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Original Research Article

Maternal Thyroid Status in Pregnant Women and its Associations with Ferritin and Vitamin B12

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Abstract

The purpose of this study is to determine the influence of maternal thyroid status on the levels of ferritin and Vitamin B12 in pregnant women in India. The thyroid plays a crucial role in maintaining overall health. A dysfunctional thyroid can negatively affect both the mother and the developing foetus during pregnancy. However, limited research has explored the interplay between maternal thyroid function and these micronutrients in the Indian population.

Methods: A cross-sectional study design was employed, involving pregnant women attending antenatal clinics in the tertiary care center. TSH, free thyroxine(FT4), and triiodothyronine(T3) were measured in serum to assess maternal thyroid function. Ferritin and vitamin B12 levels were also measured using standardized laboratory methods. Data on demographic characteristics, medical history, and dietary intake were collected through questionnaires and medical records.

Results: In preliminary results, pregnant women were more likely than expected to have thyroid dysfunction, including subclinical hypothyroidism or hyperthyroidism. Additionally, there was a significant correlation between maternal thyroid status and ferritin and vitamin B12 levels. Women with abnormal thyroid function had lower ferritin and vitamin B12 levels compared to those with normal thyroid function.

Conclusion: Due to the high prevalence of hypothyroidism in pregnant women and its association with iron and vitamin B12 deficiency. Hence early detection of thyroid status and nutritional deficiencies in this population is imperative to stop the disorder's negative effects on the mother and foetus.

Keywords: Pregnancy, Thyroid, Vitamin B12, Ferritin.

Introduction

Hypothyroidism is more prevalent in 6.47-14.32% of pregnancies, accounting for approximately 2-5% of pregnancies. [1] During the first trimester of pregnancy, the foetus completely relies on the mother's thyroid hormones until its own thyroid gland develops. At this point, an inadequate thyroid hormone supply might result in foetal brain injury, miscarriage, or early foetal growth. [2] Pregnant women's glands enlarge by 10% in iodine-rich countries and by 20–40% in iodine-deficient ones. As the daily requirement of iodine increases by 50%, there is also a rise in the production of thyroxin (T4) and triiodothyronine (T3). The reason for this is that estrogen increases the levels of thyroid-binding globulin in the blood, while the placenta produces high levels of various thyroid-stimulating hormones such as human chorionic gonadotropin (HCG). [3] During the first trimester, HCG triggers a temporary increase in levels of free thyroxin (FT4), while simultaneously causing a decrease in thyroid-stimulating hormone (TSH) levels. During the second trimester, serum FT4 levels decrease by approximately 10-15%, while serum TSH levels progressively normalize. [4]. As per certain sources, during pregnancy, the levels of serum FT3 and FT4 tend to decrease gradually from the initial to the final trimester. On the other hand, the levels of TSH tend to rise gradually throughout the entire pregnancy. These changes in the body's physiology may result in hypothyroidism. [5]. Based on our clinical experience, we have observed a rapid increase in pregnant women's TSH levels, coupled with a decrease in both hemoglobin (HB) and serum ferritin levels. Few clinical studies have also reported a correlation between iron deficiency during pregnancy and impaired thyroid function. According to Bashetti et al. [6], insufficient iron levels during the first trimester of pregnancy can be a separate risk factor for isolated hypothyroxinemia, provided that there is adequate iodine intake. As per the findings of Zimmermann et al. [7], areas with marginal iodine deficiency show a correlation between low levels of maternal iron and increased TSH levels, as well as decreased FT4 levels during pregnancy.

Adequate levels of vitamin B12 are essential for the process of cell division in pregnant women. Research has indicated that a deficiency of this vitamin is commonly observed in expectant mothers. This has become an increasingly significant concern for public health. [8] Maternal vitamin B12 deficiency can impact both the mother's and the unborn child's pregnancy outcomes. In women who are trying to get pregnant, the risk of preeclampsia, premature labor, and intrauterine development retardation increases with vitamin B12 deficiency [9]. It is quite prevalent for individuals with hypothyroidism to experience a deficiency in Vitamin B12. A lack of vitamin B12 makes hypothyroidism worse [6].

Aim and Objectives

The objective of this study is to assess the thyroid function of pregnant women during the first and second trimesters and to investigate its correlation with ferritin and vitamin B12 levels.

Material and Methods

Over the course of six months, 190 pregnant women in the first two trimesters were recruited for this cross-sectional study from the antenatal clinics of a tertiary care facility. During the study, there were three groups of women Group A, B & C. Group A consisted of pregnant women in their first 13 weeks. Group B consisted of pregnant women between the 14th and 27th weeks. Group C was made up of 66 healthy women who were not pregnant and were of similar age to the pregnant women. These wholesome women served as the controls. The number of patients who met the inclusion criteria during the study period was used to calculate the sample size.

When selecting expectant women for the sample, certain factors were considered, such as having a singleton pregnancy and carrying a healthy, viable foetus in the first or second trimester. Additionally, the women needed to attend a standard obstetric evaluation without having taken any supplements previously. To ensure accuracy, certain exclusion criteria were also established, such as having multiple children or a history of chronic ailments like diabetes, kidney disease, or thyroid disease. Using supplements within the six months prior to the trial was also a disqualifying factor. All participants provided informed consent before undergoing a thorough medical examination, including an abdominal ultrasound to determine the gestational age and pregnancy health. Laboratory tests, including thyroid function, serum ferritin and HB, and the B12 vitamin level, were also conducted as part of the standard medical evaluation at the initial prenatal appointment.

All participants had their blood drawn through venipuncture after fasting for 8-10 hours. Chemiluminescence tests were performed to measure FT4, serum ferritin, TSH, HB, and vitamin B12 levels using the Cobas 6000 analyzer e601 module from Roche Diagnostics in Munich, Germany. The normal range of different parameters, as per manufacturer, is as below:

- FT4: 12-20 pmol/l, sensitivity 0.3 pmol/l.
- TSH: 0.27- 4.20 IU/ml; sensitivity 0.005 IU/ml.
- HB: 13–150 ng/ml
- Ferritin kit: 12–15.5 g/dl
- B12: 153–710 pmol/l

As per American Thyroid Association's normal range for FT4 during pregnancy is 10.5-22.3 pmol/l. [7]

The following categories were used to categorize thyroid issues in pregnant women:

- When the TSH level was above 2.5 IU/ml, hypothyroidism was evaluated. FT4 level determines the type of hypothyroidism.
- TSH <= 0.03 IU/ml and/or FT4 > 22.3 pmol/l was regarded as signs of hyperthyroidism.
- Low FT4 (< 10.5 pmol/l) with normal TSH levels was identified as hypothyroxinemia.
- Normal TSH (2.5 ≥ TSH > 0.3 IU/ml) and FT4 (10.5 ≤ FT4 ≤ 22.3 pmol/l) was identified as euthyroid status.
- The Control Group of women who are not pregnant,
- When the TSH level was above 4.2 IU/ml, hypothyroidism was evaluated. FT4 level determines the type of hypothyroidism.
- TSH <= 0.01 IU/ml and/or FT4 > 23 pmol/l was regarded as signs of hyperthyroidism.
- Low FT4 (< 10 pmol/l) with normal TSH levels was identified as hypothyroxinemia.
- Normal TSH (4.2 ≥ TSH > 0.3 IU/ml) and FT4 (10.5 ≤ FT4 ≤ 23 pmol/l) was identified as euthyroid status.

Statistical Analysis

SPSS was used to perform bivariate, univariate, and stratified analyses. To analyze qualitative variables, Fisher exact test with Contingency tables was created. Additionally, both non-parametric and parametric quantitative variables were compared using the analysis of variance (F test) and the Kruskal-Wallis test. To analyze the correlations between different variables, we used the Pearson coefficient (r). Differences were considered significant at a p-value of 0.05 or less.

Results

The study involved 256 women in all, 190 (74.2%) of whom were pregnant. These were divided into two groups: Group A consisted of 108 (56.84%) first-trimester women, and Group B consisted of 82 (43.15%) second-trimester women. Furthermore, Group C consists of 66 (25.78%) healthy, non-pregnant women of similar age as controls. The average age of 33.6 ± 3.6 years, 27.3 ± 7.1 years, and 30.1 ± 9.9 years for Groups A, B & C respectively. In terms of body mass index, Group C was significantly different from Groups A and B (p=0.014) (Table 1).

TSH levels in pregnant women in Groups A and B were comparable to those in Group C and were not noticeably lower. The FT4 levels in Groups B and C were much lower than those in Group A. Additionally, compared to Group C, pregnant women in Groups A and B had considerably lower levels of vitamin B12. Additionally, compared to Group C, pregnant women in Groups A and B had lower HB concentrations. Although serum ferritin levels did not differ substantially between Groups A and B, Group C's levels were greater, as indicated in Table 2.

For the study groups, thyroid status was assessed according to the American Thyroid Association's guidelines for the diagnosis and treatment of thyroid illness during pregnancy. [11]. Euthyroidism was much more common in non-pregnant women than in pregnant women. Contrarily, just 3.2 % of non-pregnant women had hyperthyroidism, which was absent in pregnant women. Pregnant women in Groups A and B experienced the same prevalence of hypothyroxinemia (2%), which was absent in Group C. The thyroid status of the tested Groups did, however, differ statistically significantly (p=0.002). For Group A, a non-significant negative correlation exists between TSH, and Ferritin & HB. However, TSH was a highly significant positive correlation between TSH & Vitamin B12 (r=0.27, p=0.010). For Group B, TSH had a significant negative correlation with HB & Vitamin B12 but not for Ferritin. Additionally, for Group C, TSH was strongly inversely correlated with HB (r=-0.45, p< 0.002) and slightly inversely correlated with Ferritin & Vitamin B12(Table 3).

Upon analyzing the free thyroxin for Group A, it had a significant positive correlation with HB & ferritin, and a negative non-significant correlation with Vitamin B12(r=-0.13 and p= 0.25). For Group B, FT4 had a positive correlation with Ferritin, HB & Vitamin B12 but was significant only with Ferritin (r=0.35 and p= 0.004). For Group C, a significant positive correlation with HB & Vitamin B12 and non-significant negative correlations with Ferritin (r=-0.18 and p= 0.16) (Table 4).

Table 1: The characteristics of the study patients

	Group A [N=108 (42.18%)]	Group B [N=82 (32.03%)]	Group C [N=66 (25.78%)]	F-test	p-Value
Age (years)	33.6 ± 3.6	27.3 ± 7.1	30.1 ± 9.9	4.90	0.003
BMI (kg/m2)	24.7 ± 2.3	25.1 ± 4.4	27.4 ± 7.2	3.78	0.014

Table 2: Distribution of key Parameters across study Groups

	Group A	Group B	Group C
TSH	2.32 ± 2.43	2.48 ± 1.23	2.49 ± 1.14
FT4	13.71 ± 2.28	13.56 ± 1.98	12.38 ± 2.39
B12	189.20 ± 73.9	134.61 ± 72.83	423.65 ± 157.26
HB	12.52 ± 1.71	11.78 ± 1.35	13.18 ± 1.80
Ferritin	26.19 ± 16.28	23.46 ± 19.69	32.72 ± 32.36

Table 3: Haemoglobin, ferritin, and vitamin B12 levels in relation to thyroid-stimulating hormone in various study Groups

TSH	Group A		Group B		Group C	
	r	p	r	p	r	p
HB	−0.19	0.09	−0.42	< 0.002	−0.45	< 0.002
Ferritin	−0.08	0.53	−0.25	0.046	−0.09	0.47
Vitamin B12	0.27	0.010	−0.22	0.09	−0.07	0.63

Table 4: Haemoglobin, ferritin, and vitamin B12 levels in relation to free thyroxin in various study Groups

FT4	Group A		Group B		Group C	
	r	p	r	P	r	p
HB	0.28	0.007	0.18	0.3	0.27	0.015
Ferritin	0.3	0.27	0.35	0.004	−0.18	0.16
Vitamin B12	−0.13	0.25	0.06	0.73	0.17	0.4

Discussion

Women all throughout the world experience thyroid problems, and the prevalence rises during pregnancy [8]. In most underdeveloped nations, pregnant women frequently have dietary shortages of critical nutrients, such as iron, folic acid, and vitamin B12. Nutritional deficiencies, especially those of vitamin B12 and iron, as well as thyroid disorders can affect the mother and the baby in ways that affect growth and development and raise the risk of perinatal mortality. [9]

As by Zha et al. [10], we also discovered that TSH levels in the first two trimesters of pregnancy were non-significantly reduced when compared to controls. In contrast, Baghel et al. [11] found that pregnant women had considerably greater TSH levels than non-pregnant women. Pregnant women exhibited considerably higher TSH levels than non-pregnant women, according to Abdelhafiz et al. [12]. They concentrated their investigation on pregnant women who were in the middle and late stages. Our study's mean TSH level was marginally lower than Chandrasekhara et al.'s. [13] They looked at thyroid conditions in expectant mothers.

We found that pregnant women's FT4 levels considerably fell from the first to the second trimester. Zha et al. [10] found that FT4 levels fell steadily from the first to the last trimester. In contrast, Baghel et al. [11] discovered that first-trimester pregnant women's FT4 levels were considerably lower than controls.

FT4 and HB were positively correlated, while TSH and HB, and ferritin were negatively correlated. Similar findings were made by Refaat [14], who looked at the prevalence and traits of anaemia associated with thyroid problems in Saudi women who weren't pregnant. Subclinical hypothyroidism is more prevalent than subclinical hyperthyroidism, according to studies by Hasanato et al. [15] and Al Eidan et al. [16]. According to our data, the three most prevalent thyroid diseases in pregnant women in the first two trimesters were overt hypothyroidism, subclinical hypothyroidism, and hypothyroxinemia. In addition, there was a positive correlation between serum FT4 and HB and ferritin, but a negative correlation between TSH and HB and ferritin.

According to Refaat [8] and Zimmermann [17], hypothyroidism is the most common disease. The incidence of anaemia and its impact on thyroid function in pregnant Indian women are examined in Shaheen and Hasan's study [14].

Our findings confirmed Yu et al.'s [18] study, which compared screening for thyroid dysfunction in pregnant Egyptian women on a broad scale. The physiological and hormonal changes led higher prevalence of Hypothyroidism marked by lower TSH in pregnant women as compared to non-pregnant women. The higher FT4 level in Group A as compared to Group B & Group C. According to a study by Baghel et al. [11], ferritin levels were not statistically different between pregnant and non-pregnant women. Iron and vitamin B12 levels were significantly lower during the first trimester of pregnancy than in non-pregnant women. This result was in line with the outcomes of the investigation. In contrast to Bashetti et al.'s [10] study, we discovered that vitamin B12 was positively correlated with TSH in the first trimester and negatively correlated with TSH in the second trimester.

Conclusion

While TSH and HB and ferritin were adversely connected, serum FT4 and both were positively correlated. These findings also emphasise the important necessity for early thyroid status detection and fast therapy initiation. Therefore, it should be thought about screening expectant women for maternal thyroid dysfunction as soon as feasible, especially in a nation like India. More research is needed to rule out a clear connection between thyroid function and iron status in order to prevent the condition's harmful effects on the mother and baby and to achieve a normal pregnancy outcome. Further, thorough multicentre investigations are advised in order to fully comprehend the relationship between thyroid profile and vitamin B12. Therefore, early detection of these deficiencies will be helpful for commencing supplements to prevent adverse pregnancy consequences.

Study limitation

Our study does, however, have certain restrictions. First off, as a probable source of thyroid issues, we did not investigate autoimmune thyroid illness. In addition, the population in iodine-deficient or -excessive areas should be included in the study. The impact of iron and Vitamin B12 insufficiency and maternal thyroid dysfunction on foetal development requires more study. Lastly, since our investigation was conducted in a single centre, a multicentre study would be preferable.

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