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Original Research Article

# Study of Relationship between Iron Deficiency and Thyroid Function in Females of the Reproductive Age Group of Southern Odisha, India

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**Conflict of interest: Nil**

**Abstract:**

**Background:** Iron deficiency is one of the overlooked causes of thyroid dysfunction. It is revealed that the prevalence of iron deficiency was very high in non-pregnant Indian women and was associated with a higher serum TSH and lower FT4 level.

**Aim:** This study was planned to find out the relationship between these two conditions, so that iron supplementation can be adopted to avoid the morbidity and mortality associated with thyroid dysfunction.

**Method:** The current study was a cross sectional observational study done between 2018 to 2020 in M.K.C.G. Medical College and Hospital, Berhampur, Odisha, India. In this study 50 non-pregnant females of the reproductive age group (15 to 45 years) were taken for study.

**Results:** We found that 68% of females were iron deficient and 32% of females were having normal iron stores. TSH was raised in 35.29% in the iron deficient group as compared to 6.25% in the non-iron deficient group with a p value of 0.001. Serum TSH of 37 females out of 50 was normal (<4 mIU/L) and 13 females were having raised serum TSH (>4 mIU/L). The mean serum TSH was higher in the iron deficient group as compared to non-iron deficient group. 20% of the females had low FT4 (<0.7 ng/dl) and 80% had normal FT4. It was observed that FT4 was decreased in the ferritin deficient group as compared to group with normal ferritin. FT4 and serum ferritin were significantly associated with each other with p value of < 0.0001. The prevalence of mild and severe hypothyroxinemia was markedly higher in women with Iron deficient than those without (p<0.005).

**Conclusion:** We concluded from our study that the prevalence of iron deficiency was very high in non-pregnant Indian women and was associated with a higher serum TSH and lower FT4 levels.

**Keywords:** Iron deficiency, Thyroid function, Women, Reproductive.



## Introduction

Iron deficiency results in the depletion of iron dependent intracellular enzymes. Iron is a component of TPO which is responsible for oxidation of Iodide and binding of Iodine to tyrosyl residue of thyroglobulin. Besides decreasing the synthesis of T3 and T4, iron deficiency also reduces peripheral conversion of T4 to T3.

Thyroid hormones influence hematopoiesis by increasing erythropoietin production or hematopoietic factors by non-erythroid cells. Anemia has been observed in 20-60% of patients with hypothyroidism. Both iron deficiency and hypothyroidism affect each other's metabolism. Thus, simultaneous correction of both should be done earlier in order to achieve adequate response.

In our study, females of the reproductive age group (non-pregnant) have been taken as the study population. The reason being iron deficiency and thyroid disorders are more prevalent in non-pregnant females and very few studies have been done worldwide.

**Methods:** The study was conducted at the Department of Medicine, M.K.C.G.M.C.H., Berhampur. Approval was taken from the Institutional Ethics Committee of M.K.C.G. Medical College. Informed consent was obtained from all the participants.

**Study period:** 2018 to 2020.

**Nature of study:** Cross Sectional Observational Study.

**Study population:** 50 females of reproductive age group (15-45 yrs.) who are non-pregnant admitted to female medicine ward of M.K.C.G. M.C.H, Berhampur.

**Inclusion criteria:** non-pregnant females of reproductive age group (15-45 yrs).

**Exclusion criteria:**

- Patients on iron or thyroxine supplements
- Patients with dimorphic anemia
- Patients with acute infections
- Patients with DUB or acute GI bleed
- Patients with CKD
- Those patients who do not want to participate in the study.

The participants were evaluated as per the standard case record form specially concentrating on-

1. Age
2. Detailed history
    - History of present illness
    - Past history of goiter, thyroid disease
    - Medication history of iron and thyroid supplements
    - Obstetric history (LMP, gravida, para, abortion, live)
    - History suggestive of acute infection
3. Physical examination
    - Height, weight
    - BMI: Wt.(kg)/Height. ($m^2$)
    - Pulse rate, blood pressure, respiratory rate, temperature.
    - Pallor, icterus, cyanosis, clubbing, lymphadenopathy, pedal edema.
4. Baseline routine investigations: Urine pregnancy test, CBC, LFT, FBS, RFT, Urine R/M
5. Special investigations like: Serum FT4, Serum TSH, Serum Ferritin, Total Serum Iron, Serum vitamin B12 and folic acid.

Based on serum ferritin value, the study population was divided into two groups. First group with serum ferritin < 15 µg/L was defined as iron deficiency. Second group with serum ferritin >15 µg/L was defined as non-iron deficient. Serum FT4, TSH values were then compared between the two groups.

**Normal reference range:**

- Serum iron: 60-170 µg/dl
- Serum ferritin: > 15 µg/L
- Serum TSH: 0.4 to 4 mIU/L
- Serum FT4: 0.7-1.8 ng/dl
- Subclinical hypothyroidism-TSH 4-10 mIU/L with a normal FT4.
- Overt hypothyroidism-TSH > 4 mIU/L with a decreased FT4.

**Sample collection:** Fasting blood samples were collected in vacutainer tubes for the determination of ferritin, FT4, TSH etc. Following clotting, the samples were centrifuged at approximately 1000 rpm for 10 minutes and the serum was obtained and stored at -20º C until analysis.

**Serum TSH:** TSH was measured using TSH immunometric assay kit using the VITROS ECi/ECiQ immunodiagnostic system.

**Serum FT4:** Free T4 was measured by using FT4 competitive immunoassay kit with the VITROS ECi/ECiQ immunodiagnostic system.

**Serum Ferritin:** Serum ferritin was measured using the VITROS ECi/ECiQ Immunodiagnostic System.

**Serum Iron:** It was measured using Colorimetric assay.

**Observation:**

50 non-pregnant women of the reproductive age group were analyzed to look for a correlation between Iron deficiency and thyroid function. In our study group of 50 patients, the patient's age ranged from 15 – 45 years. The mean age of females in our study was 30.54 ± 2.42 years. Maximum females (63%) were in the age group of 26 – 35 yrs. The mean BMI of the females in our study was 21.17 ± 1.83 (range 18.5–29.9). Maximum females (94%) were in the BMI range of 18.5–24.9. 20 (40%) have mild anemia, 11 (22%) have moderate and 3(6%) have severe anemia. Mean hemoglobin of the study group is 10.12 and standard deviation is 1.68.

34 (68%) have serum iron below 60 µg/dl, 3 (6%) have serum iron between 61 – 100 µg/dl and 13 (26%) have serum iron above 100 µg/dl. The mean and standard deviation of serum iron in the study group is 62 ± 35.33 µg/dl. 34 (68%) have serum ferritin <15 µg/L and 16 (32%) have serum ferritin ≥15 µg/L. The mean and standard deviation of serum ferritin in the study group is 17.42± 14.02 µg/L. 13 (26%) have serum TSH >4 mIU/L and 37 (74%) have serum TSH ≤4 mIU/L. The mean and standard deviation of serum TSH in the study group is 4.59 ± 1.35 mIU/L. 10 (20%) have serum FT4 <0.7 ng/dL and 40 (80%) have serum FT4 0.7 – 1.8 ng/dL. The mean and standard deviation of serum TSH in the study group is 0.8 ± 0.15 ng/dL. So, in our study group 3 females had raised TSH with normal FT4, i.e., 6% had subclinical hypothyroidism.

**Table 1: TSH according to ferritin status**

| | | **Ferritin normal** N=16 | **Ferritin deficient** N=34 | **P value** |
|---|---|---|---|---|
| **TSH (mIU/L)** | Mean ± SD | 2.01 ± 0.45 | 4.86 ± 1.54 | < 0.004 |
| | Median | 1.94 | 4.12 | |
| | Min-Max | 2.01 ± 0.45 mIU/L | 1.5 – 9.0 | |
| | Inter quartile Range | 1.820 – 2.100 | 1.910 – 7.250 | |

The mean value of serum TSH in patients who were ferritin deficient was 4.86 ± 1.54 (range 1.5 – 9.0) and in the normal serum ferritin group, it was 2.01 ± 0.45 (range 1.2 – 3.7) with P value <0.004.

**Table 2: Relationship between Serum ferritin and serum TSH**

| | | **Ferritin (µ/L)** | | **Total** | **P value** |
|---|---|---|---|---|---|
| | | <=15 | >15 | | |
| **TSH (mIU/L)** | Not Raised | 22 (64.71%) | 15 (93.75%) | 37 (74%) | 0.004 |
| | Raised | 12 (35.29%) | 1 (6.25%) | 13 (26%) | |
| **Total** | | 34 (68%) | 16 (32%) | | |

In the ferritin deficient group, 12 females (35.29%) had raised serum TSH level and in normal ferritin group, only 1 female (6.25%) had raised serum TSH level. It was found that serum ferritin level was associated with serum TSH level with P value of < 0.004.

**Table 3: Correlation between TSH and ferritin**

| | | **Ferritin (mcg/L)** |
|---|---|---|
| **TSH (mIU/L)** | Correlation Coefficient | -0.335 |
| | Significance Level P | <0.004 |
| | N | 50 |

It was observed that serum TSH levels and ferritin were negatively correlated with correlation coefficient of -0.335 and significant P value of 0.004.

**Table 4: FT4 according to ferritin status**

| | | **Ferritin normal** N=16 | **Ferritin deficient** N=34 | **P value** |
|---|---|---|---|---|
| **FT4 (ng/dl)** | Mean ± SD | 1.2 ± 0.05 | 0.66 ± 0.15 | < 0.005 |
| | Median | 1.21 | 0.65 | |
| | Min-Max | 1.1 – 1.26 | 0.63 – 0.79 | |
| | Inter quartile Range | 1.175 – 1.245 | 0.64 – 0.73 | |

The mean value of FT4 in the ferritin deficient group was 0.66 ± 0.15 (range 0.63 – 0.79) and in the normal ferritin group was 1.2 ± 0.05 (range 1.1 – 1.26) with P value <0.005.

**Table 5: Correlation between ferritin and FT4**

| | | **Ferritin (mcg/L)** |
|---|---|---|
| **FT4 (mg/dl)** | Correlation Coefficient | 1.212 |
| | Significance Level P | <0.005 |
| | N | 50 |

A positive correlation was obtained between FT4 and ferritin with correlation coefficient of 1.212 and P value of 0.005.

**Discussion:**

The mean age of the study population was 30.54 ± 2.42 years, and the range was 15 – 45 years, which was comparable to the study done by Zimmerman et al [4], Fu et al [2] and Yu et al [3]. The mean BMI of the females present in our study was 21.17 ± 1.83 kg/m$^2$ and range was 18.5 – 29.9 kg/m$^2$. Maximum females (95%) were in the range of 18.5 to 24.9 kg/m$^2$ and none of the females had BMI of more than 30 kg/m$^2$.

We found that age and BMI levels were comparable between both iron deficient and non-iron deficient groups. (30.45 vs 29.38 years and 20.82 vs 21.93kg/m$^2$ respectively). The mean total serum iron of the females was 62 ± 35.33 µg/dL and range was 10 - 120 µg/dL. We found that 68% of the females were iron deficient (< 60 µg/dL) and 32% were having normal iron stores (> 60 µ/L).

The mean serum ferritin was 17.42± 14.02 µ/L and range was 3.2 – 55.4 µ/L. We found that 68% of the

females were iron deficient (ferritin < 15 μ/L) and 32% were having normal iron stores (ferritin > 15 μ/L). The mean ferritin level was comparable to the study done by Veltri et al [1]. But the percentage of iron deficient cases was higher in our study as compared to other studies. It was found that TSH was raised in 35.29% in the iron deficient group as compared to 6.25% in the non-iron deficient group with a p value of 0.001. Serum TSH of 37 females out of 50 was normal (<4 mIU/L) and 13 females were having raised serum TSH (>4 mIU/L). The mean value of serum TSH in patients who were ferritin deficient was 4.86 ± 1.54 mIU/L (range 1.5 – 9.0) and in normal serum ferritin group, it was 2.01 ± 0.45 mIU/L (range 1.2 – 3.7) with P value <0.005. The results were comparable in all studies. The mean serum TSH was higher in the iron deficient group as compared to non-iron deficient group.

The mean FT4 of the females was 0.8 ± 0.15 ng/dl and range was 0.63 – 1.26 ng/dl. We found that 20% of the females had low FT4 (<0.7 ng/dl) and 80% had normal FT4. The mean value of FT4 in the ferritin deficient group was 0.66 ± 0.15 ng/dl (range 0.63 – 0.79) and in the normal ferritin group was 1.2 ± 0.05 (range 1.1 – 1.26). It was observed that FT4 was decreased in the ferritin deficient group as compared to group with normal ferritin. We found that FT4 and serum ferritin were significantly associated with each other with p value of < 0.0001. The prevalence of mild and severe hypothyroxinemia was markedly higher in women with Iron deficient than those without (p<0.005). This supports the fact that TPO, an enzyme necessary for thyroid hormone synthesis, is dependent on serum iron. 13 females had raised serum TSH (> 4 mIU/L and < 10 mIU/L) and 10 females had decreased FT4 level. Therefore, 3 females (6%) with raised TSH and normal FT4 were considered to have subclinical hypothyroidism.

We divided our study population in two groups based on the serum ferritin level as an iron deficient group and non-iron deficient group. We found that 68% were iron deficient and 32% were non-iron deficient. Then we compared FT4, and TSH value between the two groups.

The mean FT4 of the females was 0.8 ± 0.15 ng/dl and range was 0.63 – 1.26 ng/dl. We found that 20% of the females had low FT4 (<0.7 ng/dl) and 80% had normal FT4. The mean value of FT4 in the ferritin deficient group was 0.66 ± 0.15 (range 0.63 – 0.79) and in the normal ferritin group was 1.2 ± 0.05 (range 1.1 – 1.26). We found that FT4 and serum ferritin were significantly associated with each other with p value of < 0.005. Serum mean TSH levels were significantly higher in the Iron deficient group as compared with the non-Iron deficient group (4.86 ± 1.54 mIU/L vs 2.01 ± 0.45 mIU/L; p< 0.004). A positive correlation was obtained between FT4 and ferritin with correlation coefficient of 1.212 and P value of 0.005. It was observed that serum TSH levels and ferritin were inversely correlated with correlation coefficient of -0.335 and significant P value of 0.004.

J Luo et al [5] studied the evidence and evaluated the relationship between iron deficiency and thyroid disorders. They observed iron deficiency may adversely affect thyroid function and autoimmunity of pregnant and reproductive age women and it is very necessary for monitoring iron status and early treatment of iron deficiency. Hassan N et al [6] studied the frequency of thyroid disorders in iron deficiency anemic pregnant women. A total of 180 women with the first trimester of pregnancy presented with iron deficiency anemia were studied. In their study, they found the frequency of thyroid disorders is 23.5% in anemic pregnant women presenting in the first trimester of pregnancy. Reyes R M et al [7] et al investigated the effects of iron status on thyroid function in mildly iron deficient pregnant women of Belgium. 1241 numbers of pregnant women in Belgium were studied during the first and third trimester of pregnancy. They found that iron deficiency is a determinant of serum FT4 and T4 in pregnant women.

**Limitations of our study**

- First, the study had a low sample size. Moreover, all the females were attending the same hospital. So, it might not represent the general population.
- Second, we did not measure the iodine levels in the study group. Thus, we should evaluate the association of iron status and thyroid function under different iodine levels.

**Conclusion**

Iron deficiency is one of the overlooked causes of thyroid dysfunction. This study was planned to find out the relationship between these two most common conditions, so that iron supplementation can be adopted to avoid the morbidity and mortality associated with thyroid dysfunction. Iron deficiency and thyroid dysfunction goes hand in hand. The role of iron in thyroid function has received little attention. So, it must be explored to establish the causal relationship between iron deficiency and thyroid dysfunction. Any iron deficiency should be evaluated and treated to combat thyroid dysfunction. Nutritional supplements should be encouraged in iron deficient endemic areas. Screening programs to unmask subclinical hypothyroidism should be held on a regular basis.

**Abbreviations:**

- TPO - Thyroid Peroxidase
- LFT - Liver Function Test
- RFT - Renal Function Test
- CBC - Complete Blood Count
- FT4 - Free T4

- BMI - Body Mass Index
- FBS - Fasting Blood Sugar
- DUB - Dysfunctional Uterine Bleeding
- LMP - Last Menstrual Period
- T3 - Triiodothyronine
- T4 - Tetraiodothyronine
- TSH - Thyroid Stimulating Hormone
- OPD - Outpatient Department
- TIBC - Total Iron Binding Capacity
- CKD - Chronic kidney disease

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