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The Serological Basis of the Correlation between Iron Deficiency Anemia and Thyroid Disorders in Women: A Community Based Study

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Authors' contributions

This work was carried out in equal collaboration among all the authors specially where author RI and SAA prepared the research methodology and experimental design. Author RI conducted the lab work following the instructions of author SAA. The initial result sheet was prepared by authors SAA and KMA. The data were curated and formatted for further statistical analysis by author AR. The comprehensive and complicated data were statistically analyzed by authors AR, NNK and SAA. Besides, author MRI prepared all necessary literatures for writing the Introduction and Discussion section with the assistance of authors KMA, AR, NNK, MF, MHR, MNUB, SA and AZ. All authors read and approved the final manuscript.

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ABSTRACT

Objectives: Iron Deficiency Anemia (IDA), a global public health problem may have an inimical effect on thyroid function, especially in women and children. This study was conducted to inspect the correlation between IDA and thyroid disorders in women of Bangladesh.

Methods: A cross-sectional study was conducted among 452 women of different age groups in particular regions of Bangladesh presenting anemic symptoms and were confirmed anemic after testing of serum hemoglobin levels less than 12 g/dL. To identify the correlation between iron deficiency anemia and thyroid disorders; serum samples were tested quantitatively through standardized methods considering serum iron, total iron-binding capacity (TIBC), ferritin, thyroid-stimulating hormone (TSH), free thyroxin (FT4), and vitamin D levels as parameters. Post clinical diagnosis statistical analysis, graphical presentations of the complex clinical data was generated using advanced computer programming language and bio-analytical tools.

Results: A positive correlation between hypothyroidism and IDA in women was discovered in this study as 24.69% of patients with IDA from 0-60 years were found suffering from hypothyroidism simultaneously; with the highest percentage (38.46%) amongst the 31-40 years of age and 26% of iron-deficient females of reproductive age (15-49 years) were suffering from hypothyroidism. Moreover, the association between congenital hypothyroidism and IDA was noticed in 50% of cases above all.

Conclusion: Hypothyroidism was found quite common among the women of different age groups who were previously reported with acute to chronic anemia symptoms due to iron deficiency.

Keywords: Iron Deficiency Anemia (IDA); hypothyroidism; Thyroid-Stimulating Hormone (TSH); Total Iron-Binding Capacity (TIBC); ferritin; Free Thyroxin (FT4); reproductive age; and congenital hypothyroidism.

1. INTRODUCTION

Anemia is one of the world's leading causes of health issues associated with a decline in the total amount of hemoglobin (Hb) than its normal range. Hemoglobin carries oxygen to the body tissues to meet physiological needs [1]. According to the World Health Organization (WHO), Hb concentration below 13.0 g/dL in men and 12.0 g/dL in women are considered abnormal [2]. It is more prevalent in women than men, among children than adults, and in the poor than the well to do [3]. Its predominance is significantly higher among individuals living in the agricultural nations (89%) due to having low financial status and lack of medical care [4]. It has recently reported that, 1.62 billion (24.8%) of the world's population are affected by anemia globally, where 40% pregnant women and 42% children aged below 5 years old are more vulnerable than any other cohort [5]. Numerous factors influencing anemia include deficiencies of hematopoietic materials (ex. iron, vitamin A, folate, zinc, and vitamin B12), parasitic infestations (ex. Malaria, Toxoplasmosis, etc.), inherited hemoglobin diseases (ex. Thalassemia, Sickle Cell Anemia, etc.), and several inflammatory disorders [6]. Among these factors, iron deficiency (ID) has been reported in nearly 50% of all anemia reported worldwide [7]. Tough iron is available in nature, ID is the most common micronutrient deficiency and the leading cause of anemia [8]. Anemia due to ID presents with many signs and symptoms including unusual fatigue, impaired immune function, headaches, dyspnea, pale conjunctiva, restless legs, pica, and so on [9,10]. It happens at all phases of the existent cycle of life, though is more predominant in pregnant ladies, children, and teenagers [11]. Overall, women of reproductive age (15 to 49 years) are found more prone to iron deficiency anemia because iron is lost as a result of bleeding during menstruation and childbirth. Besides, the cause of IDA includes a low dietary iron intake or absorption, an extensive iron-restricted dietary habit, elevated iron requirement during adolescence and pregnancy, chronic gastrointestinal (GI) blood loss, polyps or carcinoma and so on [12]. The daily dietary iron intake is recommended as 18 mg for women of reproductive age instead of 27 mg during pregnancy and 8 mg for men [13].

Iron is a basic component of numerous key cellular life cycles; however, the abundance of iron is toxic to cell [14], as it promotes the

'Fenton reaction' which impairs macromolecules via excess free radicals [15,16]. Thus, screening and definitive diagnosis of IDA in women depends upon the testing for hemoglobin, total iron-binding capacity (TIBC), ferritin, and occasionally an inflammatory biomarker (Hepcidin) [17]. On the other hand, thyroid abnormality is one of the most widely documented endocrine issues in clinical practice; and its prevalence depends on age, sex, race, geology and dietary iodine consumption [18]. Ethnicity, sexual orientation, and age regulate thyroid concentrations in the body, but surprisingly, thyroid anomalies are very common to the female than the male of any ages [19,20]. Thyroid diseases can be classified in several ways based on the etiology, function, pathology and clinical evolution [21]. The major disorders of the thyroid gland are hyperthyroidism and hypothyroidism. Primary hypothyroidism usually results from under secretion of thyroid hormone and secondary hypothyroidism is caused by the lack of TSH production from the pituitary gland [22]. About 5% of the world population is suffering from primary hypothyroidism which is diagnosed biochemically when TSH (thyrotrophin) level is more than the normal reference range 0.4–4.0 mIU/L [23], as well as serum FT4 (free thyroxin) and FT3 (free tri-iodothyronine) are either normal or decreased in case of subclinical or overt/ symptomatic hypothyroidism respectively [24]. On the other hand, Hyperthyroidism is a condition when synthesis, as well as secretion of thyroid hormone, is increased from the thyroid gland. Moreover, it is defined as thyrotoxicosis if clinical signs and symptoms are noticed due to the presence of excessive thyroid hormones in the circulation, produced from the thyroid gland and/or the extra-thyroid sources [25]. Though disorders of the thyroid are diagnosed generally as isolated conditions, they can be forerunner or sign of a future Polyglandular Autoimmune Syndromes (PAS) [26]. Patients with IDA can suffer from secondary and subclinical hypothyroidism and treatment with iron can be curative [27]. On the contrary, another study on children found that the level of thyroid hormones didn't change before and after the correction of anemia due to iron deficiency [28]. The coexistence of anemia and thyroid abnormalities is often found, although the mechanism is still uncertain. IDA decreases plasma total thyroxin (T4) and tri-iodothyronine (T3) fixations, lessens fringe transformation of T4 to T3 and may cause an increment of circulating thyrotropin (TSH). IDA reduces thyroid hormones which are responsible for the erythrocyte precursor cells' proliferation, thus forming a vicious circle. Hyperthyroidism also causes anemia due to the derangement of iron metabolism and oxidative stress [29]. Furthermore, iron deficiency in early pregnancy can lead to hypothyroidism due to autoimmunity as explained by increased antibodies against thyroid peroxidase enzymes (TPOAb) [30].

This study was attempted to discover the relation between IDA and thyroid disorders in women of selective locations of Bangladesh considering different serological profiling through comprehensive serological study.

2. MATERIALS AND METHODS

2.1 Clinical Diagnosis

The cross-sectional research work was conducted based on Jashore and Khulna Community in Bangladesh, from July to October 2020, among 452 women of different age groups (0 to 81+ years) who had anemic symptoms and were confirmed anemia after testing of serum hemoglobin levels (<12 g/dL). To identify the correlation between iron deficiency anemia and thyroid disorders few selective tests were conducted such as- serum iron, TIBC, ferritin, TSH, FT4 and vitamin D. The levels of iron (µg/dl) and total iron-binding capacity (TIBC, µg/dl) were quantitatively analyzed to figure out their relativity to anemia development along with their ferritin levels (ng/dl). In addition to that, serum thyroid-stimulating hormone (TSH, µIU/ml) and free thyroxin (FT4, ng/dl) levels of these patients were assayed to study the status of their thyroid malfunction depending on age groups alike anemia detection. Few healthy women were tested for the same serological profiling for using as standard in this study to compare with the anemic-thyroid disorder patients. Finally, the data were analyzed to evaluate whether or not there is any correlation between IDA and thyroid disorders in women.

In this research, to identify the anemic women, the iron (µg/dl) and TIBC (µg/dl) level of the patients' serum were tested quantitatively through the procedure of the Dimension® clinical chemistry system using 'Dimension®IRON Flex® reagent cartridge (DF85)' and 'Dimension®Flex® Reagent IBCT', Siemens Healthcare Diagnostics Inc., USA, respectively following their established methodology [31]. The ferritin level (ng/dl) was tested quantitatively with 'Beckman Coulter Access Ferritin Calibrators (S0-S5)' following [32].

Thyroid disordered patients were diagnosed using 'ADVIA®Centaur™ TSH-3 Kit, Siemens, USA, for assaying TSH level (μIU/ml) [33] and 'ADVIA®Centaur™ FT4 Kit, Siemens, USA, for FT4 level (ng/dl) detection [34]. Vitamin D level (ng/ml) was measured from the anemic-thyroid disordered women of all age groups following Beckman Coulter 25(OH) Vitamin D assay [35].

2.2 Statistical Tools

The statistical analysis and graphical presentation of the complex clinical data were generated using 'R programming' (version R-4.0.2, for Linux) and 'GraphPad Prism' (version 8.2, for Mac OS) [36,37]. The one-way ANOVA test, Brown-Forsythe test, Bartlett's test, and Tukey's multiple comparisons test 'p values' were conducted using GraphPad Prism 8.2 [38], while mean with standard deviation (SD) was calculated using R programming 4.0.2 [39].

3. RESULTS

The correlation of iron (μg/dl), TIBC (μg/dl), ferritin (ng/dl), TSH (μIU/ml), FT4 (ng/dl), and vitamin D (ng/ml) level in the serum are highly correlated with the thyroid dysfunctions of the anemic patients of all age groups analyzed in the research especially from the age 0 to 60 years women (Fig. 1).

3.1 Correlation Depending on the Iron Concentration in the Serum (μg/dl) (*)

Iron was found interlinked with thyroid dysfunctions among the anemic women tested in this study. The overall One-way ANOVA test among the female patients ranged 0 to 60 years of age (P value was 0.0001) and slightly deflecting from the 61 to 70 years age group (P<0.0024), and are all significant in the scale of P<0.05 (Fig. 1*). 'Tukey's multiple comparison test' reveals that TIBC and iron are highly correlated with each other among the patients of all the age groups (P<0.0001), while P<0.0024 between 61-70 years. TSH is correlated with the fluctuations of iron level as P<0.0001 and P<0.0297 from 0-50 years with P<0.0001 and P<0.0297, respectively (Fig.1*).

3.2 Correlation Depending on the TIBC Concentration in the Serum (μg/dl) (**)

In this study, a strong relationship was found between iron and TSH in the patients of 0-40 years but was not consistently significant over 40 years. Iron and TSH correlation values (P) were 0.0062; 0.025 and 0.0001 for 0-10 years, 11-20 years and 21-30 years, respectively. TIBC is highly significant in relation to TSH (P<0.0001), with no significance between iron and TSH for 31-40 years (Fig. 1**).

3.3 Correlation Depending on the Ferritin Concentration in the Serum (ng/dl) (***)

The overall ANOVA test P value was 0.0001 for 0-30 year's women. The values are also significant for 41-50 years and 51-60 years possessing P<0.0028 and P<0.0064, respectively (Fig. 1***). After analyzing the level of ferritin, it was found that, the P values between iron and TSH were 0.0001 and 0.0034 for 0-10 years and 21-30 years respectively. Besides, a correlation between TIBC and TSH was phenomenally significant such as 0.0008; 0.0001; 0.0122, and 0.0157 as corresponding to 11-20 years; 31-40 years; 41-50 years, and 51-60 years, respectively (Fig. 1***).

3.4 Correlation Depending on the TSH Concentration in the Serum (μIU/ml) (Ψ)

It's very notable that, P<0.0001 for the overall ANOVA analysis from 0-60 years of women (Fig. 1Ψ) and also for 61-70 years (Table 1). A strong correlation between iron deficiency (serum iron <28 μg/dl) and hypothyroidism (serum TSH >4.5 μIU/ml) was observed in this study (Fig.2ABC). The levels of serum TSH were found increased in iron-deficient patients of 0-60 years, on an average 24.69% cases and highest among the 31-40 years of age group which is 38.46% (n=5/17=29.41% in 0-10 years of age (y), n=3/18=16.67% in 11-20 y, n=12/45=26.67% in 21-30 y, n=10/26=38.46% in 31-40 y, n=3/16=18.75% in 41-50 y, n=2/11=18.18% in 51-60y). For the rest of the age groups, P was 0.0001 between TIBC and TSH level (Fig. 1Ψ).

3.5 Correlation Depending on the FT4 Concentration in the Serum (ng/dl) (Ψ*)

ANOVA revealed the overall value of P was 0.0001 for the women of all the groups except 11-20 years where P<0.0043 (Fig. 1Ψ*) and (Table 1). The correlation between TIBC and TSH was found highly significant 0.0001 for all

except 21-30 years because of having P<0.0001 between iron and TSH.

3.6 Correlation Depending on the Vitamin D Concentration in the Serum (ng/ml) (α)

Overall ANOVA test P was found 0.0001 for each of the age groups except the 21-30 years where P was <0.0004 and non-significant among 0-10 years (Fig. 1α). In that case, iron was found in significant correlation to the TSH referring P values as 0.0008; 0.0032; 0.0086 and 0.0001 for patients aged 21-30 years, 31-40 years, 41-50 years and 51-60 years, respectively. Over 60 years of age, the correlation was non-significant (Table 1).

3.7 Iron and TSH Profiling from the Reproductive-aged Patients

Overall Two-way ANOVA test P<0.0001 in Fig. 2A demonstrated a significant correlation between serum iron and TSH. In the reproductive age group of females (15-49 years), decreased iron levels (<28 µg/dl) were found associated with increased TSH levels. Considering serum TSH more than 2.5, 4 and 4.5 µIU/ml; 45%, 28% and 26% (n= 45/100, 28/100 and 26/100) iron-deficient females were found hypothyroid. For both cases of Iron vs. TSH $\geq$ 2.5 and Iron vs. TSH $\geq$ 4.5; P values were found <0.0001 in both the test types such as the overall two-way ANOVA test and Multiple comparison test/Tukey's t-tests (Fig. 2B).

3.8 Iron and TSH Profiling from Congenital Hypothyroid Patients

Data analysis of the diversified and fluctuating profile of iron and TSH in case of female patients aged 0 to 14 years revealed a highly significant result. The overall two-way ANOVA test result shows P<0.0001 in the scale of significance P<0.05. Among the female patients of the mentioned age range, 10.71% (n=6/56) were diagnosed or suspected as hypothyroid congenitally as increased levels of serum TSH (>6 µIU/ml) were observed. Congenital hypothyroidism was found associated with iron deficiency (<28 µg/dl) in 50% of female patients of this age group (Fig. 2C).

4. DISCUSSION

This study was conducted to find out the relationship among the iron, TIBC, ferritin, FT4, TSH, and Vitamin D levels in anemic women. The remarkable fluctuation of these parameter levels among different age groups of patients was noticed (Fig. 1). In different age groups, the iron levels were remarkably lower than the normal people (Fig. 1A). This is because in anemic patients due to iron deficiency, the iron level is significantly lower than the normal [40]. One-way ANOVA test, Brown-Forsythe test, and Bartlett's test P values also statistically demonstrated that iron levels were significantly lower in anemic patients evaluated. The statistical analysis reveals that, the lower iron level is highly significant among all the age groups except 70 years or more. Because the iron deficiency is more prevalent among the elderly population due to their inability to absorb adequate iron [41], chronic inflammation, elevated levels of circulating 'Hepcidin', poor diet, and some medications (e.g. aspirin), etc. these factors are responsible for systematic iron depletion [42,43].

In the United States, the risk of unexpected anemia was frequently found by clinicians in persons 65 or more years older [44]. In addition, depending on the iron concentration (iron <20 µg/dl) (*), overall statistical analysis cast a highly significant result among different parameters such as Iron vs. TIBC, Iron vs. TSH of different age groups of patients (Fig. 2*). Iron vs. TIBC and Iron vs. TSH statistical analysis relying on this iron profile depicted that both TIBC and TSH are highly correlated with iron deficiency. However, as the iron level remains statistically highly significant, the TIBC level has to be non-significant because depleted iron level increases the transferrin protein capacity to carry iron more firmly. When the iron level is depleted in the body, the ferritin level is also depleted as it is the main blood protein that contains iron and the primary form of stored iron of cells. It reflects the total amount of iron stored in the body as well as the amount that circulates throughout the blood [45]. In this research, we also observed that the ferritin level is lower among different age groups of patients as it is in the normal pre-menopausal and post-menopausal women (Fig. 2C). Ferritin is lower in pre-menopausal women than the post-menopausal women as iron is lost through menstrual blood which is one of the means of iron loss in women. That's why there is a slight increase in ferritin levels among the 61-70 and 71-80 years old women; alternatively among the other age group of women it is lower and closes to the normal premenopausal women. Similarly, depending on the ferritin concentration (ferritin

<15 ng/ml) (***), the overall statistical analysis reported a significant correlation between TIBC and TSH among the different age groups of patients (Fig. 1***).

On the other hand, the fluctuations of TIBC level are increased among the different age group of patients than the normal (Fig. 2B). TIBC is a distinctive ~ 80 kDa bilobal glycoprotein that quantifies the blood's efficiency to bind iron with transferrin [46]. Transferrin is synthesized in and secreted by the liver. When iron deficiency occurs, the aggregation of serum transferrin level is escalated, presumably attempting to augment the use of little iron that is available [47]. Statistical analysis depending on TIBC concentration (TIBC >450 µg/dl) (Fig. 1**), reported a significant P-value between iron and TSH of patients from (0-40) years of age (Fig. 01**). However, TIBC is highly significant concerning TSH with a P-value of less than 0.0001, whereas between iron and TSH for (31-40) years no significance was found (Fig. 1**). To sum up, in this investigation we noticed that iron level and ferritin level is decreased among the different age groups of 452 anemic women patients and the TIBC level is increased. It is reported that among women of reproductive ages (15 to 49 years old) in Ethiopia iron deficiency anemia is not a rare problem [48]. They systematically analyzed 970 subjects in which the overall prevalence rate of iron deficiency anemia was 18.0% and the prevalence was highest among 31-49 years old. A similar result was also retrieved from pregnant women in Southern Ethiopia where the prevalence of anemia was 23.2% [49]. Besides, other studies conducted in different parts of Ethiopia demonstrate greater prevalence than this for example 32.8%, 36.6%, and 39.9% [50-52]. The secret behind the varied prevalence might be due to the different socio-economic conditions, dietary patterns, etc. across the different parts of the same country. However, the concordance of relevance is not only related to iron deficiency, several other factors such as low hemoglobin due to inherited disorders, deficiencies of folic acid and Vitamin-B12, parasitic infestations are also considered for having anemia [53].

In this experiment, iron deficiency (serum iron <28 µg/dl) and hypothyroidism (serum TSH >4.5 µIU/ml) were found strongly inter-related (Fig.1 and Fig. 2); though [54] also showed an association between hyperthyroidism and IDA. Serum TSH levels were found increased in iron-deficient patients of 0-60 years, on an average of 24.69% cases and the highest 38.46% in the 31-40 years of age group. It requires a prospective and randomized controlled study to make this inference directly.

No specific change of serum FT4 was observed in the anemic patients of this study population (Fig. 1), though the association of ID with low serum FT4 and FT3 level was detected in a study on the adult population of Spain without having any change in TSH level [55]. It has also noticed that females suffer from diseases of thyroid more than male and mainly at their forties; these dysfunctions affect all the parameters of blood without platelets [56]. Therefore, it should be the standardized practice of investigating thyroid diseases before commencing iron therapy as well as cases of refractory anemia should also be checked for the possible presence of thyroid disorders. Moreover, a significant correlation between serum iron and TSH was noted in women of reproductive age group (15-49 years) and P-value was calculated <0.0001 in the overall two-way ANOVA test (Fig. 2A). Among the iron-deficient women of 15-49 years, 26% suffered from hypothyroidism. Both the overall Two-way ANOVA test and Multiple comparison test/Tukey's t-test show P<0.0001 for both the Iron vs. TSH > 2.5 and Iron vs. TSH > 4.5 (Fig. 2B).

The association between iron deficiency and thyroid autoantibody production especially in childbearing or reproductive age groups of women is also noticed in another study [57]. To be more specific, Thyroid peroxidase antibodies (TPOAbs) but not thyroglobulin antibodies (TgAbs) are markedly raised in iron-deficient both pregnant (in the first trimester) and non-pregnant women of childbearing age [22]. Furthermore, among the female patients of 0-14 years in this study, 10.71% were hypothyroid congenitally and 50% of them had concurrent iron deficiency (Fig. 2C). In contrast, men and women of pre and post-menopausal period don't have any notable heterogeneity between their serum levels of thyroid hormones and iron; which is also similar to these research findings [55].

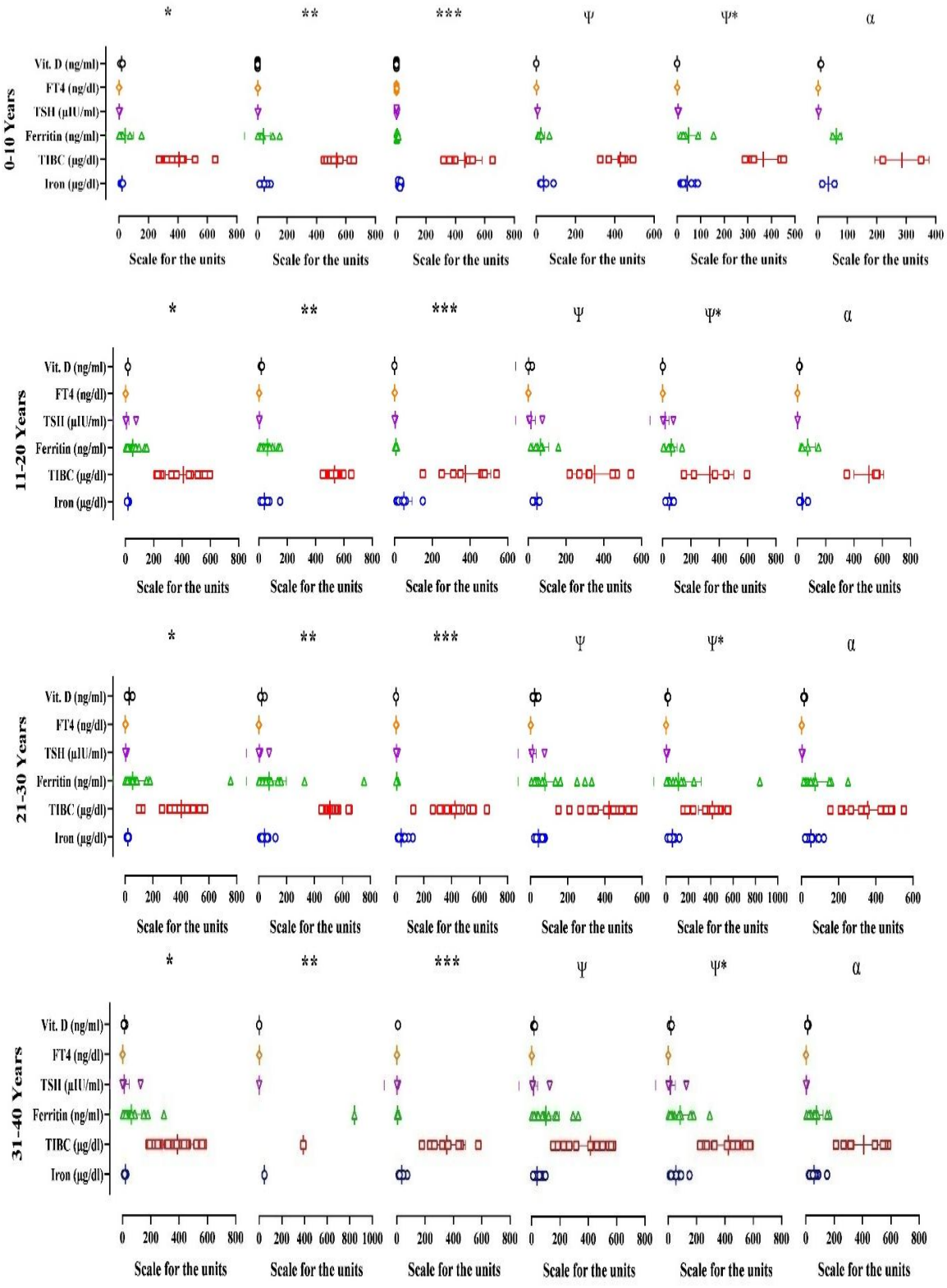
In this study, fluctuations of the serum TSH (µIU/ml), Iron (µg/dl), and vitamin D (ng/ml) (α) levels of the different age groups of patients were analyzed (Fig. 3). Vitamin D levels in anemic and hypothyroid patients were checked and statistical analysis revealed a significant association between vitamin D levels and iron as well as

Table 1. Tabular representation of different fluctuating levels of iron (µg/dl) (*), TIBC (µg/dl) (**), ferritin (ng/dl) (***), TSH (µIU/ml) (Ψ), FT4 (ng/dl) (Ψ*), and Vitamin D (ng/ml) (α) among 61 to 70 years old women patients

	Iron (µg/dl, ≤20)						TIBC (µg/dl, ≥450)						Ferritin (ng/ml, ≤15)						TSH (µIU/ml, ≥5)						FT4 (ng/dl, ≤0.7)						Vit. D (ng/ml, ≤20)					
	*	**	***	Ψ	Ψ*	α	*	**	***	Ψ	Ψ*	α	*	**	***	Ψ	Ψ*	α	*	**	***	Ψ	Ψ*	α	*	**	***	Ψ	Ψ*	α	*	**	***	Ψ	Ψ*	α
20	458	23	1.2	0.66		43	171	525	1.69	0.66		80	256	14.8	6.54	0.55	19.94	73	203	55	74	0.24	16.3	73	206	55	74	0.24		50	462	16	0.89	0.74	14.3
18	427	4	1.1	1.09	P_0						P_0		18	427	4	1.1	1.09		87	334	38	7.1	0.84	19.94	78	219	35	1.52	0.37		29	365	63	6.5	1.21	16.3
14	512	26	0.39	2.15															29	365	63	6.5	1.21		20	458	23	1.2	0.66		80	256	14.8	6.54	0.55	19.94
																			50	350	250	75	0.77		80	256	14.8	6.54	0.55	19.94	43	171	525	1.69	0.66	12.4
																			75	488	21	5.2	0.96		43	171	525	1.69	0.66	12.4						
																			31	315	80	6.52	1.1		165	329	20	0.21	0.55							
																			51	316	90	6.3	1.25		120	185	88	3.69	0.56							
																			80	256	14.8	6.54	0.55													
																			60	375	137	5.2	0.96													

thyroid hormone levels (Fig. 1) except among 0-10 years (Fig.1α) and more than 60 years age groups (Table 1). For instance, the evidence of a significant correlation between hypothyroidism and hypovitaminosis D with hypocalcemia that varies with the severity and degree of hypothyroidism has been found in a research of Saudi Arabia [58]. Similarly, vitamin D concentration may be slightly lower than average in hypothyroid patients as shown in another experiment [59]. The deficiency of vitamin D is more prevalent among elderly women due to their insufficient intake of vitamin D [60] and this picture is also very obvious in this research. Besides, low vitamin D levels are found to cause ID and increase the risk of IDA. Another study revealed that vitamin D supplementation can cause an improvement of the condition of the patients who are being treated with levothyroxine due to Hashimoto's thyroiditis but with normal vitamin D status by reducing thyroid autoantibodies [61]. In contrast, few researchers found no significant association between iron-deficient patients and subnormal vitamin D patients [62, 63].

Molecular analysis of selective genes using RT-PCR technology [64] along with gel electrophoresis and gene sequencing can ensure the very profiling of the patients responsible genes for interconnecting IDA with TSH abnormalities. How the supplementary drugs act on the reshuffling of the IDA and TSH anomalies should be analyzed screening the opsonization process, which runs through secondary immune response inside the patients' circulatory system [65] as part of next-generation disorder mechanism study.


0-10 Years
11-20 Years
21-30 Years
31-40 Years
Vit. D (ng/ml)
FT4 (ng/dl)
TSH (µIU/ml)
Ferritin (ng/ml)
TIBC (µg/dl)
Iron (µg/dl)
Scale for the units

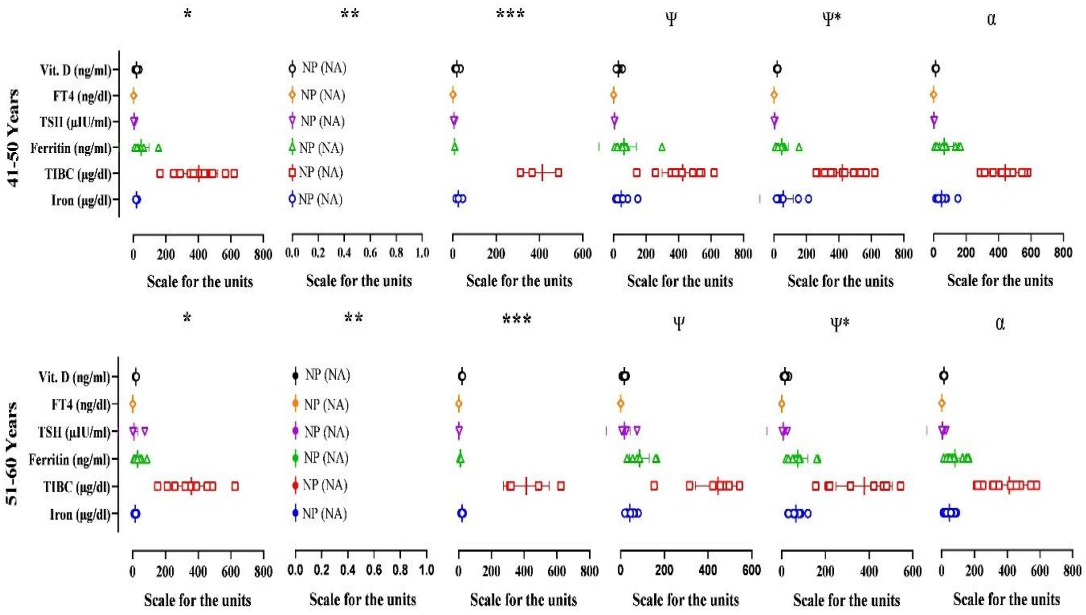


Fig. 1. Illustration of the diversified fluctuations of the iron and TIBC level depending on the age groups and taking serological standards like concentration of serum iron (≤20µg/dl) (*), TIBC (≥450µg/dl) (**), ferritin (≤15ng/dl) (***), TSH (≥5µIU/ml) (Ψ), FT4 (≤0.7ng/dl) (Ψ*), and Vitamin D (≤20ng/ml) (α) among different age groups (0-60 years) of women patients. Surprisingly, no patients out of 452 women were tested aged 41-60 depending on the standard level of TIBC (≥450µg/dl) (**). The scale of significance of the statistical significance were considered in scale of significance P<0.05

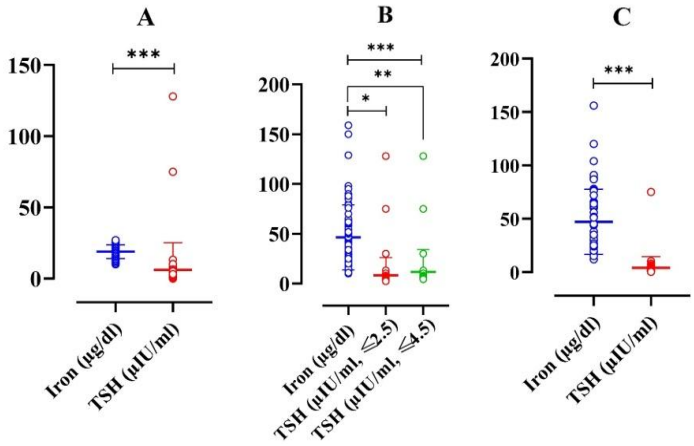


Fig. 02. Demonstration of the correlative Iron and TSH profiling of the female patients, where decreased iron level (<28 µg/dl) were associated with increased TSH level among reproductive age groups of females (15-49 years), where overall two-way ANOVA test P value was <0.0001 (***) (A). Considering serum TSH {Iron vs. TSH (≤2.5) vs. TSH (≤4.5)} iron-deficient females were found hypothyroid in reproductive age groups of females, where the two-way ANOVA test P values were <0.0001 for both the correlations between iron (<28 µg/dl)-TIBC (≤2.5) and overall multiple comparison among the three groups (***) (B). Females with congenital hypothyroidism (aged between 0 to 14 years) was found associated with iron deficiency (<28 µg/dl), resulted with overall two way ANOVA test as P<0.0001 (in value of significance P<0.05) as correlated with their corresponding TSH level (µIU/ml)

5. CONCLUSION

In this serological study, a significant correlation between IDA and hypothyroidism among different age group of women were found. As the reasons behind these are still ambiguous, further studies should be done with the larger number of samples. Integration of molecular analysis of the patients will help us to understand the genetic basis of the IDA hypothyroidism co-existence among the female iron deficient anemia patients of both the acute and chronic stages, more precisely and comprehensively.

CONSENT AND ETHICAL APPROVAL

The study protocol was approved by the Committee of Ethical Issues in Clinical Research of JMC, Bangladesh Medical & Dental Council (BMDC) with the collaboration of Dr. Sharmin Ahmed (Lecturer, Dept. of Pharmacology, JMC). All necessary forms were signed by each of the patients who participated in the study cordially, as dated on July 24, 2020. The endorsement of the patients and Ethical Committee criteria directly follows the Declaration of Helsinki and the Health Ministry of Bangladesh. All necessary documents have been conserved by the corresponding author, which will be shared upon conditional requests.

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COMPETING INTERESTS

Authors have declared that no competing interest exists.

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