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# Association of thyroid dysfunction and anemia in pregnancy: A cross sectional study

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***Abstract*---**Background: Thyroid dysfunction in pregnancy is clinically important as insufficient thyroxine is associated with an increased risk of premature birth, low birth weight and miscarriage. This prospective, cross sectional study, single-center study was carried out to identify the thyroid dysfunction in pregnancy in Indian antenatal mothers. Methods: This prospective, cross sectional study, single-center study was conducted in the Department of Obstetrics and Gynecology, Indian Institute of Medical Science & Research, Warudi, Badnapur, Jalna, India. The study period was of 20 months from January-2018 to August-2019. One hundred and sixty six antenatal mothers with age population in range of 18-35 years were included in the study. All the study subjects were randomly selected & rendered to serological testing's like T3, T4, TSH. All The study protocol was performed in accordance with the principle of the declaration of Helsinki and after approval by the Institutional ethical scientific committee. The data was entered and tabulated in MS-Excel 2007, and statistical analysis was performed by using Statistical Package for the Social Sciences (SPSS 22.0). Data had been summarized as mean for numerical variables and count and percentages for categorical variables. Results: Mean age of the study population was 22.8 years. Mean level of hemoglobin was recorded at 12.67 g/dL. The current

study recorded 55, 70 and 41 women in first, second and third trimester, respectively. Level of T3, T4 and TSH was 130.107, 9.83 and 2.49 was recorded in women in their first trimester. Similarly, level of T3, T4 and TSH was 129.30, 9.75 and 2.48 was recorded in women in their second trimester. Whereas, level of T3, T4 and TSH was 129.14, 9.79 and 2.48 was recorded in women in their third trimester.Hypothyroidism, euthyroidism and Hyperthyroidism was seen in 25.3%, 71.7% and 3.0% respectively.Anemia was seen in 66.7%, 44.5% and 40% in Hypothyroidism, euthyroidism and Hyperthyroidism patient. Conclusion: The current study imply that reporting observed values of TSH, T4 and T3 in 1st, 2nd and 3rd trimester of pregnancy will add to available literature. Early and effective treatment of thyroid disorder ensures a safe pregnancy with minimal maternal and neonatal complications.

***Keywords*---**Thyroid, Pregnancy, TSH, T3, T4.

## Introduction

Pregnancy is a time of complex hormonal changes.[1] In women with normal thyroid function, there is an increase in thyroxine (T4) and triiodothyronine (T3) production, which results in inhibition of thyroid-stimulating hormone (TSH) in the first trimester of pregnancy, due to a high human chorionic gonadotropin (hCG) level that stimulates the TSH receptor because of partial structural similarity.[2] Thyroid disorders are encountered frequently during pregnancy and the postpartum period.[3] Thyroid disease is the second most common endocrine condition encountered in women of childbearing age after diabetes. Most of these conditions are treatable, and may affect mother and fetus adversely if they are not evaluated and managed appropriately.[4]

Thyroid disorders are common in pregnancy and the most common disorder is subclinical hypothyroidism. Due to the complex hormonal changes during pregnancy, it is important to remember that thyroxine requirements are higher in pregnancy.[5]

According to recent American Thyroid Association (ATA) guidelines, the recommended reference ranges for TSH are 0.1 to 2.5 mIU/L in the first trimester, 0.2 to 3.0 mIU/L in the second trimester, and 0.3 to 3.0 mIU/L in the third trimester.[6] Maternal hypothyroidism is an easily treatable condition that has been associated with increased risk of low birth weight, fetal distress, and impaired neuropsychological development. Hyperthyroidism in pregnancy is less common as conception is a problem.[6] In view of this, the current prospective, cross sectional study, single-center study was carried out to identify the thyroid dysfunction in pregnancy in Indian antenatal mothers.

## Materials and Methods:

This prospective, cross sectional study, single-center study was conducted in the Department of Obstetrics and Gynecology, Indian Institute of Medical Science &

Research, Warudi, Badnapur, Jalna, India. The study period was of 20 months from January-2018 to August-2019. One hundred and sixty six antenatal mothers with age population in range of 18-35 years and singleton pregnancy were included in the study. Patients with pregestational thyroid dysfunctions, multiple pregnancy and gestational trophoblastic disease were excluded from the study. All the study subjects were randomly selected & rendered to serological testing's like T3, T4, TSH.

Estimation for TSH was conducted using the Enhanced Chemiluminescence method. Estimation of free T3 and free T4 was subsequently carried out when TSH levels were abnormal. Cut off values used for TSH were those indicated by the American Pregnancy and Thyroid Association: 1st trimester: 0.1–4.0mIU/L, 2nd trimester: 0.2–4.5mIU/L, 3rd trimester: 0.3-5mIU/L. Normal free T4 level is 0.7 to1.8 ng/dl and free T3 level is 1.7 to 4.2 pg/ml.[6]

Patients with normal fT4 and high TSH were considered to have subclinical hypothyroidism (SCH); those with low fT4 and high TSH were considered to have overt hypothyroidism; those with normalfT4 and low TSH were considered to have subclinical hyperthyroidism; and those with highT4 and low TSH <0.1 mIUwere considered to have overt hyperthyroidism.[6]

Women were chosen irrespective of age, parity, residence and socioeconomic status. Women with multiple pregnancies, a known case of thyroid disorder, or any pre-existing medical disorder were excluded. Informed consent was taken from the patients in the study group. Further, measurement of hemoglobin (Hb), LMP and gestation age was recorded. All The study protocol was performed in accordance with the principle of the declaration of Helsinki and after approval by the Institutional ethical scientific committee.

**References for statistical methods:**

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**Statistical analysis**

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version (IBM SPSS Statistics, Somers NY, USA) software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Normality of the continuous data, was tested by Kolmogorov–Smirnov test and the Shapiro–Wilk test. Continuous data was represented as mean and standard deviation. ANOVA (Analysis of Variance) was the test of significance to identify the mean difference between more than two groups for quantitative data. Graphical representation of data was done by bar

diagram. p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

**Results**

Table 1
Distribution of Profile of the study population

| | | Count | % |
|---|---|---|---|
| Age | 18 to 20 years | 61 | 36.7% |
| | 21 to 25 years | 76 | 45.8% |
| | 26 to 30 years | 24 | 14.5% |
| | >30 years | 5 | 3.0% |
| | Mean ± SD | 22.77 ± 3.884 | |
| Male child | 0 | 122 | 73.5% |
| | 1 | 31 | 18.7% |
| | 2 | 11 | 6.6% |
| | 3 | 2 | 1.2% |
| Female child | 0 | 111 | 66.9% |
| | 1 | 42 | 25.3% |
| | 2 | 9 | 5.4% |
| | 3 | 3 | 1.8% |
| | 4 | 1 | 0.6% |
| Gestational age | First Trimester | 50 | 30.1% |
| | Second Trimester | 75 | 45.2% |
| | Third Trimester | 41 | 24.7% |
| Thyroid Status | Hypothyroid | 42 | 25.3% |
| | Hyperthyroid | 5 | 3.0% |
| | Euthyroid | 119 | 71.7% |

Mean age of the study population was 22.77 ± 3.884 years. Mean level of hemoglobin was recorded at 12.67 ± 4.67 g/dL. 18.7% had 1 male child and 25.3% had female child. 30.1% were in First trimester, 45.2% were in second trimester and 24.7% were in third trimester. 25.3% had Hypothyroidism, 3% had hyperthyroidism and 71.7% were euthyroid (Table 1).

Table 2
T3, T4 and TSH in 1st, 2nd and 3rd trimester of pregnancy among study population

| | | T3 | | T4 | | TSH | |
|---|---|---|---|---|---|---|---|
| | | Mean | SD | Mean | SD | Mean | SD |
| Gestational Age | First Trimester | 122.63 | 28.94 | 15.66 | 62.99 | 2.54 | 3.70 |
| | Second Trimester | 137.11 | 23.59 | 7.00 | 2.28 | 2.58 | 2.04 |
| | Third Trimester | 131.24 | 25.29 | 8.04 | 11.44 | 2.32 | 1.11 |
| | Total | 131.30 | 26.30 | 9.87 | 35.03 | 2.50 | 2.50 |
| | P value | 0.01* | | 0.373 | | 0.863 | |

Mean T3 levels was highest in Second Trimester (137.11± 23.59) and lowest in first trimester (122.63 ± 28.94). There was significant difference in Mean T3 levels with respect to Gestational age. There was no significant difference in T4 and TSH with respect to Gestational age.

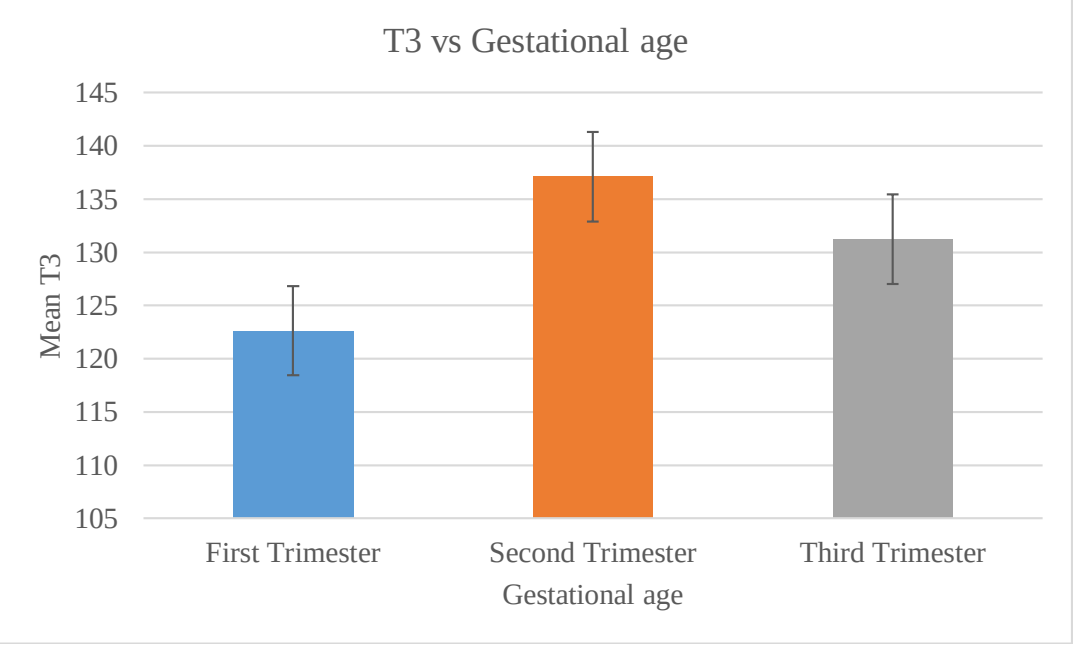


Figure 1: Bar diagram showing T3 levels with respect to Gestational age

Table 3
Association between Gestational age and Thyroid Status

| | | Thyroid Status | | | | | |
|---|---|---|---|---|---|---|---|
| | | Hypothyroid | | Hyperthyroid | | Euthyroid | |
| | | Count | Row N % | Count | Row N % | Count | Row N % |
| Gestational Age | First Trimester | 11 | 22.0% | 1 | 2.0% | 38 | 76.0% |
| | Second Trimester | 21 | 28.0% | 3 | 4.0% | 51 | 68.0% |
| | Third Trimester | 10 | 24.4% | 1 | 2.4% | 30 | 73.2% |

x 2 =1.187, df =4, p = 0.880

In the study among subjects in First Trimester, 22% had Hypothyroid and 2% had Hyperthyroidism. Among subjects in Second Trimester, 28% had Hypothyroid and 4% had Hyperthyroidism and among subjects in Third Trimester, 24.4% had Hypothyroid and 2.4% had Hyperthyroidism. There was no significant association between Gestational age and Thyroid Status.

Table 4
Association between Anemia and Thyroid Status

| | | Thyroid Status | | | | | |
|---|---|---|---|---|---|---|---|
| | | Hypothyroid | | Hyperthyroid | | Euthyroid | |
| | | Count | % | Count | % | Count | % |
| Anemia | Present | 28 | 66.7% | 2 | 40.0% | 53 | 44.5% |
| | Absent | 14 | 33.3% | 3 | 60.0% | 66 | 55.5% |

x 2 =6.287, df =2, p = 0.043*

Among subjects with Hypothyroidism, 66.7% had Anemia. Among subjects with Hyperthyroidism, 40% had anemia and among subjects with euthyroid status, 44.5% had anemia. There was significant association between Thyroid Status and anemia.

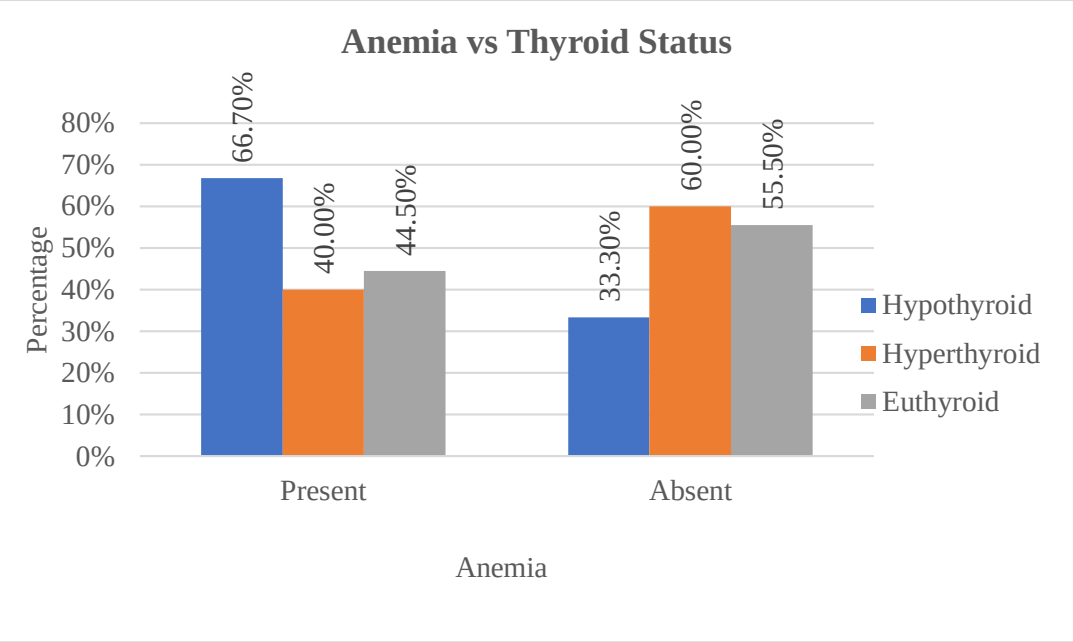


Figure 2: Bar diagram showing Association between Anemia and Thyroid Status

**Discussion**

Pregnancy is a stress test of maternal thyroid function.[7] The prevalence of thyroid dysfunction in pregnant women is high. Subclinical hypothyroidism occurs in 10% of all pregnancies.[8]

Pregnancy results in a number of important physiological and hormonal changes that alter thyroid function mainly due to the influence of two main hormones: human chorionic gonadotropin (HCG) and estrogen. There is a change in the level of thyroxinebinding globulin (TBG), total thyroid-hormone level and thyroid stimulating hormone (TSH) during normal pregnancy. The thyroid gland increases in size (by about 10-15%) during pregnancy and the half-life of TBG increases from 15 min to 3 days and concentration increases 3 times by 20 weeks. 3 For the first 10-12 weeks of pregnancy, the fetus is completely dependent on the mother for the production of thyroid hormone. By the end of the 1st trimester, the fetus's thyroid begins to produce its own hormone. The fetus, however, remains dependent on the mother for ingestion of adequate amounts of iodine, which is essential to make the thyroid hormones. [9]

World Health Organization has revised the reference of Median Urinary Iodine ( M UI) for adequate iodine nutrition in pregnancy from 150 to 250 µg/L and the Recommended Dietary Allowance (RDA) for iodine in pregnancy from 200 to 250 µg/L. [9] Iodine deficiency significantly raises the risk of still births and abortion amongst pregnant women and also leads to decreased availability of iodine to the fetus. It retards neurologic development in the fetal stage and also impairs cognitive development thereby leading to learning disability and lowered achievement motivation in later stages of childhood.

In the study done by Rajput R et al [10] the levels of thyroid harmones with references to the trimester during the pregnancy was found to be inconsistent in various studies done through out India, this difference of thyroid levels during the pregnancy is due to different ethnicity and other factors like maternal iodine consumption, laboratory assay method and further concluded that reference range of thyroid levels should be with respect to the region and ethnicity. Further Kalra S et al [11] concluded that recent 2017 recommendation of ATA of a revised URL for TSH of 4.0 mIU/L is high and should instead be 3.0 mIU/L in the 1st trimester and 3.5 in 2nd and 3rd trimester.

It is recommended that all pregnant women should be screened at 1st antenatal visit by measuring TSH levels. TSH cut off should be lower rather than keeping it on 4.0 mIU/L. However, the trimester specific TSH cut off recommended are:[9]
• 1st trimester 2.5 mIU/L;
• 2nd trimester, 3.0 mIU/L;
• 3rd trimester, 3.0 mIU/L.

Effects of hypothyroidism in pregnancy are anemia, low birth weight and mental retardation in neonate. Thyroid disorder is common in women of reproductive age, and it is the most common endocrine disorders after diabetes in this age. Prevalence of thyroid disorders in pregnancy and its maternal and fetal complications in pregnant women vary greatly in different regions depending upon many factors. To date, there are few studies of thyroid function and pregnancy in Maharashtra, India. The geographic location may be a factor in prevalence of thyroid disorder, because the amount of iodine in common salt and consumption of salt may vary from region to region.[12,13]

The observed levels of T3, T4 and TSH in the 1st, 2nd and 3rd trimester of pregnancy in the present study is comparable to the results observed in study conducted by Wang et al.[14] and Ajmani et al.[15]. Variations in different areas may be due to non-uniformity in the study setting or in laboratory techniques, personal human error, and differences in sample size. In India, the prevalence of hypothyroidism in pregnancy is much higher compared to that in Western countries.[16] Iodine deficiency could be a contributing cause.

In the study done by Bijay Vaidya et al [17] nearly 2.6% of the study subjects reported raised TSH level and prevelance of raised TSH in high risk group was found to be statistically significant. In other studies done by Usha Agarwal et al [18] the prevalance of hypothyroidism was found to be 31.8% with mean TSH value of more than 2.5 among the study subjects , further Anemia in hypothyroidism was found to be around 19 % which is much lesser when compared to the findings of our study .

In another study done by Nidhi Singh et al [19] the prevelance of hypothyrodisim was found to be 69.95% with most patients with overt hypothyroidism had mild anemia 26 (68.4%), while in sub-clinical hypothyroid patients' group most of the patients had moderate anemia. In the overt hypothyroid and subclinical hypothyroid group dimorphic anemia was the most prevalent form of anemia with 52.6% and 74.6% respectively.

The percentage of households consuming iodised salt in India, as per the Iodine Network Global score card 2010, is 51%.[20] Many women would be unnecessarily diagnosed as having SCH and may be subjected to the therapeutic burden of LT4 treatment.[21] The current study imply that reporting observed values of TSH, T4 and T3 in 1st, 2nd and 3rd trimester of pregnancy will add to available literature.

The association between hyperthyroidism status and anemia was found to be due to reduced erythrocyte survival duration which is due to alteration in the iron metabolism and utilization of iron in the body with increased oxidative stress and increased hemolysis contributing to the anemic status among the subjects with hyperthyroidism.

Similarly the presence of subclinical and overt hypothyroidism also leads to be anemic status among the subjects due to deficits in the production of healthy erythrocytes from the reticuloendothelieal system. It is also proven that the T3 and T4 has its influence on erythroid precursor proliferative capacity thus altering the regulation of hematopoiesis. T3, T4 and TSH plays a direct role in the erythropoiesis and also acts as a direct beta 2 adrenergic receptor mediated stimulation of red cell precursor. T4 is also known to has its effect on the initiation and completion of hemoglobin protein chains in vivo and further enchances red blood cell productions. Further thyroid harmones are also shown to promote erythropoiesis by increasing the production of erythropoietein by the kidneys.

Further among those with thyroid dysfunction also also found to be suffering from chronic inflamortory status, malnutrition and malabsorption all results in altered absorption of micronutrients and further nutrients which is essential in haemoglobin production

## Conclusion

Thyroid disorders are common in pregnancy, and the most common disorder is subclinical hypothyroidism. Early and effective treatment of thyroid disorder ensures a safe pregnancy with minimal maternal and neonatal complications. Association of maternal anemia, preeclampsia, and increased cesarean delivery, presence of LBW babies, low Apgar score and increased number of NICU admission should also be assessed along with the current study variables.

## Limitations

This study included sample size of only 166 subjects, whom do not represent or generalize the whole population.

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