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Original Article

Evaluation of Iron Status with Abnormalities of Thyroid Function in Children

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ABSTRACT

Introduction and aim: Iron deficiency can negatively affect thyroid function. This research was done to find out whether children's thyroid levels and iron status are related.

Methodology: A cross-sectional research of 300 children attending the outpatient clinic of Pediatric Department at Damietta General Hospital, was carried out., Their ages were between 6 and 12 years. Hemoglobin (Hb), serum irons, overall iron binding capacities, triiodothyronine (t3), thyroxine (t4), thyroid releasing hormones, free thyroxine, free triiodothyronine, and percent transferrin saturation were measured in blood samples.

Results: In the group, there were 235 children who were euthyroid (78.3%), overtly hypothyroid (1.7%), subclinically hypothyroid (17.7%), as well as subclinically hyperthyroid (2.3%). Children who were anemic and iron-deficient frequently had hypothyroidisms, both overt and subclinical. When compared to non-anemic and iron-sufficient children, Hb levels and transferrin saturation showed a strong positive association ($r = 0.322$, $p < 0.001$), although FT3 and FT4 showed only modest correlations ($r = 0.069$, $p = 0.358$, and $r = -0.022$, $p = 0.676$, respectively). In comparison to non-anemic and iron-sufficient kids, the likelihood of hypothyroidisms (overt and subclinical) in anemic and iron-deficient kids was 6.624 (95% CI: 3.233-11.796, $p < 0.001$) and 1.828 (95% CI: 1.182-3.338, $p = 0.034$), accordingly.

Conclusion: Children frequently have anemia, iron insufficiency, and thyroid dysfunctions. Children in this group who were iron-deficient and anemic showed impaired thyroid functions.

Keywords: Thyroid Dysfunction; Iron Deficiency; Anemia; Thyroid Hormone; Children.



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INTRODUCTION

Multiple micronutrient inadequacies continue to be a serious problem for general health in developing nations⁽¹⁾. Particularly in susceptible populations like pregnant women and children, these deficits have a negative impact on growth and development⁽²⁾. Thyroid function is also hampered by a lack of trace minerals like iron, zinc, and selenium. Numerous physiological processes and metabolic processes are impacted by thyroid hormones^(3,4).

While deficits result in hypothyroidisms, an excess of thyroid hormones produce hyperthyroidism. In underdeveloped nations like Egypt, anemia and preventive brain injury are thought to be most frequently caused by iron deficiency⁽⁵⁾. Schoolkids in Egypt have been reported to have a significant prevalence of iron deficiency and anemia^(6,7). The development of children is impacted by iron deficiency, whether or not anemia is present, and thyroid metabolism is negatively impacted in numerous ways⁽⁸⁾. According to investigations, thyroid function and iron status are related⁽⁹⁾. In research conducted in Egypt by Metwalley et al., it was discovered that children in primary schools with iron deficiency anemia were more likely to experience intellectual impairment and subclinical hypothyroidisms⁽¹⁰⁾. Because of the higher rate of anemia and iron deficiency in the Egyptian population, evaluating thyroid function in these inhabitants might assist identify any possible implications of anemia on thyroid metabolism⁽³⁾. Additionally, the Egyptian population has indicated increasing cases of thyroid disease. On the other hand, it is uncertain what causes thyroid issues in this area⁽¹¹⁾.

According to a theory, low iron levels significantly impact thyroid functions, increasing the prevalence of thyroid diseases⁽¹²⁾. Therefore, there may also be a connection between thyroid dysfunction and micronutrient deficiencies in this population. The current report was conducted to examine the potential consequences of iron deficiency on thyroid functions in children, taking into consideration the low iron condition and increased prevalence of thyroid dysfunction in the community of Egypt. Children were specifically randomly chosen between the ages of 6 and 12 who attended at the outpatient's clinic at Damietta general Hospital, Pediatric Department then blood samples were tested to look into the potential association between thyroid function and iron level.

PATIENTS AND METHODS

Study design: To explore the association between iron levels and thyroid functions, both thyroid function and iron status were estimated in a cross-sectional manner.

Study setting and duration: Children attending outpatient clinic at Damietta general hospital, Pediatric Department, were the subject of the study. The study was conducted during the period from August 2019 to November 2019.

Patients: Children around 6 and 12 years' old who had parental consent were randomly recruited in the experiment. 300 kids in all were selected for the research. On the basis of the estimated incidence of thyroid dysfunction (20%) and iron insufficiency (30%) in children, sampling size was estimated.

Exclusion criteria: Children who were lower than 6 years old, having other associated anemia, chronic disease or acute illness, had a history of blood transfusion or iron therapy within the last four months, cases suffering

thyroid disorders and treated with thyroid hormones or had family history of thyroid disorders, and hadn't a parental consent was cut off from the research.

Dataset collection and materials: Age, sex, and three milliliters of venous blood were taken from every kid as demographic data. The materials were sent to the laboratory in refrigerated containers. By using the cyanmethemoglobin technique, Hb was assessed during 24 hours of sample collection, while other variables were calculated within a week as described previously⁽¹³⁾. Applying commercially available kits, colorimetric techniques were used to assess serum iron and total iron binding capacity (TIBC) (Roche Diagnostics). TIBC level and serum iron were used to estimate transferrin concentration (14). HUMAN Diagnostics' ELISA kits were utilized to detect the thyroid hormones free triiodothyronine (fT3), free thyroxine (fT4), and thyroid stimulating hormones (TSH). Regarding females, the normal values range for serum iron was 37-145 g/dl, while for males it was 59-158 µg/dl, and for TIBC it was 274-385 µg/dl. The kit manufacturer also said that the usual normal value for thyroid hormones was TSH (0.39-6.16 mIU/L), fT3 (1.4-4.2 pg/ml), and fT4 (0.8-2.2 ng/dl).

Ethical approval: A written consent was obtained from each child parents to participate in the current study. The Ethical committee of Damietta general hospital has approved the study.

Statistical analysis: The report's output data were imported into Spreadsheet and examined with SPSS software version 19. With the exception of TSH, which were reported as median, and predictor data as number, continuous data were presented as mean ± SD (percentages). For categorical, the chi-square analysis was used at a 95% confidence level, while the independent t analysis, one-way ANOVA, Man Whitney analysis, and Kruskal Wallis testing were employed for continuously data. To determine the association between the iron assessment process and thyroid hormones at a 95percentage confidence level, Spearman's rho correlations analysis and Pearson correlations were performed amongst parameters. A 95percentage confidence interval was used to assess the relative hazard for hypothyroidisms in anemic and iron-deficiency individuals versus non-anemic and iron-sufficiency individuals.

RESULTS

According to the current findings, 53.3% (n = 160) of the participants in the research were males, and 46.7% (n = 140) were females. The range TSH varied from 3 to 7 mIU/L, with median value = 5.1 mIU/L. In the study sample, the average value for Free T4 (ng/dl), Free T3 (pg/ml), Transferrin saturation(%), TIBC (µg/dl), and Serum iron (µg/dl) were 1.3 ± 0.5, 2.6 ± 0.9, 19.9 ± 13.7, 373.9 ± 90.1, 71.6 ± 34.5 and 12.75 ± 2.1 respectively. Table (1) displays the levels of biochemical markers in relation to anemia and iron levels. Iron deficiency and adequate individuals had identical median TSH levels (p = 0.04), while anemic individuals had higher median TSH levels (p < 0.001). In iron sufficient versus iron deficient individuals, fT3 was considerably greater (p = 0.004). According to the study findings, 78.3% (n = 235), 1.7% (n = 5), 17.7% (n = 53), and 2.3% (n=7) of the study participants' children had euthyroidism, overt hypothyroidism, subclinical hypothyroidism, and subclinical hyperthyroidism, respectively. Table (2) displays thyroid function in relation to anemia and iron shortage. In a similar manner, table (3) displays the concentration of Hb and iron condition

markers in the sample participants according to thyroid functional state. There was a significant difference in the thyroid function state according to Transferrin saturation, TIBC ($\mu\text{g/dl}$), Serum iron ($\mu\text{g/dl}$) and Hb (gm/dl) ($p = <0.001, 0.023, 0.029$ and 0.003 respectively). Hb levels and transferrin saturation indicated a strong positive correlation ($r = 0.322, p < 0.001$), however fT3 and fT4 indicated only modest correlations ($r = 0.069, p = 0.358$, and $r = -0.022, p = 0.676$, respectively). In comparison to non-anemic and iron-sufficient kids, the likelihood of hypothyroidisms (overt and subclinical) in anemic and iron-deficient kids was 6.624 (95% CI: 3.233-11.796, $p < 0.001$) and 1.828 (95% CI: 1.182-3.338, $p = 0.034$), accordingly (Figures 1 and 2).

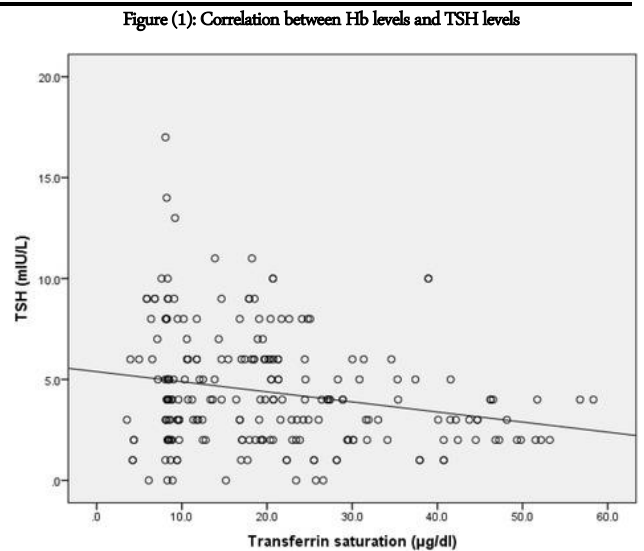
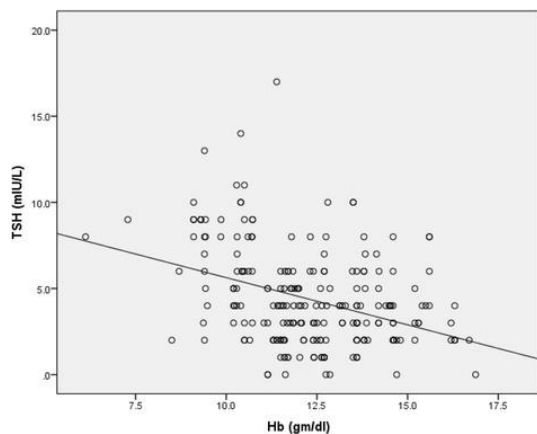


Table (1): Biochemical variables in sample populations regarding anemia and iron levels

Variables	Total	Anemia level		P value	Iron level		P value
	N=300	Anemic N=110	Non-anemic N=190		Iron deficiency N=130	Iron sufficiency N=170	
TSH (mIU/L)	5.1 (3;7)	6.0 (4; 9)	3.32 (3; 6)	<0.001	5.0 (4; 8)	5.0 (3; 7)	0.04*
Free T4 (ng/dl)	1.3 ± 0.5	1.3 ± 0.6	1.3 ± 0.5	0.637	1.3 ± 0.6	1.3 ± 0.5	0.642
Free T3 (pg/ml)	2.6 ± 0.9	2.5 ± 0.8	2.9 ± 0.8	0.24	2.5 ± 0.9	3.1 ± 0.6	0.004*
Transferrin saturation (%)	19.9 ± 13.7	15.1 ± 6.7	24.5 ± 14.7	<0.001*	10.1 ± 1.9	29.2 ± 11.8	<0.001*
TIBC ($\mu\text{g/dl}$)	373.9 ± 90.1	425.7 ± 79.9	374.5 ± 90.01	<0.001*	448.3 ± 82.3	354.9 ± 75.9	<0.001*
Serum iron ($\mu\text{g/dl}$)	71.6 ± 34.5	56.5 ± 22.9	77.7 ± 37.5	<0.001*	38.5 ± 13.8	95.6 ± 29.2	<0.001*
Hb (gm/dl)	12.75 ± 2.1	9.58 ± 2.3	13.6 ± 1.9	<0.001*	10.7 ± 2.3	13.8 ± 1.9	<0.001*

With the exception of TSH, the data was presented as mean ± SD (expressed as median with IQR). P value was determined using a 95% confidence level.

Table (2): Thyroid function state in study sample considering anemia and iron levels

Parameters	Total	Anemia level		P value	Iron level		P value
	N=300	Anemic N=110	Non-anemic N=190		Iron deficiency N=130	Iron sufficiency N=170	
Subclinical hyperthyroidism, n (%)	7 (2.3 %)	2 (0.6 %)	5 (1.7 %)	1.0	5 (1.7 %)	2 (0.6 %)	0.43
Subclinical hypothyroidism, n (%)	53 (17.7 %)	38 (12.7 %)	15 (5 %)	<0.001	31 (10.3 %)	22 (7.33 %)	0.214
Overt hypothyroidism, n (%)	5 (1.7 %)	5 (1.7 %)	-	0.032	5 (1.7 %)	-	0.091
Euthyroidism, n (%)	235 (78.3 %)	70 (23.3 %)	165 (55 %)	<0.001	95 (31.7 %)	140 (46.7 %)	0.023

Numbers (percentages) are used to describe the data. P-value was determined using a 95% confidence level.

Table (3): Biochemical characteristics in sample population regarding thyroid functions

Variables	Euthyroid	Hypothyroid*	Subclinical hyperthyroid	P value
	N = 235	N = 58	N = 7	
Transferrin saturation (%)	22.6 ± 14.3	15.7 ± 9.2	15.1 ± 9.01	0.003
TIBC ($\mu\text{g/dl}$)	369.8 ± 85.3	420.3 ± 105.9	382.5 ± 112.2	0.029
Serum iron ($\mu\text{g/dl}$)	75.2 ± 35.6	58.1 ± 25.5	51.6 ± 24.4	0.023
Hb (gm/dl)	11.9 ± 1.9	9.9 ± 3.2	13.8 ± 3.4	<0.001

The dataset was presented as mean ± SD (expressed as median with IQR). Either overt or subclinical hypothyroidism was included in the hypothyroid cohort, as indicated by the asterisk (*). P-value was determined using a 95% confidence level.

DISCUSSION

In areas where appropriate iron is not available in the typical diet, iron shortages are particularly prevalent⁽¹⁵⁾. In 35.2% and 43.6% of the youngsters, correspondingly, anemia and iron deficiency have been detected. Among the study children, anemia and iron deficiency have indeed been reported to be extremely common. Anemia and iron deficiency, were found in 34.5% and 43.4% of the school children, correspondingly, according to research by Khatiwada *et al.*⁽¹⁶⁾. In the study by Baral *et al.*, Khatiwada *et al.* and Khatiwada *et al.*, the anemia incidence was 48% (among those aged 6-59 months), 65.6% (among those aged 10–19 years), and 37.9% (among those aged 4–13 years), correspondingly⁽¹⁷⁾. Anemia is thought to be most frequently brought on by iron deficiency in underdeveloped nations⁽¹⁸⁾. The current results provide more evidence that iron deficiency is the most prevalent origin of anemia in children, as seen by the anemic children's low iron state indicators. Anemia is very common in underdeveloped nations due to a lack of appropriate iron in the diet as well as other chronic illnesses such hookworms' infestations, malaria, and hereditary factors⁽¹⁸⁾.

The most prevalent thyroid dysfunction among children, according to the current study is euthyroidism (78.3%), which is trailed by subclinical hypothyroidism (17.7%), then subclinical hyperthyroidism (2.3%), and finally overt hypothyroidism (1.7%). 13.6% of people in a facility in Eastern Nepal experienced hyperthyroidism, and 17.1% experienced hypothyroidism, according to the research carried out by Baral *et al.*⁽¹⁹⁾. Thyroid dysfunction, especially subclinical hypothyroidism, was described in previous investigations among eastern Nepali individuals with chronic conditions such diabetes mellitus and chronic renal disorders. The increasing percentage of thyroid autoimmune diseases and the lack of micronutrients like iron in the research participants could be the cause of their high risk of hypothyroidism^(20, 21).

In the current research, hypothyroidism (both overt and subclinical) was found to be considerably fewer Hb levels and indicators of iron status than euthyroid, and that a higher percentage of hypothyroidism (both overt and subclinical) participants had iron deficiency and anemia. These findings are in line with those of earlier research by Bremner *et al.* and Banday *et al.*^(22, 23). Bremner *et al.* discovered that individuals with subclinical hypothyroidism had significantly reduced serum iron levels than euthyroid people ($p=0.001$), while Banday *et al.* noted that many individuals with primary hypothyroidism had iron insufficiency^(22, 23).

The mechanism of hematopoiesis is thought to be impacted by thyroid disorders, and thyroid hormonal insufficiency can result in bones marrow suppression and/or a reduction in erythropoietin synthesis because of a decreased need for oxygen. Additionally, thyroid hormones have been discovered to control transferrin gene expression⁽²⁴⁾.

The current results indicate that anemic individuals typically have greater TSH levels than non-anemic individuals; nevertheless, fT3 and fT4 do not appear to be different. Likewise, children with iron deficiency were found to have considerably lower fT3 levels than children with adequate levels of iron. In research by Metwalley *et al.*, iron-deficient children with hemoglobin status between 10.9 and 7 gm/dl had considerably greater

serum fT3 and fT4 concentrations than those with Hb values below 7 gm/dl ($p < 0.01$ for both), and markedly decreased serum TSH concentrations ($p < 0.05$)⁽¹⁰⁾. In a separate survey performed in Bangladesh amongst the general public, serum TSH scores were markedly increased ($p < 0.05$) and serum fT4 levels were significantly lower ($p < 0.05$) in subjects with iron deficiency than in control subjects, but serum fT3 levels were almost identical between the two groups⁽²⁵⁾. The current research shows that hypothyroidism is linked to anemic and iron-deficient children, and that hypothyroidism is at heightened hazard in children who are anemic and iron-deficient. Our results support the notion that thyroid metabolism may be impaired by iron shortage, as documented in other investigations. Thyroid peroxidase, an enzymatic that contains heme, catalyzes the first two phases in the creation of thyroid hormones. Severely iron shortage can interfere with the synthesis of thyroid hormones, reduce thyroid peroxidases activity, and cause hypothyroidisms⁽²⁶⁾. According to investigations, iron deficiency anemia (IDA) affects thyroid metabolism, decreases plasma total T4 and T3 levels, and slows periphery T4 to T3 conversions⁽²⁷⁾.

We found a negative correlation between transferrin saturation and Hb with TSH in the current investigation. Bremner *et al.* earlier investigation found substantial correlations between free T3 and hemoglobin, as well as an inverse association among TSH and serum iron and transferrin saturate⁽²²⁾. The concentrations of free T4 and Hb also showed a weakly positively statistically significant correlation ($r = 0.217$, $p = 0.033$), according to Bivolarska *et al.*⁽²⁸⁾. Although numerous researches have shown the interdependence of thyroid and iron metabolism, as well as the potential for each of them to play a regulatory role, others have shown no connection between thyroid hormones and anemia or iron shortage^(24-26, 29). Akhter *et al.* found that neither the iron-deficient nor the normal control group's serum TSH, fT3, or fT4 levels significantly correlated with Hb concentrations⁽²⁵⁾.

Limitations:

The article's cross-sectional design makes it unattainable to draw a reliable conclusion on the relationship of cause and effect between thyroid dysfunctions and iron insufficiency. Though anti-thyroid peroxidase antibodies (anti-TPO) had not been measured in the community, thyroid autoimmunity's high incidence could also be a factor in the research population's highly risk of thyroid dysfunctions.

Conclusion:

The study confirms a substantial relationship between iron state and thyroid functions as well as a higher incidence of thyroid dysfunctions, anemia, and iron shortage among the children under the study. Thus, it appears that thyroid malfunction, especially hypothyroidism, is linked to anemia and iron shortage. Future research should focus on determining the causes of lower thyroid hormones in anemic and iron-deficient youngsters and larger sample sizes.

Conflict of interest disclosure: None to disclosed.

Financial disclosure: None.

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