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Original Research Article

Prevalence and complications of hypothyroidism during pregnancy in western Uttar Pradesh

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ABSTRACT

Background: This study was designed to know the prevalence of hypothyroidism during pregnancy in western part of Uttar Pradesh and its potential complications. A prospective and comparative clinical study to know prevalence of thyroid disorder in pregnancy and pregnancy outcome was done.
Methods: Eight Hundred eighty seven pregnant cases from Department of Obstetrics and Gynaecology, Chattrapati Shivaji Subharti Hospital, Meerut were enrolled in the study from the year 2018 to 2020. Detailed history and physical examination was done. Thyroid Function test (FT3, FT4, TSH and Anti-TPO) were performed after the confirmation of pregnancy. Patients were followed up during entire pregnancy. Thirty seven patients dropped out from the study.
Results: In this study, prevalence of thyroid disorder was 27.28% which was high when compared to other regions in India and in other parts of Asia. Subclinical hypothyroidism and Overt hypothyroidism was 16.57% and 10.71% respectively. Subclinical hypothyroidism was more prevalent and hidden, leading to the poor obstetrical outcome and fetal complications. Rate of miscarriage was high in overt hypothyroid patients.
Conclusions: Due to the immense impact that the maternal thyroid disorder has on maternal and fetal outcome, prompt identification of thyroid disorders and timely initiation of treatment is essential. Thus, universal screening of pregnant women for thyroid disorder should be considered especially in a country like India where there is a high prevalence of undiagnosed thyroid disorder.

Keywords: Hypothyroidism, Overt or subclinical hypothyroidism, Thyroid peroxidase (TPO)

INTRODUCTION

Thyroid disease is a common endocrine disorder affecting women of reproductive age, second only to diabetes mellitus. Worldwide, iodine deficiency is the most common cause of hypothyroidism. In iodine-sufficient regions, the most common causes are autoimmune thyroiditis and iatrogenic hypothyroidism after treatment for hyperthyroidism. The thyroid undergoes physiological changes during pregnancy. Normal pregnancy is associated with an increase in renal iodine excretion, an increase in thyroxine binding proteins, an increase in thyroid hormone production, an increase in HCG level and thyroid stimulatory effects of HCG. All of these factors influence thyroid function tests in pregnant patients. Maternal thyroid function changes during pregnancy and inadequate adaptation to these changes results in thyroid dysfunction. Some of these alterations in thyroid function occur due to increased thyroid hormone-binding globulin (TBG) concentration, increased iodine clearance in the kidneys, and thyrotrophic effect of human chorionic gonadotropin (HCG).[1]

An elevated TSH indicates primary hypothyroidism and serum T4 level will help to categorize this as either overt

or subclinical hypothyroidism. The main pregnancy complications of hypothyroidism are anaemia, preeclampsia, prematurity, low-birth weight (LBW), fetal distress in labor, fetal death, and congenital hypothyroidism, and neurocognitive deficits in children. Subclinical hypothyroidism might be associated with preterm delivery and low Apgar score.

Five factors alter thyroid function in pregnancy: the transient increase in HCG during the first trimester, which stimulate the TSH-R, the estrogen – induced rise in TBG during the first trimester which is sustained during the pregnancy, alteration in immune system, leading to the onset, exacerbation or amelioration of an underlying autoimmune thyroid disease, increased thyroid hormone by the placenta and increased urinary iodide excretion, which can cause impaired thyroid production.[2]

The strength of evidence relating maternal hypothyroidism to low IQ in children, strongly suggests that the screening of thyroid function in the early gestation and treatment with Levothyroxine in hypothyroid women would be beneficial. Levothyroxine is the mainstay of treatment for maternal hypothyroidism. The increment of dose adjustment gener-ally is based on the degree of TSH elevation.

Presently there is a lack of information of Indian data on the prevalence and effect of Hypothyroidism in pregnancy. Keeping this in mind, Present study has been designed in our Department to evaluate the prevalence of hypothyroidism in pregnant women according to new ATA guideline 2017 with maternal and perinatal outcome.

METHODS

This was a prospective analytical study which was conducted in the Department of Obstetrics and Gynaecology, Chattrapati Shivaji Subharti Hospital, Meerut over a period of two years (October 2018 to October 2020), after clearance and approval from ethical committee of the institution. 887 candidates were enrolled after taking informed consents. Pregnant women fulfilling the inclusion criteria were the part of the study. Informed and written consent to participate in this study was obtained.

Detailed history and clinical examination were performed with special regards to maternal age, parity, gestational age, smoking, alcohol consumption or any other addiction, socio-economic status, religion, medical and surgical history.

Symptoms of hypothyroidism were asked for past history of hypothyroidism and details of previous thyroxine supplementation was noted and we also looked for the clinical features suggestive of thyroid dysfunction. Serum samples were collected for investigation as specified below including serum TSH , FT3, FT4 estimation which was done by using siemens flex by chemiluminescences immunoassay(CLIA) technique in ADVIA Centaur XP machine using microplate luminometers utilizing monoclonal antibody directed against a distinct antigenic determinant on the intact TSH molecule which serves as principle of the Assay.

In women with a raised S.TSH>4.0mIU/L indicating hypothyroidism, as per new 2017 ATA guidelines as mentioned below, the tests for FT3, FT4 and Anti TPO antibody were done.

Those with raised TSH but normal FT4 were considered as subclinical hypothyroidism. Women with raised TSH with low FT4 were considered as case of Overt hypothyroidism and the Anti TPO test was done by EUROIMMUN TPO ELISA IgG test kit-human diagnosis, Germany which were first washed in ELISA WASHER and then read on ROBONIK ELISA analyser.

The ELISA test kit provides a semiquantitive in vitro assay for human autoantibodies of the IgG class against thyroid peroxidase (TPO) in serum or plasma. Values with ratio >1(more than 50 IU/ml) were considered as Anti TPO positive and ratio <1(less than 50 IU/ml) were considered as Anti TPO Negative. TSH values were repeated every six weeks in patients given levothyroxine for hypothyroidism till TSH values of < 2.5mIU/L is attained.

These women were followed during delivery regarding anaemia, preeclampsia, gestational diabetes and obstetric complication such abruption placenta, overall rate of caesarian section, vaginal delivery and post-partum haemorrhage were noted. Neonatal outcomes including incidences of low birth weight, prematurity, intrauterine growth restriction, Apgar score at 1 and 5 minute, neonatal intensive care unit admission and foetal demise were also noted.

Statistical analysis

Descriptive statistics was performed by calculating mean and standard deviation for the continuous variables. Categorical variables are presented as absolute numbers and percentage.

The software used for the statistical analysis were SPSS (statistical package for social sciences) version 25.0. Chi-square test was used to investigate whether distributions of categorical variables differ from one another. The p-value was taken significant when less than 0.05 ($p<0.05$).

RESULTS

In the present study, 887 pregnant women were screened, out of 887 women 645 (72.72%) were euthyroid, 147 (16.57%) women were subclinical hypothyroid and 95(10.71%) were overt hypothyroids. The prevalence of thyroid disorders in this study was 27.28% as per table 1.

Table 1: Prevalence of hypothyroidism in various groups (Distribution of women were done as per the 2017 ATA Guidelines on hypothyroidism in pregnancy).

No. of subjects					
Euthyroid (72.72%)	**Subclinical (16.57%)**		**Overt (10.71%)**		Total
	TPO +ve	TPO -ve	TPO +ve	TPO -ve	
645 (72.72%)	6 (0.68%)	141 (15.89%)	29 (3.27%)	66 (7.44%)	887 (100%)

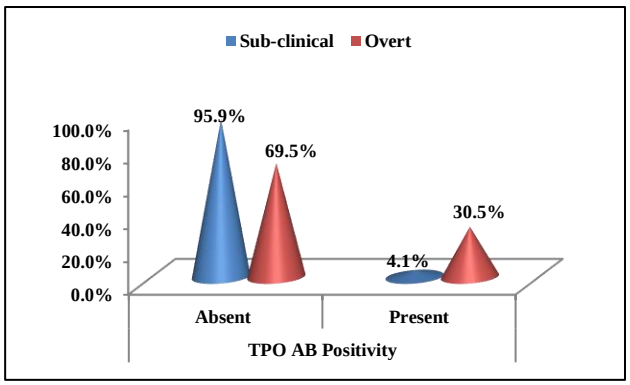

Figure 1: Distribution of women according to Anti TPO antibody positivity correlation between subclinical and overt.

On comparison of Anti TPO antibody positivity in the present study we found TPO AB Positivity was significantly more among overt hypothyroidism compared to Sub-clinical hypothyroidism with p value < 0.001 (statically significant) as per Figure 1).

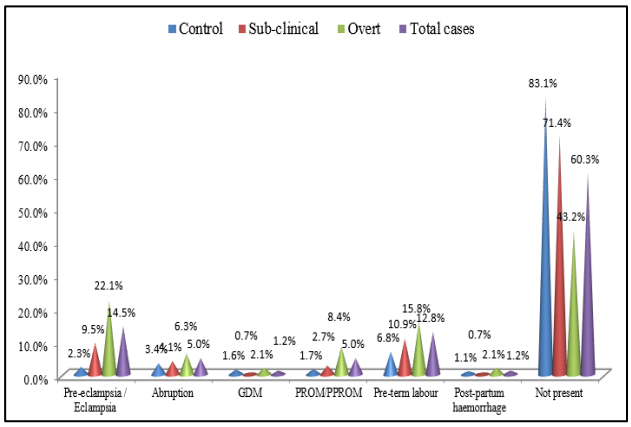

Figure 2: Women according to maternal complication in relation to their TSH levels.

On comparison of maternal complications in present study we found Pre-eclampsia/ Eclampsia (9.5%), PROM (2.7%) are significantly more among sub-clinical hypothyroid group and similarly Pre-eclampsia/ eclampsia (22.1%), Pre-term labour (15.8%) and PPROM (8.4%) were significantly more among overt hypothyroidism group compared to control as per Figure 2.

In present study, Total of N=233 after excluding number of women who aborted (9 women). These adjustments have been made in each group separately. Hence NICU admission and Low APGAR score were significantly more among sub-clinical thyroid cases compared to the controls. NICU admission, Jaundice, Prematurity and Low APGAR score were significantly more among overt thyroid cases compared to the controls as per Figure 3.

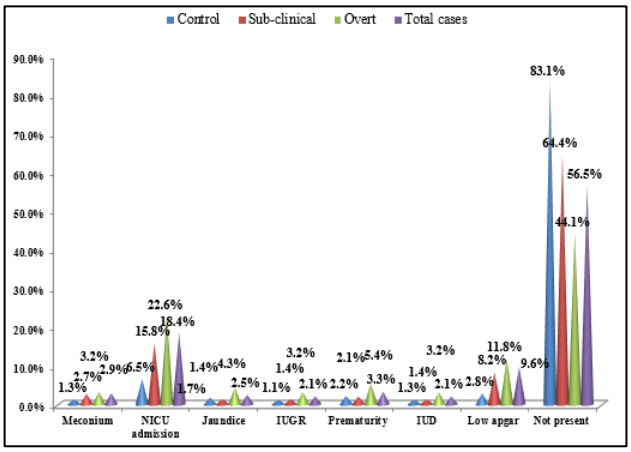

Figure 3: Distribution of women according to fetal complication in relation to their TSH levels.

DISCUSSION

This prospective analytical study conducted at department of Obstetrics and Gynecology for a period of 2 years. Total of 887 pregnant women fulfilling the inclusion criteria were part of this study.

Prevalence of hypothyroidism in pregnant women: Among 887 pregnancy women, 72.72% (n=645) were euthyroid, 16.57% (n=147) were subclinical hypothyroidism and 10.71% (n=95) were overt hypothyroid as per the 2017 ATA guideline on diagnosis of hypothyroid condition among pregnant women. In various studies the prevalence of the overt hypothyroidism is reported in range of 4.8% to 13.1 in concordance with our present study.

One of the hypothesised reasons for higher mean TSH concentration and range in India compared to western countries may be linked to the country's long-standing iodine deficiency, which has only been partially rectified in the last 20 years by iodization of salt as a national

policy. In general hypothyroidisms are concerned with iodine deficiency. Soil degradation with the washing away of iodine from the soil in hilly areas, the use of non-iodinated salts and the ingestion of various goitrogens may also have aggravates the problems. However, even with iodine salt in every household in India, the iodine concentration needed by pregnant women may not be appropriate. The dietary requirement for iodine in pregnant women is 250µg/day, far higher than that fortified by iodinated salt to provide 150µg/day. It may be one of the key reasons for the deficiency of iodine in pregnant women which subsequently leading to hypothyroidism.

In study conducted by the Dhanwal et.al, to assess the prevalence of hypothyroidism in individual sates of India. They have documented average prevalence of 13.13% pregnant women with hypothyroidism. The higher prevalence of the hypothyroidism among the pregnant is similar to various studies as cited in Table 2.

Table 2: showing the prevalence of subclinical overt hypothyroidism and hypothyroidism among the pregnant mother in various studies.

Authors	Prevalence of overt hypothyroidism	Prevalence of subclinical hypothyroidism	Prevalence of hypothyroidism (subclinical +overt)
Gedam et al[3]	4%	7.70%	11.70%
Mandal et al[4]	13.92%	32.94%	46.86%
Murthy et al[5]	3.28%	16.13%	19.41%
Our study	10.71%	16.57%	27.28%

Maternal complications

In controls, 83.1% women had an uneventful delivery. Among the pregnant women with subclinical hypothyroidism reported pre-term labor in 10.9% (n=16), followed with pre-eclampsia/eclampsia in 9.5% (n=14) and abruption in 4.1% (n=6). Likewise, in pregnant women with overt hypothyroidism, found to have pre-eclampsia in 22.1% (n=21) followed by pre-term labour in 15.8% (n=15) and abruption in 6.3% (n=6) pregnant women. Similarly, the anti-TPO antibody was positive among the mothers who recorded complication with the pre-eclampsia/eclampsia, followed by pre-term labour and abruption in both the subclinical and overt hypothyroidism cases.

There is a significant maternal complications among the subclinical and overt hypothyroidism compared to the mothers with euthyroid state. Similar to our findings the study conducted by Kiran et. al., documented the significant association of pregnancy outcome with the hypothyroidism and TSH levels measured. Some studies demonstrated that TSH > 2.5 uIU/mL does not have a significant relationship with abortions or any cause of pregnancy loss.[6] In study by Gahlawat et. al, documented a higher rate of abortion among the hypothyroid group of pregnant women compared to euthyroid group similar to our study with abortion among control was 1.9% and among the pregnant women with hypothyroidism (SCH+Overt) was 3.7%.[7]

Thyroid hormones is important in placing and regulating early pregnancy, which could partly explain the association between hypothyroidism and hypertensive gestational disease like pre-eclampsia, PROM, and preterm birth. The endothelial cell dysfunction, reduction in the local nitric oxide synthesis and the impaired vasodilatation due to reduced circulating thyroid hormone is one of the mechanism of preeclampsia/eclampsia among the hypothyroidism this can further worsen the outcome with abruption, intrauterine growth retardation as secondary to pre-eclampsia and placental insufficiency and pre-term labour and prematurity.

In our study spontaneous abortion is significantly associated with hypothyroid Anti-TPO positive mothers, in concordance to our study several studies have shown that maternal hypothyroidism is associated with increased risk of abortion, stillbirth, premature delivery and hypertension caused by pregnancy.[8] Similar to study by various authors there is a significant association of the anti-TPO positive mothers with occurrence of pre-term labour, spontaneous abortion, pre-eclampsia and eclampsia.[9]

Fetal complications

The role of maternal thyroid status on the future neuropsychological development of the fetus is important at all stages of pregnancy. The maternal hypothyroidism is potentially deleterious to the cerebral development of the fetus.

In present study, the NICU admission (15.8%, n=23) and low APGAR score (8.2%, n=12) were significantly more among the subclinical hypothyroid cases compared to euthyroid controls. Similarly, the NICU admission of newborn (22.3%, n=21), followed by Low APGAR score (11.8%, n=11), prematurity (5.4%, n=5) and jaundice (4.3%, n=4) and IUD (3.2%) were significantly (except IUD) more among over hypothyroidism compared to euthyroid mothers. The placental insufficiency and hypothyroidism leads to the pre-eclampsia and placental abruptions which would lead to preterm and prematurity with the fetal distress.

Similar to our study, the hyperbilirubinemia and fetal death was higher among the subclinical and overt hypothyroidism women was higher compared to euthyroid pregnant women. They documented fetal death of 5% subclinical women and 12.5% among overt hypothyroidism. The hyperbilirubinemia was documented 21.4% babies compared to babies born to euthyroid women (16.5%).[10]

Likewise, the NICU admission and the Low APGAR score were significantly more common among the Anti-TPO positive mothers compared to anti-TPO negative mothers. Overall, the fetal complications are more among the infant born to mother with subclinical/overt hypothyroidism compared to infant born to euthyroid mother. Untreated maternal hypothyroidism in the neonate can result in preterm birth, low birth weight and respiratory distress.

Neonates delivered from women with subclinical hypothyroidism are similar to infants of women with typical TSH values in birth weight. In infants of females with subclinical hypothyroidism, other conditions associated with prematurity were increased.(93) Some studies recorded no significant association between the TPO status and the infant birth weight and other studies documented increased likelihood of low birth weight infants born to TPO+ve mothers.[11]

Post-partum thyroiditis

In present study, total 242 patients were diagnosed as hypothyroid cases out of which lost to follow up were 37 and remaining 205 patients were followed. In this study 105 (51.08%) women became Euthyroid, 45 (21.94%) became Subclincal hypothyroid and 55 (26.98%) women became overt hypothyroid. Women 55 (52.38%) who were subclinically hypothyroid with anti TPO antibody negative who were treated turned out to be Euthyroid. Similar findings were documented by Dussault JH et al, who stated for the prevention of obstetric complications women with thyroid disorders should be closely monitored during pregnancy, and their newborn children should be closely monitored for thyroid dysfunction in the first months of postnatal life.[12]

Women who sought treatment had improved maternal and fetal outcome with decreased hypothyroid symptoms. Mothers who were levothyroxine, there was a general sense of well-being and less fatigue with a positive materal and fetal outcome. Untreated women had complications that had been documented as preeclampsia/eclampsia, placenta abruption, premature labor and PROM. It is documented that the untreated and undertreated women with hypothyroidism showed similar complications of during the pregnancy and its outcome with negative effect on growing fetus as the undiagnosed hypothyroidism during early trimester.

Follow up

Total 242 patients were diagnosed as hypothyroid cases out of which lost to follow up were 37 and remaining 205 patients were followed. In this study 105 (51.08%) women became Euthyroid, 45 (21.94%) became Subclincal hypothyroid and 55 (26.98%) women became overt hypothyroid. Women 55 (52.38%) who were subclinically hypothyroid with Anti TPO negative who were treated turned out to be Euthyroid.

Limitations

Limitation of our study is lack of follow-up. Therefore further longitudinal studies with large sample size should be conducted

CONCLUSION

ATA guideline 2011 recommended the trimester specific criteria of TSH estimation in which 2.5mIU/L was taken as a cut off for diagnosis of subclinical hypothyroidism. However various review research considered this trimester specific criteria too low leading to over diagnosis and increasing therapeutic burdening of patient with LT4 treatment. Therefore ATA revised their recommendation in 2017 raising S.TSH to 4mIU/L as a cut off.

Nevertheless, the prevalence of hypothyroidism in pregnancy continued to remain high owing to country's long standing iodine deficiency. The fetal NICU admission, Jaundice, Prematurity and Low APGAR score and IUD were significantly more among overt hypothyroid mothers. Present study strongly recommends routine thyroid screening should be done at the first antenatal visit of every pregnant woman to prevent any obstetric complications in women, growing foetus and event of delivery among the Indian population.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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