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Original Article

Obstetrics and Gynaecology Section

Thyroid Disorders in Pregnancy: An Exploratory Study

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ABSTRACT

Introduction: Thyroid disorders, mostly hypothyroidism, being one of the common diseases during pregnancy, if untreated, affect the neuro-psycho development of neonates. Many factors influence thyroid function tests in pregnancy; ethnic variations or different environmental conditions being one of them.

Aim: This study was done to find the prevalence of overt hypothyroidism, subclinical hypothyroidism, overt hyperthyroidism and subclinical hyperthyroidism in the pregnant women in all trimesters.

Materials and Methods: The present cross-sectional study was carried out by the Department of Obstetrics and Gynaecology and the Department of Physiology over a period of one year. Pregnant women who consented; with uncomplicated singleton pregnancy attending the antenatal check up for first time at antenatal OPD were included for the study. Blood samples for the estimation of FT4 and TSH were collected during a specific time period of the day. Serum FT4 and TSH estimation were done using an electro-chemiluminescent immunoassay technique.

Results: Amongst the total 505 enrolled pregnant ladies 428 were included in the study. There were (n=278, 65.0%), (n=146, 34.1%) and (n=4, 0.9%) women in their first trimester, second trimester and third trimester respectively. With TSH cut off at 2.5 mIU/L, prevalence of subclinical hypothyroidism was (n=159, 37.15%) and overt hypothyroidism was (n=48, 11.21%). Prevalence of subclinical hypothyroidism was (n=13, 3.04%) when TSH cut off 4.5 mIU/L was considered. There was no significant difference in prevalence of subclinical hypothyroidism or overt hypothyroidism in pregnant ladies in different trimesters. Prevalence of subclinical hypothyroidism and overt hypothyroidism was lesser in women in primi gravida than women in multi gravida. There were no women with subclinical hyperthyroidism or overt hyperthyroidism.

Conclusion: Hypothyroidism is more prevalent among the thyroid disorders during pregnancy. Prevalence of subclinical and overt hypothyroidism is more in multiparous pregnant women, irrespective of their trimesters.

Keywords: Overt hypothyroidism, Pregnancy, Subclinical hypothyroidism, Thyroid diseases

INTRODUCTION

Thyroid disorders remain one of the common problems during pregnancy, subclinical hypothyroidism being the most common [1]. Untreated hypothyroidism in pregnancy is not only associated with adverse maternal effects but it also has cognitive and neuro-developmental impairment in the neonates [2]. Prevalence of hypothyroidism was found to be more pronounced in the Asian countries than that in the west [3]. In the west, the prevalence of Overt Hypothyroidism (OH) and Subclinical Hypothyroidism (SCH) is 0.3-0.5% and 2-3% respectively [4,5], whereas the prevalence of OH (3-4%) and SCH (4.8 to 12%) is much higher in the East [6]. Though many concerned bodies like the American Thyroid Association (2017), the Endocrine Society (2012), the World Health Organization (WHO) have not recommended universal screening for hypothyroidism of all pregnant women, still the Indian Thyroid Society recommends screening of TSH levels in all pregnant women at their first antenatal visit [7].

Normal pregnancy is associated with an increase in thyroid hormone production, thyroid stimulatory effects of Human Chorionic Gonadotropin (hCG), an increase in renal iodine excretion, and an increase in thyroxine binding proteins. All of these factors influence thyroid function tests in the pregnant patients; therefore, these tests differ in healthy pregnant women than from those of healthy non pregnant women [8,9]. Furthermore, the reference ranges for the most widely applied tests, TSH and free thyroxine (FT4), may vary significantly in different populations. It may be also due to ethnic variations or different environmental conditions [10,11].

There is a lack of reported studies regarding the prevalence of thyroid disorders during pregnancy. Prevalence of hyperthyroidism is quite low compared to sub clinical hypothyroidism in pregnancy [2]. Prevalence of SCH varies widely in different parts of the country among pregnant women [6,12,13]. Also, there seems to be an association between iron deficiency and thyroid function [14]. Study reports that the eastern zone (Odisha, West Bengal and Bihar) has the highest prevalence of anaemia compared to the national level [15]. There are a very few reported studies regarding the thyroid dysfunction in pregnancy from the Eastern India [16], especially from Odisha [17]. Those few reported studies have included the first trimester pregnant women to find out the prevalence of hypothyroidism; thus, in the present scenario, it is a requisite to find the prevalence of hypothyroidism in pregnant women in all trimesters in Odisha. With this in mind, we planned the present study to find the prevalence of overt hypothyroidism, subclinical hypothyroidism, overt hyperthyroidism and subclinical hyperthyroidism in pregnant women of all trimesters.

MATERIALS AND METHODS

The present cross-sectional study was conducted in antenatal OPD of the Department of Obstetrics and Gynaecology in collaboration with the Department of Physiology, KIMS, Bhubaneswar, Odisha, over a period of one year (March 2015 to March 2016) after clearance from Institutional Ethics Committee. After obtaining an informed written consent, pregnant women with uncomplicated singleton pregnancy attending antenatal check up for the first time in antenatal OPD, were enrolled for

the study. Pregnant women with any other associated chronic diseases, positive past history or/and a positive family history of thyroid diseases or if taking any steroids or thyroid medicines were excluded from the study. On enrolment of the participants, a detailed history was taken and they were subjected to relevant general physical examinations as per the predesigned performa. Along with recommended routine, antenatal investigations (blood investigations and ultrasonography), blood for FT4 and TSH were done for all women included in the study. Blood samples were collected between 7 AM to 11 AM in OPD settings to avoid any variation due to circadian rhythm. Serum FT4 and TSH estimation were done in the NABL accredited Central laboratory of KIMS and PBM Hospital by using the electro-chemiluminescent immunoassay (eCLIA) technique where commercially available Advia Centaur XP Siemens kit (ADVIA Centaur® ReadyPack) was used. The intra-assay coefficients of variation for FT4 and TSH are 3% and 3.4% respectively.

Laboratory reference range for FT4 and TSH were 0.89-1.76 ng/dL and 0.1 to 2.5 mIU/L respectively. Trimester specific cut off values for TSH were used to diagnose hypothyroidism and hyperthyroidism. TSH values in the first, second and third trimester of pregnancy are 0.1-2.5 mIU/L, 0.2-3.0 mIU/L and 0.3-3.0 mIU/L, respectively [8]. Women with FT4 below the reference range along with elevated TSH and or TSH ≥10 mIU/L irrespective of the FT4 level were classified as having overt hypothyroidism while those having FT4 in the normal range with TSH level between 2.5 mIU/L to 10 mIU/L were diagnosed as having SCH [18]. Women with FT4 above the reference range along with TSH value <0.1 mIU/L were classified as having overt hyperthyroidism while those having FT4 in the normal range with TSH <0.1 mIU/L were diagnosed as having sub-clinical hyperthyroidism [19]. Participants were considered euthyroid when TSH and FT4 were in their normal range.

STATISTICAL ANALYSIS

The data was entered in Excel and exported to Strata version 13.1 using which the percentages of various outcome measures were calculated. Fisher's Exact Test was applied for analysis of the outcome measures and p-value <0.05 was considered as statistically significant.

RESULTS

Amongst the total 505 enrolled pregnant ladies 428 were included in the study. Seventy seven ladies were excluded due to either presence of multiple pregnancy or positive past/family history of thyroid disorders or presence of other associated chronic disorders. The mean age of all the included participants was 23.95±3.8 years. The median of duration of gestation was 12 weeks with range 6 weeks to 38 weeks. The mean and standard deviation of FT4 level is 1.44±0.32 ng/L. The TSH shows a nonparametric distribution, thus, the median of TSH level is 2.56 mIU/L with range from 0.48 to 17.7 mIU/L.

There were (n=278, 65.0%) women in first trimester, (n=146, 34.1%) in second trimester and (n=4, 0.9%) in third trimester. Among all the women with subclinical hypothyroidism, (n=102, 64.2%), (n=54, 34.0%) and (n=3, 1.9%) of women were in their respective 1st, 2nd and last trimester of pregnancy. The [Table/Fig-1] expresses the percentage value of thyroid disorders in pregnancy. None of the participants had subclinical hyperthyroidism or overt hyperthyroidism. There is no significant difference in the prevalence of subclinical hypothyroidism or overt hypothyroidism in pregnant ladies in different trimesters. Among the overt hypothyroidism subjects, eight of them had TSH ≥10 mIU/L. [Table/Fig-2] shows the significant difference in the prevalence of subclinical hypothyroidism and overt hypothyroidism among the pregnant ladies in their different gravida. Out of all the subclinical hypothyroidism women, (n=100, 62.9%) and (n=59, 37.1%) of the women were primi gravida and multi gravid respectively. Similarly, (n=23, 47.9%) of primi gravida and (n=25, 52.1%) of multi gravida women were among the overt hypothyroidism women. There were no participants with subclinical hyperthyroidism or overt hyperthyroidism. The prevalence of subclinical hypothyroidism was (n=13, 3.04%) when the TSH cut off was considered to be 4.5 mIU/L as stated by the American Association of Clinical Endocrinologists and the Endocrine Society [20].

DISCUSSION

In healthy pregnant women, though there occurs certain physiological changes like an increase in size of the thyroid gland and increase production of thyroid hormones but chance of thyroid dysfunction may be detected in many due to pathologic process. Thus, the assessment of thyroid function is usually done during pregnancy. However, accurate assessment of maternal thyroid function during gestation remains difficult, because of a downward shift of the TSH reference range during pregnancy compared to the non pregnant TSH reference range. Elevated levels of serum hCG during the first trimester directly stimulate the TSH receptor resulting in increase in thyroid hormone production; so the decrease in serum TSH is maximum observed during the first trimester of pregnancy [19]. In this study, we have found the prevalence of subclinical hypothyroidism and overt hypothyroidism in pregnant women of all trimesters coming for the first antenatal check up in the eastern part of India.

When 2.5 mIU/L is taken as the cut off in the TSH level, the prevalence of subclinical hypothyroidism was (n=159, 37.15%) and overt hypothyroidism was (n=48, 11.21%) respectively; whereas, the prevalence of the same was (n=13, 3.04%) when the TSH cut off is taken at 4.5 mIU/L. The prevalence reported from different studies conducted in different parts of India varies because of different cut off value of TSH level. Many of the studies had a lower prevalence of subclinical hypothyroidism when compared to our results [2,21]. Sahu MT et al., in 2010 showed the prevalence of subclinical hypothyroidism and overt hypothyroidism to be 6.47% and 4.58%, which is much lower than our findings [22]. A similar study (2015) from Haryana also reported the prevalence of the same to be 21.5% and 1.3%, which is much lower than ours [23]. While the prevalence of hypothyroidism (36.07%) from a multi-centric study conducted covering nine states (where Odisha was not included) was similar to that of our result, with the TSH cut off level 2.5 mIU/L; but the prevalence (13.13%) was quite higher than our study results (3.04%) when the cut off level is 4.5 mIU/L [24]. The reports from the Mandal RC et al., study from southern West Bengal, showed lower prevalence (32.94%) of subclinical hypothyroidism than our study reports with TSH cut off at 2.5 mIU/L, but a higher prevalence (13.92%) of the same when compared to our results with TSH cut off at 4.5 mIU/L [16].

Autoimmune thyroiditis, increasing age, iodine deficiency and micronutrient deficiency like iron and selenium are many of the

Thyroid disorders*	1st Trimester (n=278)	2nd Trimester (n=146)	3rd Trimester (n=4)	Total (n=428)	p-value (Fisher's Exact)
Subclinical hypothyroidism	102 (36.7%)	54 (37%)	3 (75%)	159 (37.15%)	0.34
Overt hypothyroidism	27 (9.7%)	20 (13.7%)	1 (25%)	48 (11.21%)	0.21
Euthyroid	125 (45%)	61 (41.8%)	0	186 (43.46%)	0.19

[Table/Fig-1]: Percentage value of thyroid disorders in pregnancy.
*No participants with subclinical hyperthyroidism and overt hyperthyroidism (not mentioned in the table)

Thyroid disorders*	Primi Gravida (n=297)	Multi Gravida (n=131)	Total (n=428)	p-value (Fisher's Exact)
Subclinical hypothyroidism	100 (33.7%)	59 (45%)	159 (37.15%)	0.04 †
Overt hypothyroidism	23 (7.7%)	25 (19.5%)	48 (11.21%)	0.003 †
Euthyroid	152 (51.2%)	34 (26.6%)	186 (43.46%)	0.000 †

[Table/Fig-2]: Percentage of subclinical hypothyroidism and overt hypothyroidism participants in different gravid.
*No participants with subclinical hyperthyroidism and overt hyperthyroidism, so not mentioned in the table, † Statistical significant

factors for high prevalence of subclinical hypothyroidism [25,26]. In the present study, high prevalence of the same may be due to not only autoimmune thyroiditis but also may be due to micronutrient deficiency like iodine and or iron deficiency. Iron deficiency anemia, which is prevalent in Odisha, remains one of the factors for high prevalence of subclinical hypothyroidism [27]. Similarly, presently reported high prevalent iodine deficiency in Odisha also may be one of the causes [28].

In the present study, the prevalence of overt hypothyroidism (11.21%) was much higher than studies reported from Delhi [6], Haryana [23], Telengana [29]. Higher prevalence of overt hypothyroidism may be because of the factor that we have included pregnant women with FT4 level below the reference range along with elevated TSH between 2.5 mIU/L to 10 mIU/L and / or TSH ≥10 mIU/L irrespective of the FT4 level according to National Guidelines for Screening of Hypothyroidism during pregnancy, Maternal Health Division Ministry of Health & Family Welfare Government of India, released in December 2014. None of the previous studies have included TSH ≥10 mIU/L irrespective of the FT4 level as an inclusion for overt hypothyroidism. Same may be the reason for a higher prevalence of subclinical hypothyroidism in many of the other studies [6,16,24] compared to ours when TSH cut off is taken to be 4.5 mIU/L.

In this study, there were only four women in their last trimester that attended first time antenatal checkup and of them 75% of them had subclinical hypothyroidism and 25% had overt hypothyroidism. Similarly, distribution of prevalence of subclinical hypothyroidism and overt hypothyroidism in women in different trimesters was not significantly different. Dhanwal DK et al., showed a similar finding to that of ours but with more women in the last trimester of pregnancy [24]. In contrast, reports from a study done in Sikkim showed higher prevalence of thyroid disorders in women in their 1st trimester compared to in the 2nd trimester [30]. Gayatri R et al., reported no association between gestational age and subclinical hypothyroidism [21]. Results from a Japanese study showed increase in the TSH with advancing pregnancy [31]. These variations may be due to different sample size and ethnic variations.

Prevalence of subclinical hypothyroidism and overt hypothyroidism was significantly different in pregnant women in their different gravida. In the present study, prevalence of subclinical hypothyroidism and overt hypothyroidism were lesser in women in primi gravida than women in multi gravida. In contrast to our results, a study by Dubey S et al., showed that prevalence of thyroid disorders was higher in the primi gravida women than multi gravida women [30]. Another South Indian study found no association between subclinical hypothyroidism and number of pregnancy [21]. The risk of the developing goiter in multiparous women was three times higher as compared to nulliparous women. The higher prevalence of the same in multigravida women in this study may be attributed to more iodine deficiency in this group and/ or endogenous hormonal changes during pregnancy [32].

Somehow. there was not even a single case of subclinical hyperthyroidism or overt hyperthyroidism reported in this study. Even though untreated hyperthyroidism is associated with significantly higher frequency of obstetric complications, frequency of the disorder is relatively low, occurring in only 0.5-2/1000 pregnancies. Similarly, prevalence of subclinical hyperthyroidism is also very low [22].

[Table/Fig-3] shows the comparison among different studies mentioned above.

Authors	Year and place	Subclinical	Hypothyroidism	Overt hypothyroidism
		Cut off 2.5 mIU/L	Cut off 4.5 mIU/L	
Present study	2017 (Bhubaneswar)	37.15%	3.04%	11.21%
Gayathri R et al., [21]	2009 (Chennai)	----	2.8%*	----
Dhanwal DK et al., [6]	2013 (Delhi)	----	14.3%	0.7%
Rajput R et al., [23]	2015 (Rohatak)	21.5%	----	1.3%
Mandal RC et al., [16]	2016 (South Bengal)	32.94%	13.92%	----
Dhanwal DK et al., [24]	2016 (9 States)	36.07%	13.13%	----
Dubey S et al., [30]	2017 (Sikkim)	8.0%	----	2.0%

[Table/Fig-3]: Comparison of present study findings with other studies from India.
*TSH Cut off >5 mIU/L

LIMITATION

Our study is the first of its kind to provide prevalence of hypothyroidism during pregnancy in women of Odisha. Among the few limitations of our study, one is, we did not estimate the anti-thyroglobulin antibodies and thus directly cannot say autoimmunity is the cause of hypothyroidism. Second, as it is a study from a single tertiary care center, representation of the sample may not be for whole of the state. So, future multi-centric study may be planned.

CONCLUSION

Hypothyroidism is more prevalent among the thyroid disorders during pregnancy. Prevalence of subclinical and overt hypothyroidism in pregnant women is high in this region of the country. Prevalence of the same is more in multiparous pregnant women irrespective of their trimesters.

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