a conformation required for binding to target genes¹³. Moreover, zinc is also required for the activity of the enzyme 1, 5-deiodinase, which converts biologically inactive T4 to biologically active T3^{14,15}. The fact that zinc levels are lower in hypothyroidism females, it is important to note that stronger association between hypothyroidism and zinc values have been reported for women compared with men¹⁶. Our study confer a high proportion (62%) of females with hypothyroidism, but

not normal thyroid females (13%) or females with hyperthyroidism (18.3%), had serum zinc levels (<70 µg/dl). These may suggest an important mechanism through which zinc can influence higher risk of hypothyroidism in our population. Indeed, several Iraqi studies reported that nutritional zinc deficiency is prevalent in our population, particularly females at child bearing age^{17, 18}. This appears to be a new finding as previous study by Mocayo *et al*¹⁹ reported that neither zinc nor selenium correlated with thyroid function in benign thyroid disease.

The lack of correlations between serum zinc level and thyroid hormones in hyperthyroid females seems to be similar to the results of other studies^{20, 21}, but in contrast to others^{22, 23}. This discrepancy of our results as compared to those of other studies may be related partly to the nutritional zinc status. However, several factors are known to make a negative impact on zinc status, particularly in females. Of these pregnancy and lactation are the factors which cause the most marked negative effects on serum zinc levels^{24, 25}. The current study has shown a similarity in serum zinc levels among hyperthyroid females and normal thyroid females, although none of the studied females were pregnant. Another probable explanation is that TSH has significant influence in the variation of zinc concentration in normal and changed human thyroid tissues²⁶.

The results confirm that zinc deficiency may play a role in thyroid function. We have shown positive correlations between FT3 and FT4 with zinc and negative correlation between TSH and zinc in hypothyroid females. Efforts to increase

zinc status in patients with hypothyroidism may help to normalized thyroid hormone levels.

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پوخته

هه‌لسه‌نگاندنا باری ریژاناستین زینک د سیروما خوینی دال دهف وان نافرمتین ناریشه د سایروده رژین دا

پیشه کی: گریدان دنافبه راریژا نزمیا ناستین زینک ی د خوینی دا ب کارین سایروده رژین قه ب پتر ژ ریکه‌کی.

نارمانج: نارمانج ژفه‌کولینی نهوه هه‌لسه‌نگاندنا باری ریژاناستین زینک ی د سیروما خوینی دال دهف وان نافرمتین ناریشه د سایروده رژین دا هه‌ین، بین سرمدانا یه‌کا رژیین ئینکرویدینی کری ل نه‌خوشخانا نازادی یا فیرکرنی ل پاریزگه‌ها دهوک.

ریکنیفه‌کولینی: فه‌کولین ل سر 225 نافرمتا هاته‌کرن بین ناماده‌بوین ل یه‌کا رژیین ئینکرویدینی بو ده‌ستنیشانکرنا دو‌ماهی د کیماسیا کارئ سایروده رژین دا و 100 نافرمتین دی کو سایروده رژینا وان ناسایی کاردکعت وه‌ک کوما کونترولی یان بنهما.

نه‌نجام: نه‌نجامان دیارکر کو ناستین زینکی د سیروما خوینی دا یا کیم بو بشیوه‌کی دیار لدهف نافرمتین ناریشه د سایروده رژین دا هه‌ین (16.3 ± 62.2 مایکروگرام/دیسلیتر) ب هه‌قبهرکرن دگهل نافرمتین ناریشه د زیده چالاکیا سایروده رژین دا هه‌ین (13 ± 80.5 مایکروگرام/دیسلیتر) و نافرمتین ساخلم (13.2 ± 86.2 مایکروگرام/دیسلیتر)، (ص=0.001).

هاته‌قه‌دیتن کو کیم بونه‌کا دژوار د ناستی زینکی دا یا هه‌ی (>50 میکروگرام/دیسلیتر) کو دبیته بلندترین لدهف نافرمتین ناریشه د سایروده رژین دا هه‌ین (25%) ب هه‌قبهرکرن دگهل نافرمتین ناریشه د زیده چالاکیا سایروده رژین دا هه‌ین (3.0%)، د هه‌مان دم دا چ بارین کیم بونه‌کا دژوار د ناستی زینکی د کوما ساخلمان دا نه‌بون.

د کوما ناریشه د سایروده رژین دا هه‌ین دیار بو کو په‌یوه‌ندیه‌کا نهرینی یا زینکی دگهل 10.00 FT3, P=0.007, FT4, P=0.001 و دیار بو کو په‌یوه‌ندیه‌کا نهرینی یا دگهل TSH, P>0.001 دا هه‌ی، هه‌روه‌سا و دیار بو کو په‌یوه‌ندیه‌کا نهرینی یا زینکی دگهل TSH, P>0.001 ژ ی هه‌ی، و دیار بو کو په‌یوه‌ندیه‌کا نهرینی یا زینکی دگهل پبه‌رینسروشتی بین هورمونین سایروده رژین دا هه‌ین. و چ په‌یوه‌ندیه‌کا مه‌زن دنافه‌را زینکی و هه‌ر ئیک ژ TSH, FT3, FT4 د کومین ساخلم و ناریشه د زیده چالاکیا سایروده رژین دا هه‌ین نه‌بوو.

ده‌نه‌نجام: کیمبون د ناستین زینکی د خوینی دا دبیته نه‌گه‌ری ژ کارکه‌فتنا سایروده رژین د نافرمتان دا. زیده‌کرنا زینکی د قی کومی دا دی بیته هاریکار بو راسته‌کرنا ناستانین سایروده رژین.

الخلاصة

حالة مستويات مصّل الزنك في الإناث المصاحب مع خلل في الغدة الدرقية

الخلفية والأهداف: لقد تم ربط مستويات الخارصين المنخفضة في الدم بوظائف الغدة الدرقية في أكثر من طريقة واحدة. الهدف من الدراسة الحالية هو تقييم حالة مستويات الخارصين في مصّل الدم لدى الإناث اللواتي يعانين من خلل في وظائف الغدة الدرقية و تأكيد العلاقة مع هورمونات الغدة الدرقية .

المواضيع و طرق البحث: تم اجراء الدراسة على 225 حالة من الإناث اللواتي حضرن وحدة الغدد الصماء للتشخيص النهائي من الخلل في وظيفة الغدة الدرقية و 100 من الإناث مع وظيفة الغدة الدرقية العادية بمثابة المجموعة الضابطة.

النتائج: اظهرت النتائج ان مستويات الخارصين في مصّل الدم كانت اقل بشكل ملحوظ في الإناث المصابين بخمول الغدة الدرقية (16.3 ± 62.2 ميكروغرام/ديسيلتر) بالمقارنة مع الإناث المصابين بزيادة نشاط الغدة الدرقية (13 ± 80.5 ميكروغرام/ديسيلتر) والإناث الأصحاء (13.2 ± 86.2 ميكروغرام/ديسيلتر), ($P=0.001$) تم العثور على انتشار نقص الخارصين الشديد (>50 ميكروغرام/ديسيلتر) لتكون اعلى بكثير لدى الإناث المصابين بخمول في الغدة الدرقية (25%) بالمقارنة مع الإناث المصابين بزيادة نشاط الغدة الدرقية (3.0%), بينما لم تكن هناك اي حالة لنقص شديد للخارصين بين مجموعة الأصحاء.

في المجموعة الخمول في الغدة الدرقية لوحظ ارتباط ايجابي من الخارصين مع هورمون الغدة النخامية. ولم تكن هناك ارتباط كبير بين الخارصين وكل من TSH, FT3, FT4 في مجموعة الأصحاء ومجموعة زيادة نشاط الغدة.

الاستنتاجات: انخفاض مستويات الزنك في الدم قد يؤدي إلى قصور الغدة الدرقية عند الإناث. قد تساعد الجهود المبذولة لزيادة حالة الزنك في هذه المجموعة على تصحيح مستويات غير طبيعية من هرمونات الغدة الدرقية