PREVALENCE OF THYROID DISORDERS IN PREGNANCY AT A TEACHING HOSPITAL

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ABSTRACT

BACKGROUND

Thyroid disorders are the second most common endocrinological disorders seen in pregnant women. Thyroid hormone plays a crucial role in pregnancy both in the development of a healthy baby and in maintaining the health of the mother. Several studies have shown a rising prevalence of thyroid disease in India and in South Asian countries. The diagnosis of thyroid disease in pregnancy is difficult as many of the signs and symptoms of thyroid disease are also common to pregnancy.

The aim of the study is to determine the prevalence of thyroid disease in pregnant women.

MATERIALS AND METHODS

This is a hospital-based cross-sectional study. 333 antenatal women were screened in their first visit to the antenatal clinic by serum TSH, fT3, fT4. Statistical analysis of the results was done.

RESULTS

283 women out of 333 antenatal women screened were found to be euthyroid. 50 women were detected to be having thyroid disorder. 45 women had subclinical hypothyroidism, one woman had overt hypothyroidism and four women had subclinical hyperthyroidism. 4 women had hypothyroidism prior to pregnancy. The overall prevalence of thyroid disorders in pregnancy in our study was found to be 16.21%.

CONCLUSION

The prevalence was found to be high in our study and in several studies from India and in its neighbouring countries. This is probably due to iodine deficiency being prevalent in several areas in our country. The prevalence of subclinical hypothyroidism is high. This all the more stresses the need for universal screening of pregnant women for thyroid disease in our country.

KEYWORDS

Thyroid Disorder, Subclinical Hypothyroidism, Pregnancy, Prevalence.

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BACKGROUND

Thyroid disorders are the most common endocrinological disorders affecting women of childbearing age and typically manifest during reproductive years. They are the second most common endocrinological disorders found in pregnancy. Thyroid hormone plays a crucial role in pregnancy. Maternal thyroid disease during pregnancy can influence the pregnancy outcome and foetal development adversely. Pregnancy is associated with significant, but reversible changes in maternal thyroid physiology. Inadequate adaptation to these changes results in thyroid dysfunction. There is a moderate increase in the size of thyroid gland by 10-20%.[1] Oestrogen mediated increase in the levels of thyroid-binding globulin results in a larger volume of distribution of thyroid hormone in pregnancy. There is an increase in urinary iodine excretion due to increase in the glomerular filtration rate and increase in the deiodinase activity of the placenta, which increases the thyroid hormone metabolism. There is a decrease in the level of Thyroid-Stimulating Hormone (TSH) with an increase in human chorionic gonadotropin concentration. Thus, pregnancy is a stress test for thyroid, resulting in hypothyroidism in women with limited thyroidal reserve or iodine deficiency.

Maternal thyroxine is important for foetal neural development throughout the pregnancy. Before birth, the foetus is entirely dependent on the mother for thyroid hormone until the foetal thyroid gland becomes functional by 8-10 weeks of gestation. The maternal thyroid hormones transferred through the placenta is the main source for foetal growth and development. Thyroid hormone is critical for normal foetal brain development, neuronal multiplication, migration and structural organisation. A lack of adequate maternal thyroid hormone may result in irreversible effects and maybe harmful to the foetal brain development and may lead to poor cognitive development and mental retardation in the child. Haddow et al[2] showed that 7 to 9 year old children of women known to be

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hypothyroid during gestation showed impaired psychological development when compared to children of same age whose mothers had normal thyroid function during pregnancy. Vermiglio et al[3] observed that attention deficit and hyperactivity disorder were more common in the children born to mothers with early gestational hypothyroxinemia.

Thyroid disorders include Subclinical Hypothyroidism (SCH), Overt Hypothyroidism (OH), subclinical hyperthyroidism and overt hyperthyroidism, isolated hypothyroxinemia. The prevalence of subclinical hypothyroidism (raised TSH and normal or low T4) is 2-2.5%.[4] Endemic iodine deficiency is the most common cause of hypothyroidism worldwide.[4] In iodine sufficient areas, the most frequent cause of hypothyroidism is autoimmune thyroid disease (positive thyroid peroxidase antibodies and or thyroglobulin antibodies). Thyroid autoantibodies are detected in nearly 50% of pregnancies with SCH and 80% with OH.[1]

Overt hypothyroidism occurs in about 5% of all women who have high TSH levels. It is associated with a prevalence of 0.3%-0.5%.[4] It is well established now that untreated maternal overt hypothyroidism and subclinical hypothyroidism are associated with adverse foetal and obstetric outcomes.[1] They include miscarriages, anaemia in pregnancy, preeclampsia, abruptio placenta and postpartum haemorrhage while intrauterine death,[5] premature birth,[6] low birth weight,[7] increase in neonatal respiratory distress and more admissions to NICU have been described in babies born to mothers with hypothyroidism. There is a greater prevalence of SCH in women who delivered before 32 weeks.[8] There is even an association between thyroid autoimmunity and adverse obstetric outcome, which is independent of thyroid function.[8] Higher maternal TSH levels even within the normal reference range are associated with an increased risk of miscarriages,[9] foetal and neonatal distress and preterm delivery.[10] Treatment of overt hypothyroidism has been shown to prevent the obstetric and neonatal complications. R. Negro et al[11] showed a significant reduction in adverse obstetric outcome even in low-risk women who were screened for subclinical hypothyroidism. Recently, it was concluded that an elevated TSH at 36 weeks of gestation in an otherwise healthy woman was a predictor for breech presentation at term and increased risk of the foetus presenting in a breech position by two and a half times that of an individual with normal TSH levels at 36 weeks of gestation.[12] Recent studies[13,14] reported that caesarean section for foetal distress was significantly high among women with subclinical hypothyroidism. Higher incidence of foetal distress in hypothyroid women may be attributed to the irreversible placental effect of abnormal thyroid status along with thyroid peroxidase antibodies.

The prevalence of hyperthyroidism (undetectable or low TSH, elevated fT4 levels) in pregnancy is around 0.1-0.4%.[4] It causes maternal complications such as miscarriage, placental abruption, preterm delivery, preeclampsia and neonatal hyperthyroidism. Subclinical hyperthyroidism (normal circulating levels of T4 and T3, but subnormal TSH levels) occurs in 1.7% of pregnant women and is not associated with adverse pregnancy outcomes.[4] Isolated maternal hypothyroxinemia has no adverse effects on perinatal outcome.[15]

The prevalence of thyroid disease among pregnant women varies from 2.5% in the western countries to 26% in India.[4,16-21] Their prevalence shows wide geographic variation due to ethnicity, different cut-offs of TSH used, iodine intake, presence of goitrogens in the diet, prevalence of antithyroid antibodies, deficiency of micronutrients like selenium, iron in the diet. Prevalence of thyroid disease is more in Asian countries. The most recent recommendations of the American Thyroid Association do not endorse universal screening of pregnant women for thyroid diseases.[1] In India, the entire population is prone to iodine-deficiency disorders due to deficiency of iodine in the soil of the subcontinent and consequently the food derived from it.[22] Vizianagaram district is endemic to iodine deficiency.[23] So, this study was undertaken to assess the prevalence of thyroid disease among pregnant women as there are no similar studies in this region.

MATERIALS AND METHODS

Type of study- This is a hospital-based cross-sectional study.
Site of study- This study was undertaken in the Department of Obstetrics and Gynaecology, Maharajah's Institute of Medical Sciences, Nellimarla, Vizianagaram District, Andhra Pradesh, after obtaining institutional ethics committee approval.
Study period- May 2014 to April 2016.

Inclusion Criteria

All the pregnant women in their first antenatal visit irrespective of gestational age.

Exclusion Criteria

1. Pregnant women with medical disorders like diabetes and hypertension.
2. Pregnant women with multiple pregnancy.
3. Those not willing to participate in the study.

History regarding age of the pregnant woman, socioeconomic status, gestational age, past and present medical history, treatment history in case of preexisting thyroid disease, family history, personal history and obstetric history was taken through a structured questionnaire. Informed consent of the pregnant women was taken. Apart from routine tests, 5 mL of fasting venous blood sample was taken and analysed for fT3, fT4 and TSH levels by chemiluminescent immunoassay method. The reference ranges of the test values taken in this study were as per the guidelines of American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. As per these regulations, if trimester specific ranges for TSH are not available in the laboratory, the following normal reference ranges are recommended. 1st trimester- 0.1-2.5 mIU/L, 2nd trimester- 0.2-3.0 mIU/L, 3rd trimester- 0.3-3 mIU/L; fT4 level of 0.7-1.8 ng/mL and fT3 level of 1.7-4.2 pg/mL was taken as normal.

Based on these values, pregnant women were classified into-

Subclinical hypothyroidism- Elevated serum TSH with normal fT3 and fT4 level.

Overt hypothyroidism- High serum TSH with fT3 and fT4 less than normal range.

Subclinical hyperthyroidism- Low serum TSH with normal fT3 and fT4 level.

Overt hyperthyroidism- Low serum TSH with fT3 and fT4 more than normal range.

Subclinical and overt hypothyroid women were treated with Eltroxin in consultation with endocrinologist. Those with preexisting thyroid disease increment in the dose of Eltroxin was done as advised by the endocrinologist.

Statistical Analysis- The results were analysed by statistical package for social sciences 16 using mean, median and chi-square test. P value was calculated to assess the association between the variables tested. A P value of less than 0.05 was taken as significant.

A total of 333 antenatal women were screened. 42% of the women with thyroid disease belonged to 21 to 25 years age group (Table 1). 54% of women with thyroid disease were multigravidae (Table 2). 38% of women with thyroid disease were detected in first trimester, 38% in second trimester and 24% in third trimester in the present study (Table 3). Out of the 333 women screened, 283 women were euthyroid. 46 women had high levels of TSH. Out of these, 45 women had subclinical hypothyroidism with a prevalence rate of 13.51% and one woman had overt hypothyroidism with a prevalence rate of 0.3%. Four women showed low levels of TSH with normal fT3 and fT4 values. Thus, the prevalence of subclinical hyperthyroidism was found to be 1.2%. No cases of overt hyperthyroidism were detected. Four women had hypothyroidism prior to pregnancy. So, the overall prevalence of thyroid disorders among pregnant women in the present study was found to be 16.21% (Table 6).

RESULTS

Age in Years	Number of Women Screened (%)	Number of Women with Normal Thyroid Profile	Number of Women with Abnormal Thyroid Test (%)
16-20	78 (23.35%)	64	14 (28%)
21-25	161 (48.34%)	140	21 (42%)
26-30	77 (23.05%)	65	12 (24%)
31-35	13 (3.89%)	11	2 (4%)
36-40	4 (1.19%)	3	1 (2%)
Total	**333**	**283**	**50 (15.01%)**

Table 1. Age Wise Distribution of Pregnant Women Screened

Chi-square=1.35, P value=0.8528 (not significant).

Parity	Number of Women Screened (%)	Number of Women with Normal Thyroid Profile	Number of Women with Thyroid Disorder (%)
Primi	195 (58.55)	172	23 (46)
Multisecond Gravida	96 (28.82)	81	15 (30)
Third Gravida	28 (8.38)	18	10 (20)
Fourth Gravida	11 (3.29)	9	2 (4)
Fifth Gravida	3 (0.89)	3	0
Total	**333**	**283**	**50**

Table 2. Party Wise Distribution of Pregnant Women Screened

Chi-square=11.63, P value=0.0203 (significant).

Trimester	Number of Women Screened (%)	Number of Women with Normal Thyroid Profile	Number of Women with Thyroid Disorder n (%)
First	171 (51.19)	152	19 (38)
Second	125 (37.53)	106	19 (38)
Third	37 (11.07)	25	12 (24)
Total	**333**	**283**	**50**

Table 3. Trimester Wise Distribution of Pregnant Women Screened

Chi-square test-10.84, P value-0.004 (significant).

TSH level	Number of Women	%	Mean±SD
Normal	283	85	2.26±1.41
High- 1. Subclinical hypothyroidism 2. Overt hypothyroidism	45 01	13.8	5.11±1.74 3.48±0
Low- 1. Subclinical Hyperthyroidism 2. Overt Hyperthyroidism	4 Nil	1.2 -	0.05±0.03 -
Total	**333**	**100**	**-**

Table 4. Distribution of Serum TSH Levels

Age Group	Subclinical Hypothyroidism	Overt Hypothyroidism	Subclinical Hyperthyroidism	Overt Hyperthyroidism	Total
16-20	13	-	1	-	14
21-25	19	1	1	-	21
26-30	10	-	2	-	12
31-35	2	-	-	-	2
36-40	1	-	-	-	1
Total	**45 (90%)**	**1 (2%)**	**4 (8%)**	**Nil**	**50**

Table 5. Age Wise Distribution of Pregnant Women with Different Thyroid Disorders

Study	Place of Study	Prevalence Rate (%)
Present study	Vizianagaram District, A.P.	16.21
P.V. Bandela et al	Rayalaseema Region, A.P.	18.7
Rama Saraladevi et al	Warangal District, Telangana	11.6
V.R.M. Nabhi et al	Hyderabad District, Telangana	26
A. Singh et al	Hyderabad	8.25
A.S. Nangia et al	New Delhi	13.25
R. Rajput et al	Haryana	26.5

Table 6. Comparison of Prevalence Rates of Thyroid Disorders in Pregnancy in Different Studies

DISCUSSION

Out of the 333 women screened, 85% belonged to lower socioeconomic status and 78% belonged to rural areas. In a study by Pandit V Bandela et al,[24] the prevalence of thyroid disease was more in the tribal (37.5%) and rural women (10.8%), 42% of women with thyroid disease belonged to 21-25 years age group in the present study. This may be due to more women in this age group being screened for thyroid disease. This is comparable with the study done by Savitha S Konin et al.[25] Increasing maternal age is associated with a higher incidence of thyroid dysfunction in the present study though not statistically significant. The mean age of the antenatal women was 23±3.66 years in the present study.

195 women screened were primigravidae while 138 women were multigravidae. In the present study, 54% of the women who were detected to be having thyroid disorder were multigravidae, which is statistically significant. This may be explained by the increase in the prevalence of antithyroid antibodies with increasing age and parity. This is comparable with the study done by Sapana C Shah et al.[26]

38% of women with thyroid disease were detected in first trimester, 38% in second trimester and 24% in third trimester in the present study (Table 3). Many women were undetected till second and third trimesters. This is comparable with the studies done by Srinivas Rao et al at Hyderabad.[18] The association between thyroid disease and trimester was found to be statistically significant. This may be due to the physiological changes resulting in hypothyroidism in later stages of pregnancy in iodine deficient women who were euthyroid in first trimester.

The prevalence of thyroid disorders in pregnancy in the present study was found to be 16.21%, which is comparable with the studies done by Dhanwal DK et al[17] (14.3%) and Ajmani Sangita Nangia et al (12.7%).[27] But, a TSH value cutoff of 4.5 miu/L was taken in the study by Dhanwal DK et al.[17] The prevalence rate in our study is also comparable with the study of Pandit V Bandela et al (18.7%) done in Rayalaseema region of Andhra Pradesh.[24] In the present study, 1.2% of pregnant women had hypothyroidism prior to pregnancy. The prevalence of hypothyroidism was found to be 15.01% and hyperthyroidism was found to be 1.2%. This is comparable with the prevalence rate obtained in the study by Ajmani Sangita Nangia et al[27] (12% and 1.25%, respectively). A high incidence rate of 15.01% in our study maybe due to iodine deficiency in Vizianagaram district. A recent study by Kumar A et al[28] showed that only 68% of the household of Vizianagaram district are using iodised salt. The prevalence of thyroid disease is found to be high in Asian countries especially in India. According to a recent study by C S Pandav et al,[22] the whole of Indian subcontinent is found to be deficient in iodine and iodine deficiency is the commonest cause of hypothyroidism in developing countries.

The limitation of our study is that we have not screened the antenatal women for antithyroid antibodies. However, studies done by A.S. Nangia et al[27] and Neelam Aggarwal et al[14] showed that 52% and 57% of hypothyroid women were positive for antithyroid peroxidase antibodies, respectively. In a study by Alpana Singh et al,[20] 36.6% of hypothyroid

women had antithyroid peroxidase antibodies. 57% of women with subclinical hypothyroidism had thyroid peroxidase antibody positivity. Thyroid peroxidase antibody positivity has been found to be associated with adverse pregnancy outcomes such as preterm premature rupture of membranes, preterm labour, postpartum thyroiditis, recurrent miscarriage and postpartum depression. Permanent hypothyroidism develops in 20% to 40% of women following postpartum thyroiditis and is more likely with a higher TSH and/or thyroid antibody levels.[29] So, long-term follow up with annual thyroid function tests is recommended in these women. Maternal subclinical hypothyroidism, hypothyroxinemia and euthyroidism with elevated thyroid peroxidase antibody titres were all significant predictors of lower motor and intellectual development at 25 to 30 months.[30] Positive thyroid antibodies during pregnancy warrants treatment at a lower TSH level. Berbel et al[31] reported that a delay of 6 to 10 weeks in iodine supplementation of hypothyroxinemic mothers at the beginning of gestation increases the risk of neurodevelopmental delay in the progeny. So, screening for thyroid disease should be ideally be prenatal or at the earliest following conception so that treatment can be given promptly. TSH, fT4 and thyroid peroxidase antibodies maybe done as the initial screening test for thyroid dysfunction in pregnancy. The American Thyroid Association recommends high-risk targeted screening strategy at present.[1] This includes those who have a personal or a family history of thyroid disease, a personal history of type 1 diabetes or other autoimmune disorders. Clinical signs suggestive of thyroid disorders, goiter, thyroid antibodies, history of previous therapeutic head or neck irradiation, a history of miscarriage or preterm delivery or infertility. B Vaidya et al[32] in their study observed that with high-risk screening strategy at least one third of women are likely to be missed. Weiwei Wang et al[30] in their study concluded that a case finding strategy for screening thyroid function in high-risk group would miss about 81.6% of women with hypothyroidism and 80.4% of women with hyperthyroidism and in mildly iodine deficient areas. Thyroid function testing early in gestation seems to be only partly effective in identifying thyroid under function in pregnant women. In a study by Moleti M et al,[33] it was suggested that if screening is limited to first trimester over 40% of pregnant women with hypothyroidism could be missed. However, there is no evidence to recommend TSH monitoring in every trimester for all antenatal women, a case can be made for targeted screening at 26 to 32 weeks.[34] Dosiou et al,[35] Donnay CS et al,[36] L.D. Premawardhana et al[37] observed that universal screening was cost saving in the scenario of untreated maternal hypothyroidism resulting in low child intelligence with levothyroxine therapy being preventive. Thung SF et al[38] concluded that screening for subclinical hypothyroidism in pregnancy will be a cost-effective strategy under a wide range of circumstances. Universal screening is to be considered especially in our country with a high prevalence of hypothyroidism in pregnancy.

Dietary iodine deficiency during pregnancy leads to hypothyroxinemia. Iodine deficiency is the leading cause of preventable intellectual deficit.[1] While severe iodine deficiency results in cretinism, mild-to-moderate iodine deficiency has been associated with attention deficit and hyperactivity disorders. So, iodine supplementation should be started prenatally or at least at the earliest in pregnancy. The beneficial effects of iodine on offspring development appeared to be lost if supplementation is started after 10 to 20 weeks.[1] WHO recommends 250 mcg/day of iodine for pregnant and lactating women. Medications like iodine-containing antiasthmatic drugs and expectorants are to be prescribed carefully. Sustained iodine intake from diet and dietary supplements exceeding 500 to 1000 mcg/day should be avoided due to the risk of foetal hypothyroidism.[3] Selenium supplementation during pregnancy and in the postpartum period also reduces thyroid inflammatory activity and the incidence of postpartum thyroid dysfunction and hypothyroidism.[39]

CONCLUSION

Our study showed a high prevalence of thyroid disorders in pregnancy in Vizianagaram district. Majority of these being subclinical in nature. Universal screening becomes all the more relevant as they are asymptomatic. High thyroid peroxidase antibody positivity among Indians and iodine deficiency being prevalent in the whole of the subcontinent. Universal screening of all antenatal women for thyroid disorders should be implemented in our country starting right from the primary healthcare level. Women of reproductive age group need to be educated about prenatal care, consumption of iodised salt and early screening in pregnancy.

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