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Original Article

Thyroid Disease and Anaemia Among Early Pregnant Iraqi Women

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ABSTRACT

***Aims**: Iron deficiency anaemia and thyroid disease are common obstetrical problems. Both cause a wide range of complication, empathizing feto-maternal wellbeing. We verify iron deficiency anaemia effect on thyroid hormones during the first trimester. **Methods**: A cross-sectional study at Al-Yarmouk Teaching Hospital enrolled 100 primigravidae in their first trimester of a singleton pregnancy. Participants were subdivided into anaemic cases (50/100) and healthy controls (50/100) based on serum haemoglobin. We evaluated serum haemoglobin, ferritin, iron, Total Iron-Binding Capacity (TIBC)and T3, FT4, and TSH for all. **Results**: Both groups were comparable in age, body mass index, and gestational age. Higher serum levels of haemoglobin, ferritin, iron TSH, T3 were seen in the healthy controls versus anaemic cases; all differences were meaningful. Only TIBC and serum FT4 was significantly higher in anaemic cases. The ROC curve highlighted the validity of study markers in diagnosing anaemia. Serum iron was the most sensitive blood indices associated with anaemia, followed by ferritin, with a sensitivity of 94%, 84%, respectively. **Conclusion**: Thyroid disorders were very common in anaemic patients. As a result, women's iron levels must be enhanced, and thyroid disease screening can begin early in pregnancy. Screening for both will unravel hidden differences and improve pregnancy outcome.*

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INTRODUCTION

Iron deficiency anaemia (IDA) is a common nutritional deficiency. The prevalence is 9–22% among menstruating women[1]. IDA is defined as reducing the blood haemoglobin levels to less than 12 mg/dL for females and less than 11 mg/dL for pregnant women. The first stage of IDA involves the depletion of tissue iron stores. Serum ferritin, an iron storage protein, is a sensitive and reliable biomarker of body iron storage [2].

Serum Hemoglobin levels and a peripheral blood smear is a good starting point to diagnose anaemia. Other aiding tests: total iron-binding capacity (TIBC), serum ferritin (SF) [3]. The etiological causes of anaemia must be determined before appropriate treatment starts. Hemodilution is the primary cause of a decreased haemoglobin level. Iron deficiency anaemia can be affected by a negative iron balance caused by elevated iron demand and unequal iron flow to the fetus [4].

Anaemia may occur as a result of hypothyroidism's negative impact on the hematologic system. Pregnancy changes affect the endocrine system. TSH levels decrease in the first trimester of a healthy pregnancy as a hormonal adaptation to hCG's stimulating effect on the TSH receptors, with peak hCG values between 7 and 11

weeks of pregnancy. Other considerations, such as iodine consumption, gender, gestational age, and laboratory assay procedures, may influence the reference ranges of thyroid function tests (TFTs) and contribute to conflicting results. [5,6].

According to Yu B et al. [7], the use of non-pregnant normal population comparison values as a basis for diagnosis causes 5.7-18.4 % of misdiagnoses in clinical practice. The American Thyroid Association (ATA) proposed using a gestational age and area-specific reference point for TSH because the risk of misclassification was as high as 10.5% in the first trimester. [8]. Thyroid dysfunction associating anaemia is a common yet underappreciated clinical disorder. Different types of anaemias may develop as a result of thyroid dysfunction, most frequently is IDA. Minerals needed for a normal functioning thyroid gland is Iodine and Iron [9]. The latter is crucial for thyroid peroxidase function (hem-dependent enzyme) needed for incorporation of iodine to form thyroid hormones.

Should IDA develops and iron level decreases, low FT4 production and high serum TSH levels will result [10]. Interestingly, Thyroid hormones play has a direct stimulating effect on the proliferation of erythrocyte precursors, in addition to the effects exerted on the kidneys as it enhances erythropoiesis by up-regulation of erythropoietin gene expression and increased production of erythropoietin [11,12]. Though earlier literature discussed the association of thyroid hormones and anaemia, still their results were conflicting. We aimed to verify the role of thyroid hormones in the anaemic Iraqi population during the first trimester of pregnancy.

METHODS

Study design and setting

A cross-sectional case-control study was conducted from May2018-till June 2019 in the outpatient department of obstetrics and gynaecology department in AL-Yarmouk Hospital, a tertiary centre hospital that receives thousands of cases every month. Approved by Institute Ethical Committees. all the procedures were explained to the participants, and written informed consent was obtained.

Data collection procedure

Study participants were attendee for routine obstetrical evaluation. They were primigravidae aged 18-35years in the first trimester of singleton pregnancy and should not initiate any vitamin preparation. Pregnancy dating was confirmed by the history of a regular cycle or an early dating ultrasound. With a detailed medical, gynaecological, and obstetrical history, we excluded cases with: diabetes, hypertension, whether chronic or gestational, a previous history of renal disease, blood dyscrasia alcohol consumption, evidence of mal-absorption, smokers were excluded.

One hundred participants fulfil inclusion criteria. They were subdivided into two groups based on their serum haemoglobin levels; Hb <11 mg/dL is anaemia cases(N=50/100); otherwise, they were healthy controls(N=50/100). Both groups were age and body mass matched. We evaluated serum haemoglobin, ferritin, iron, Total Iron-Binding Capacity (TIBC) and Thyroid Function Test for every participant.

After one night fast, five ccs of blood were aspirated in EDTA vials to calculate haemoglobin with an automated haematology analyzer DxH520 (Beckman Coulter Sn BC010420. Germany). Iron deficiency anaemia was defined as a haemoglobin level less than 11 mg/dL in pregnant women. According to World Health Organization (WHO) criteria, serum iron level less than 65µg/dl and ferritin less than 30ng/ml. Normal range of TIBC (274-400) µg/dL. Serum ferritin, iron, and TIBC were assessed using Chemistry Analyzer AU480 (Beckman Coulter Sn2018011735, Japan). Blood samples for the calculation of the Thyroid profile were taken in separate gel vials and centrifuged at 3000 rpm for 10 min to separate serum. The thyroid function was analyzed by Immunoassay system Access 2 (Beckman colter, Inc.A99558A. Germany). The reference values for thyroid hormones followed the

recommendation of the ATA in the first trimester [8]. The TSH 0.3–4.0 µIU/mL, FT4 (0.7-1.9) ng/ml and T3(80-200) µIU/mL.

Statistical Analysis

It was performed using SPSS-21 (Statistical Packages for Social Sciences- version 21). Independent t-test and one way ANOVA were used to assess the differences between means. The Reciever operating characteristic curve (ROC curve) was used to identify the validity of markers as an indicator of anaemia. The markers were further compared based on the cutoff values, sensitivity, specificity and 95% confidence interval(95%CI). The analysis was performed using MedCalc Software. P⩽ 0.05 is considered significant

RESULTS

A comparative case-control study took place at the Al-Yermuk Hospital enrolled 100 primigravidae in their first trimester. They were subdivided into two groups based on their serum haemoglobin levels; Hb <11 mg/dL is anaemia; otherwise, they were healthy controls.

The demographic characteristics of study participants were comparable in terms of age, body mass index, and gestational age. After taking the laboratory analysis, the result was shown in table 1.Higher serum levels of haemoglobin, ferritin, iron TSH, T3 was seen in the healthy controls versus anaemic cases; all differences were statistically meaningful as P<0.05. Only TIBC and serum FT4 was significantly higher in anaemic cases. The ROC curve was constructed to highlight the validity of study markers in diagnosing anaemia; the results were summarized in Table 2, which showed the markers cutoff values, respective sensitivity, specificity, 95% Confidence interval and standard errors. The most sensitive blood indices associated with anaemia were serum iron, followed by ferritin and total iron-binding capacity (TIBC), as associated sensitivity was 94,84and 80%.

Table 1. The result of blood analysis of the two study groups presented as Means, standard deviations (SD) and respective P values.

Study variables	Mean±SD of Control N=50/100	Mean±SD of Anaemia Cases N=50/100	P-value
Hb mg/dL	14.25±0.52	8.96±0.66	<0.0001
Ferritin ng/ml	55.51±27.45	22.74±5.74	<0.0001
TIBC µg/dL	216.48±82.53	304.44±58.53	<0.0001
Iron µg/100mL	101.77±23.28	33.38±15.43	<0.0001
TSH µIU/mL	2.34±0.76	1.23±2.18	0.001
T3 µIU/mL	159.32±26.07	62.78±12.63	<0.0001
FT4 ng/ml	1.28±0.16	7.95±12.63	<0.0001

FT4: free thyroxin, T3: triiodothyronine, TIBC: Total Iron-Binding Capacity, TSH: thyroid-stimulating hormone

Table 2. Showing the sensitivity and specificity and respected cutoff value for the study parameters

Marker	Cutoff point	Sensitivity	Specificity	95% CI [b]	SE [a]
Ferritin ng/ml	≤25	84.00	85.71	0.8 to 0.94	0.04
TIBC µg/dL	>294	80.00	73.50	0.7 to 0.86	0.05
Iron µg/100mL	≤59	94.00	100.00	0.95 to 1.0	0.004
TSH µIU/mL	≤0.71	81.60	100.00	0.74 to 0.90	0.05
T3 µIU/mL	≤82	77.00	96.00	0.96 to 1.0	0.000
FT4 ng/ml	>1.63	79.00	95.00	0.96 to 1.0	0.00

FT4: free thyroxin, T3: triiodothyronine, TIBC: total iron-binding capacity, TSH: thyroid-stimulating hormone, CI: confidence interval, SE: standard error of the mean.

DISCUSSION

IDA has been linked with many bad obstetrical and neonatal outcomes. The correlation of IDA and thyroid dysfunction has been a focus of interest as it forms a surrogate cause for a poor milestone in newborns and impaired cognitive outcome and intellectual performance in school-aged children [4,9]. Moreover, mild thyroid insufficiency and subclinical hypothyroidism throughout pregnancy can increase the incidence of spontaneous miscarriage, abruption placentae, preterm birth, fetal distress, and preeclampsia[13-15].

The current study showed reduced blood indices markers among the anaemic cases. The level of TSH and T3 was reduced, but FT4 and TIBC were significantly higher in anaemic cases in line with earlier studies[16-18].

The reduced activity of thyroid peroxidase (TPO), a heam dependant protein, in response to reducing serum iron is the reason for lower FT4 production and higher serum TSH levels, signifying the impact of IDA on thyroid metabolism regulation and its contribution to the endemic goitre [19].

Teng X et al. [20] explored the association of IDA with hypothyroxinemia in a cohort study recruiting 723 pregnant women. The study discussed a positive association for iron status and the serum FT4 rather during the first and second trimester rather than the third trimester. Furthermore, IDA cases showed a higher rate of clinical hypothyroidism with low serum FT4 during the second or third trimester than for healthy pregnancy. The study considered IDA as an independent indicator for hypothyroidism.

It is not unusual to know that IDA might be the haematological mask of hypothyroidism and the leading symptom to reach the diagnosis. If we face unsuccessful therapy with oral iron preparations, further investigation may underly a thyroid dysfunction [12].

Godinez et al.[21] investigated the impact of IDA and iron treatment on the thyroid functions before and after treatment. TSH levels in the IDA population were higher before therapy, while FT4 levels were lower. FT4 values improved dramatically after iron therapy. According to the authors, secondary and subclinical hypothyroidism exists in patients with IDA and is reversed upon iron supplementation.

Yang Y et al.[22] evaluated the thyroid dysfunction influence on gestational anaemia in a meta-analysis study of a Cochrane database in 2019. The analysis demonstrated a higher IDA risk among pregnant during the first trimester to the second trimester. The risk was significant for cases with overt hypothyroidism and not for subclinical cases.

Our data highlighted serum iron as the most sensitive blood indices associating with IDA (sensitivity was 94%, 95%CI 0.95 to 1.0). Xiaohui Yu et al. [23] declared a direct correlation with serum iron and an inverse correlation with serum transferrin receptor (TfR) concentration. He conducted his results at the time of delivery and

calculated TfR. Our study was conducted in the first trimester, and instead of using TfR concentrations, we used TIBC to reduce the possible dilution effect caused by blood volume expansion, resulting in a more precise reflection of iron status during pregnancy comparison to TfR concentrations [23].

The gold standard for evaluating iron stores is serum ferritin; it is the first variable to changes when iron stores fall, regardless of recent iron intake. There were lower levels in the anaemic cases than the healthy controls in line with Shuxiang Li et al. and Flora Veltri et al. studies [24,25].

The current study showed that; at a 25 ng/ml cutoff value, serum ferritin had 84% sensitivity, 85% specificity, and 95% CI (0.8 to 0.94). As for Flora Veltri et al. study, they declared a lower serum ferritin cutoff value of <15 ng/ml with a specificity of 98% and a sensitivity of 75% for IDA [25]. The importance of evaluating iron stores cannot be overstressed since various health consequences of deficient or depleted iron stores take a long time to present themselves as iron deficiency anaemia. A plane haemoglobin level can only give a tip of the iceberg of what lies beneath [26].

The study limitation, iodin and autoimmune antibodies are fundamental causes for hypothyroidism; both were out of this study scope. The study was a single-centre study; collection from multiple centres would have added a more diverse reading. Strengths, we collected all related parameters for both anaemia and thyroid hormones and presented them with detailed statistical analysis to understand the interchangeable relation of these two common alignments

CONCLUSION

First-trimester pregnant women with IDA could be regarded as a high-risk group for the development of maternal hypothyroxinemia, so we recommend screening for both during first-trimester antenatal care visits to improve the obstetrical service outcome for both the mother and the baby.

Disclaimer

The article has not been previously presented or published and is not part of a thesis project.

Conflict of Interest

There are no financial, personal, or professional conflicts of interest to declare.

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