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Prevalence and Association of Thyroid Dysfunction with Anemia/Body Iron Status among Northern Border Saudi Population

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ABSTRACT

Objective: *To find the prevalence and association of thyroid dysfunction with anemia/body iron status among Northern Border Saudi population.* ***Materials and methods:*** *The present cross-sectional study included 150 male and female participants visiting the out-patient clinic in Arar Central Hospital, Arar, Saudi Arabia. Blood samples were collected for estimation of thyroid hormones, RBC count, hemoglobin, MCV, MCH, TIBC, serum iron and ferritin.* ***Results:*** *Thyroid disorders were detected in 61.33% of the studied population and hypothyroidism (73 cases out of 92) was more prevalent than hyperthyroidism (19 cases out of 92) with higher prevalence observed among female participants (60.27%) as compared to males (39.72%). Higher prevalence of anemia (60.27%) and iron deficiency (49.31%) was observed among hypothyroid group as compared to hyperthyroid and euthyroid group which was characterized by significantly lower values of erythrocyte indices (RBC count, hemoglobin, MCV, MCH) and iron parameters (serum iron, ferritin, transferrin saturation) in hypothyroid group as compared to hypothyroid and euthyroid group. Erythrocyte indices and iron parameters correlated positively with FT4 and negatively with TSH.* ***Conclusion:*** *The study demonstrates a high prevalence of thyroid abnormalities particularly hypothyroidism, accompanied by increased prevalence of anemia and iron deficiency indicating symbiotic relationship between thyroid gland function and body iron status. Future studies should be done in large samples and should include thyroid antibodies profile and urine iodine to identify the underlying mechanism and the etiological factors contributing to the development of thyroiditis-induced anemia.*

Keywords: Hypothyroidism, Hyperthyroidism, Anemia, Iron deficiency

INTRODUCTION

Among the nutritional deficiencies prevalent worldwide, iron deficiency is the most prevalent [1]. It is associated with a number of adverse health consequences including delayed psychomotor development, cognitive impairment in children [2] and damage to immune mechanisms [3]. Moreover, past studies on humans and animals indicate that deficiency of iron may alter thyroid hormone metabolism [4,5].

Thyroid hormones play a central role in normal development, differentiation, metabolic balance, and physiological function of virtually all tissues [6] and thyroid function disorders are among the most common endocrine diseases [7,8]. The occurrence of thyroid disorders varies according to the society with hyperthyroidism being the most prevalent form with a reported frequency of 2-5% worldwide and hyperthyroidism least prevalent with a frequency ranging between 0.5 and 2% in women [6,8-11]. Dysfunction of the thyroid gland has been linked to hematological abnormalities and anemia is the most prevalent disorder [12]. Studies of the patients after thyroidectomy revealed a decrease in the number of red blood cells (RBCs) in their peripheral blood [13] and 20%-60% of the hypothyroid patients were found to be anemic [9,12,14]. Anemia in hypothyroidism may be attributed to bone marrow depression, decreased erythropoietin production, comorbid diseases, or concomitant iron, vitamin B12, or folate deficiency.

Although past studies have demonstrated that Grave's disease is also associated with hematological abnormalities [11,15], anemia is not common in hyperthyroid patients, whereas erythrocytosis is common [12,14,15].

The westernization of lifestyle and nutrition transition in Saudi Arabia has increased the burden of endocrine disorders including thyroid dysfunction. Both anemia and thyroid disease, due to their high prevalence and close association, are significant clinical problems often encountered by practitioners. The majority of the existing data regarding the association between anemia and thyroid dysfunction is mainly confined to children and adolescents or pregnant women whereas replication in wide samples of the general adult population has not been carried out. Therefore, this study aims to measure the prevalence of thyroid disorders and to study their relationship with anemia/iron status in the adult and non-pregnant Saudi population.

SUBJECTS AND METHODS

Study Design

The present cross-sectional study was conducted in Arar, Saudi Arabia. Five milliliters of the blood sample was collected from 150 males and females (age range between 24 and 76 years) visiting the out-patient clinic in Arar Central Hospital, Arar, Saudi Arabia. All participants filled a questionnaire regarding their medical history and the reason for attending the medical center. To be included in the study, the participants had to be healthy with no current or past history of acute illness within at least 3 months before recruitment, no history of/current chronic medical condition, not using medication for significant clinical disease, and not taking iron or vitamin supplementation. The recruitment of participants was consecutive, and half of the blood sample (2.5 ml) was collected in tubes containing ethylenediaminetetraacetic acid (EDTA) and the rest in plain tubes.

The participants were divided into euthyroid, hypothyroid and hyperthyroid group according to their thyroid profile results. Patients with normal thyroid profile served as the "euthyroid group" and their hematological results and iron parameters were compared with those obtained from hypo and hyperthyroid group.

Exclusion criteria: Patients with pregnancy, hepatic disorder, renal diseases, polycystic ovarian syndrome, chronic medical condition, coronary heart disease, uncontrolled hypertension, diabetes mellitus, history of thyroid dysfunction, or on drug and supplements which may affect iron metabolism and thyroid function were excluded from the study.

Inclusion criteria: Saudi adult (>18 years) patients with no history of thyroid dysfunction, no chronic diseases, not on hormonal therapy and/or oral contraceptive pills, not known to be anemic, not taking vitamins and/or iron supplementation were included in the study.

Ethical consideration and patient consent: The work was approved by the Deanship of Scientific Research at Northern Border University and informed consent was obtained from all participants.

Thyroid Hormone Measurements

Thyroid hormones (Free triiodothyronine (FT3), Free thyroxine (FT4) and Thyroid-stimulating hormone (TSH)) were measured by immunoassay methods using ELISA kits. Normal reference range provided by kits for thyroid hormones were FT3 (2.80-7.10 pmol/l), FT4 (12-22 pmol/l) and TSH (0.27-4.20 µIU/L). The diagnosis and classification of thyroid abnormalities were according to the guidelines of the National Academy of Clinical Biochemistry (NACB) for laboratory diagnosis and monitoring of thyroid diseases [16]. Hypothyroidism was considered when TSH was >4.2 µIU/ml and FT4 <12 pmol/l. Hyperthyroidism was considered for TSH <0.27 µIU/ml and FT4 >22 pmol/l.

Determination of Hematological Profile

Whole blood samples (2.5 ml) collected in EDTA containing tubes were processed on Sysmex XS 500 with five-parameter differential (Sysmex, Lincolnshire, IL, USA) for the measurement of hemoglobin concentrations, RBC count, Packed cell volume (PCV), mean corpuscular volume (MCV), and mean corpuscular hemoglobin (MCH). Anemia was defined by hemoglobin (Hb) level <12 g/dl in women and <13g/dl in men [17].

Iron Parameters

Serum iron, ferritin and total iron-binding capacity (TIBC) were measured by colorimetric methods using commercial

kits. Transferrin saturation (%) was calculated as follows: (serum iron/TIBC) x100. According to the manufacturer, the normal range of iron was 9-31µmol/L. The normal range of TIBC was 42.96-80.55 µmol/L. The normal range for the ferritin kit was 13-400 ng/ml. A low transferrin saturation (<15%) was considered diagnostic of iron deficiency [18].

Statistical Analysis

Results are expressed as mean ± standard deviation (SD). The correlation/association between different variables was determined by Pearson's correlation coefficient (r). p-value<0.05 was considered significant.

RESULTS

Among the study population, 42.66% (n=64) were males and 57.33% (n=86) were females with the mean age of 37.98 and 45.34 years respectively.

Table 1 depicts the thyroid profile of the participants. The studied population was categorized into the hypothyroid, hyperthyroid or euthyroid group based on their thyroid profile. As is obvious from the results, there was a significant ($p<0.05$) difference among the values of TSH, FT3 and FT4 among the groups.

Overall, thyroid disorders were detected in 61.33% (n=92) of the studied population. Among the thyroid disorders, hypothyroidism was more prevalent (73 cases out of 92) than hyperthyroidism (19 cases out of 92) with higher prevalence observed among female participants as compared to males (Table 2).

The prevalence of anemia and iron deficiency among the studied population (n=150) was 43.33% (n=65) and 28.66% (n=43) respectively. Higher prevalence of anemia and iron deficiency was observed among hypothyroid group as compared to hyperthyroid and euthyroid group (Table 3). Figures 1 and 2 exhibit a comparison of anemia prevalence and iron status among euthyroid and thyroid dysfunction group.

The mean values of erythrocyte indices (RBC count, hemoglobin, MCV, MCH) and iron parameters (serum iron, ferritin, transferrin saturation) were significantly ($p<0.05$) lower and TIBC was significantly ($p<0.05$) higher in the hypothyroid group as compared to hypothyroid and euthyroid group (Table 4).

Correlation analysis of thyroid hormones with hematological indices and iron parameters is shown in Table 5. A significant ($p<0.05$) positive correlation of FT4 was observed with RBC count, Hb, MCV, MCH, Serum iron, ferritin and transferrin saturation whereas FT4 was significantly ($p<0.05$) negatively correlated with TIBC. On the other hand, TSH was found to have a significant ($p<0.05$) negative correlation with RBC count, Hb, MCV, MCH, Serum iron, ferritin and transferrin saturation, and a significant ($p<0.05$) positive correlation with TIBC.

Table 1 Thyroid profile of the studied population

Thyroid Status	Hypothyroid Group	Hyperthyroid Group	Euthyroid Group
	Mean ± SD	Mean ± SD	Mean ± SD
TSH (µIU/ml)	10.43 ± 2.24[a]	0.16 ± 0.05[b]	2.13 ± 0.64[c]
FT3 (pmol/l)	2.53 ± 0.78[a]	10.31 ± 1.37[b]	4.58 ± 0.98[c]
FT4 (pmol/l)	11.34 ± 1.78[a]	28.58 ± 2.79[b]	16.08 ± 2.22[c]

[a]$p<0.05$ when compared to euthyroid and hyperthyroid group; [b]$p<0.05$ when compared to euthyroid and hypothyroid group; [c]$p<0.05$ when compared to hypothyroid and hyperthyroid group

Table 2 Prevalence of thyroid dysfunction among the studied population according to gender (N=150)

Thyroid Status	Total N=150	Females N (%)	Males N (%)
Hypothyroidism	73 (48.66%)	44 (60.27%)	29 (39.72%)
Hyperthyroidism	19 (12.66%)	12 (63.15%)	7 (36.84%)
Euthyroidism	58 (38.66%)	30 (51.72%)	28 (48.27%)

Table 3 Prevalence of anemia and iron deficiency among the studied population according to their thyroid status

Thyroid Status	Total	Anemia Status		Iron Status	
	(N=150)	Anemic N (%)	Non-anemic N (%)	Iron deficient N (%)	Iron sufficient N (%)
Hypothyroidism	73 (48.66%)	44 (60.27%)	29 (39.72%)	36 (49.31%)	37 (50.68%)

Hyperthyroidism	19 (12.66%)	6 (31.57%)	13 (68.42%)	1 (5.26%)	18 (94.73%)
Euthyroidism	58 (38.66%)	15 (25.86%)	43 (74.13%)	6 (10.34%)	52 (89.65%)

Table 4 Erythrocyte indices and iron parameters in the studied population

Parameters	Hypothyroid Group	Hyperthyroid Group	EuthyroidGroup
	Mean ± SD	Mean ± SD	Mean ± SD
RBCs count (× 106/µl)	4.04 ± 0.42[a]	4.31 ± 0.41[b]	4.38 ± 0.28[b]
Hb (g/dl)	11.87 ± 1.73[c]	12.68 ± 1.09	13.17 ± 1.01[b]
MCV (fL)	81.41 ± 5.16[a]	85.22 ± 3.59[b]	85.23 ± 4.50[b]
MCH (pg)	25.09 ± 1.79[a]	27.50 ± 1.73[d]	29.11 ± 1.5[e]
Serum iron (µmol/L)	12.30 ± 2.85[a]	18.17 ± 5.18[b]	16.65 ± 5.00[b]
TIBC (µmol/L)	81.81 ± 6.24[a]	64.77 ± 10.29[d]	46.10 ± 8.55[e]
Ferritin (ng/ml)	28.10 ± 6.01[a]	69.66 ± 5.51[d]	88.2 ± 18.65[e]
Transferrin saturation (%)	15.12 ± 3.76[a]	28.30 ± 7.71[d]	36.35 ± 9.8[e]

[a]p<0.05 when compared to euthyroid and hyperthyroid group; [b]p<0.05 when compared to hypothyroid group; [c]p<0.05 when compared to euthyroid group; [d]p<0.05 when compared to euthyroid and hypothyroid group; [e]p<0.05 when compared to hypothyroid and hyperthyroid group

Table 5 Results of correlation analysis for the hematological indices and iron parameters with TSH and FT4 levels in all study participants (N=150)

Parameters	Correlation Coefficient (r)	
	TSH	FT4
RBCs count	-0.347*	0.256*
Hb	-0.321*	0.153
MCV	-0.342*	0.222*
MCH	-0.626*	0.365*
Serum iron	-0.442*	0.348*
TIBC	0.752*	-0.366*
Ferritin	-0.800*	0.488*
Transferrin saturation	-0.689*	0.358*

*p<0.05 when correlated to different parameters (RBC, Hb. MCV, MCH, Serum iron, TIBC, ferritin, Transferrin saturation)

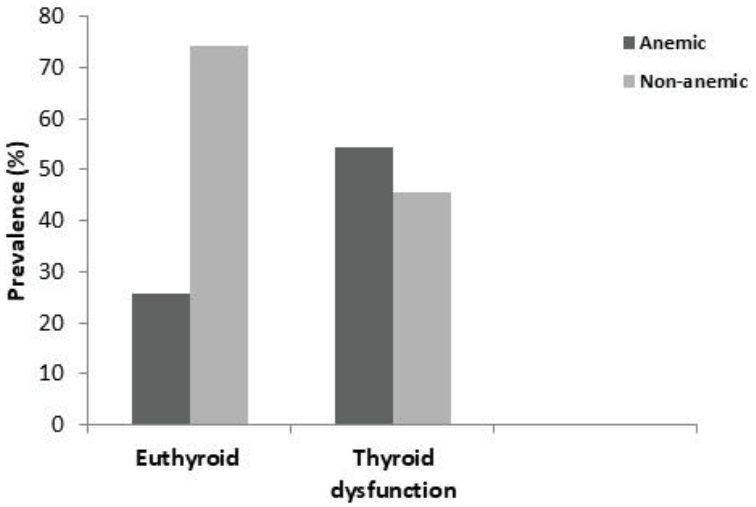

Figure 1 Comparison of anemia prevalence in euthyroid and thyroid dysfunction

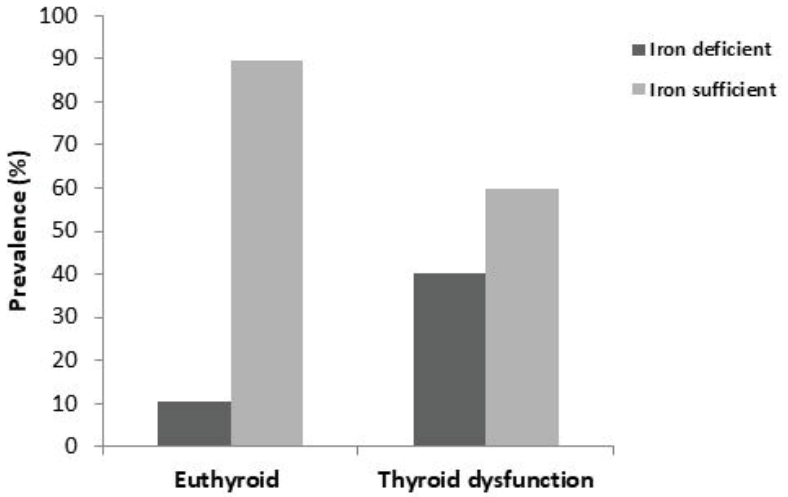

Figure 2 Comparison of iron status in euthyroid and thyroid dysfunction

DISCUSSION

Anemia is a frequent, although often underestimated, clinical condition accompanying thyroid diseases. Most of the past studies linking anemia and thyroid dysfunction are confined to pregnant women or adolescents. To the best of our knowledge, this is the first study to report the prevalence and association of thyroid dysfunction with anemia/body iron status among adult Northern Border Saudi population.

Thyroid dysfunction was observed in 61.33% of the study population with hypothyroidism being the most common disorder and hyperthyroidism the least common. A higher prevalence of hypothyroidism was observed in females as compared to males. Thyroid dysfunction is a major health problem affecting females more than males and its prevalence varies according to the society with hyperthyroidism being the most prevalent form with a reported frequency of 2%-5% worldwide and hyperthyroidism least prevalent with a frequency ranging between 0.5 and 2% in women [6,8-11]. Although, thyroid abnormalities are a frequent problem in Saudi Arabia, but there is a lack of information regarding their prevalence, types and etiological factors [19,20]. Our results demonstrate a high prevalence of thyroid abnormalities among the study population indicating that thyroid dysfunction is a common endocrine disorder in the adult population of the Northern Border region of Saudi Arabia.

Dysfunction of thyroid gland has been linked to hematological abnormalities and anemia is the most prevalent disorder and it is indicated by a decrease in the number of RBCs and hemoglobin concentration [12]. The present study correlates with the aforesaid findings as a significant decrease was observed in the number of RBCs, hemoglobin concentration, MCV, MCH and the iron status indicators between the thyroid disorder and euthyroid groups and the prevalence of anemia was higher in the hypothyroid group as compared to hyperthyroid and euthyroid group. Our findings are following the results of previous studies by Bremner, et al. and Banday, et al. [21,22] who demonstrated significantly lower serum iron concentrations in participants with subclinical hypothyroidism than euthyroid subjects. It is believed that hematopoiesis is affected by abnormalities in the thyroid gland function and thyroid hormone deficiency may lead to bone marrow repression and/or decrease in erythropoietin production due to the reduction of O_2 requirements. Thyroid hormones are also known to regulate the gene expression of transferrin [23]. The decreased prevalence of anemia with hyperthyroidism may be attributed to an increase in erythrocytosis [12,14].

Furthermore, a significant positive correlation of FT4 was observed with RBC count, Hb, MCV, MCH, Serum iron, ferritin, and transferrin saturation whereas FT4 was significantly negatively correlated with TIBC. On the other hand, TSH was found to have a significant negative correlation with RBC count, Hb, MCV, MCH, Serum iron, ferritin and transferrin saturation, and a significant positive correlation with TIBC. The significant correlations of FT4 and TSH with erythrocyte indices and iron parameters suggest that both hormones could have a role in the regulation of erythropoiesis and iron metabolism. Several studies investigated the correlation between thyroid hormones and erythrocyte indices. As reported by Bremner, et al., significant relationships between free T3 and Hb, and the inverse

relationship of TSH with serum iron and transferrin saturation were observed [21]. Bivolarska, et al. also found a slight positive statistically significant correlative association between the levels of free T4 and Hb [24]. The present study is in concordance with the findings of Bremner, et al. [21] as there was a significant decrease in erythrocyte indices in the abnormal thyroid group compared to the euthyroid group and there was a significant positive correlation of serum FT4 with the RBC count, hemoglobin concentrations, MCV, MCH, Serum iron, ferritin, and transferrin saturation. Our findings support the hypothesis that FT4 plays an important role in the regulation of erythropoiesis. Moreover, the decreased values of iron parameters and increased prevalence of iron deficiency in the hypothyroid group suggest that thyroid deficiency could affect the metabolism of iron. Our study supports the assumption that both thyroid dysfunction and serum iron are interdependent, as demonstrated by the observed significant increase in the prevalence of iron deficiency in the thyroid disorder group. Significant correlations of serum TSH positively with TIBC and negatively with serum iron and transferrin saturation further corroborate this association.

CONCLUSION

The study demonstrates a high prevalence of thyroid abnormalities among the study population indicating that thyroid dysfunction is a common endocrine disorder in the adult population of the Northern Border Region of Saudi Arabia. Thyroid dysfunction, particularly hypothyroidism was accompanied by the prevalence of anemia and iron deficiency indicating a symbiotic relationship between thyroid gland function and body iron status. Future studies should be done in large samples and should include the thyroid antibodies profile and urine iodine to identify the underlying mechanism and the etiological factors contributing to the development of thyroiditis-induced anemia.

DECLARATIONS

Acknowledgement

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Conflicts of Interest

The authors declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

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