Original research article

Prevalence of hypothyroidism among pregnant women- a prospective study

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ABSTRACT

INTRODUCTION: Hypothyroidism especially sub clinical hypothyroidism is widely prevalent in pregnant women and the rate of detection, in a developing country like India, has not kept pace with the magnitude of the problem. Since hypothyroidism can be easily detected and treated, timely detection and treatment of the disorder could reduce the burden of adverse foetal and maternal outcomes

AIM : to find out the prevalence of hypo thyroidism in pregnant women in and around Coimbatore, western part of Tamilnadu, India.

MATERIALS AND METHODS: All patients attending antenatal outpatient department in three medical college hospitals in Coimbatore, Tamilnadu in South India are included in study .Their demographic details are collected with consent study period is between Jan 2018-Dec2018

RESULTS : Total number of patients screened 32,871 The prevalence of hypothyroidism during pregnancy is estimated is 7.5%(n=2419), of which overt hypothyroidism is(n= 493)1.5%,subclinical hypothyroidism is (n=1926) 6% .of which Autoimmune thyroiditis is (n=611) 2%

CONCLUSION: Hypothyroidism in pregnancy needs early detection, prompt initiation of treatment, adequate follow-up and most importantly, sufficient education of the doctors and the patients regarding this curable condition

KEY WORDS: PREGNANCY, SUB CLINICAL, HYPOTHYROIDISM

INTRODUCTION

Thyroid physiology is perceptibly modified during normal pregnancy. These alterations take place throughout gestation, help to prepare the maternal thyroid gland to cope with the metabolic demands of pregnancy, are reversible post-partum and the interpretation of these changes can pose a challenge to the treating physician.

The most notable change is the increase in thyroxine-binding globulin (TBG). This begins early in the first trimester, plateaus during mid gestation, and persists until shortly after delivery. This is due to stimulation of TBG synthesis by elevated maternal oestrogen levels, and more importantly, due to a reduced hepatic clearance of TBG because of oestrogen-induced sialylation. This increased TBG concentration leads to an expansion of

the extra-thyroidal pool and results in elevated total T3 and T4 levels due to an increase in maternal thyroid hormone synthesis. Maternal thyroid hormone synthesis is also

increased due to an accelerated renal clearance of iodide resulting from the increased maternal glomerular filtration rate.

Enhanced metabolism of T4 in the second and third trimesters, due to a rise in placental type II and type III deiodinases, which convert T4 to T3 and T4 to reverse T3 and T2 respectively, act as further impetus to T4 synthesis. Plasma iodide levels decrease due to both increased thyroxine metabolism and increased renal iodide clearance. All these changes lead to an increase in the size of the thyroid gland in 15% of pregnant women, which returns to normal in the post-partum period. Serum hCG has intrinsic thyrotropic activity, which increases after fertilization and peaks at 10 to 12 weeks. Hence, in the first trimester , free T3 and T4 levels increase slightly and TSH levels decrease in the first trimester with a readjustment in the second and third trimesters, when hCG levels decrease. As a consequence, cut-offs to determine hypothyroidism in pregnancy are different in the first trimester and the rest of the pregnancy.

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Children born to mothers with iodine deficiency fared even worse , with a greater than 10-point average deficit in global IQ and quite a few also had attention deficit hyperactivity disorder.

Subclinical hypothyroidism is defined as increased TSH with normal concentrations of FT4 and FT3. The prevalence of subclinical hypothyroidism during pregnancy is estimated to be 2% to 5%. It is almost always asymptomatic. Women with subclinical hypothyroidism are more likely than euthyroid women to have TPO antibody positivity (31% compared to 5%).

Characteristics	**Category**	**Frequency**
Age (years)	Below 20	9,261
	21-29	12,381
	30-39	10,288
	≥ 40	941
Parity	primi	16,680
	multi	16,191
Body Mass Index (kg/m^2)	19-25	18,314
	>25	14,557
Total number of AN VISITS	0-2	9,877
	3-5	8,377
	6-10	9,834
	>10	4,783

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Characteristics	Category	Frequency
Daily Exercise	Yes	3,510
	No	29,361
Family Type	Nuclear	30,361
	Joint	2,510
Family Income in rupees P M	≤ 10,000	29 515
	>50,000	3 356
Hypothyroid		493
Sub clinical Hypo thyroid among study population	1315	

Aetiology is similar to overt hypothyroidism. Since multiple studies have shown that subclinical hypothyroidism is associated with an adverse outcome for the mother and offspring, most guideline s recommend thyroxine replacement in women with subclinical hypothyroidism. However, while thyroxine treatment has been shown to improve obstetrical outcome, it has not been proven to modify long-term neurological development in the offspring.

The prevalence of hypothyroidism during pregnancy is estimated to be 0.3–0.5% for overt hypothyroidism and 2–3% for subclinical hypothyroidism. Autoimmune thyroiditis is the commonest cause of hypothyroidism during pregnancy .Other causes include radioiodine ablation of thyroid while treating hyperthyroidism or thyroid cancer, surgery of the thyroid tumours and rarely , central hypothyroidism including lymphocytic hypophysitis or ectopic thyroid and drugs like Rifampicin and phenytoin which accelerate thyroid metabolism. However, worldwide, iodine deficiency still remains one of the leading causes of hypothyroidism, both overt and subclinical.

DISCUSSION:

Multiple studies have dwelt upon the risk of miscarriage in patients with autoimmune thyroid disease. While causality has not been established and these antibodies may only be a marker for autoimmune mediated recurrent miscarriage, more evidence is needed before dismissing antibody positivity as a cause of adverse pregnancy outcomes. Increased perinatal mortality and large-for-gestational-age infants have also been observed in a few studies.

Euthyroid women with positive thyroid peroxidase (TPO) antibodies undergoing *in vitro fertilization* (IVF) have also been reported to have higher miscarriage rates. A study by Negro *et al*., reported an association between thyroid antibody positivity and preterm delivery in euthyroid women and a possible association with neonatal respiratory distress.

Another study by Mannisto *et al*., found that thyroid dysfunction and antibodies during pregnancy seem to predict later thyroid disease. Moreover, overt hypothyroidism seemed to predict a later risk of diabetes Negro *et al* in a pioneering study, found that LT4 administration in euthyroid pregnant women with autoimmune thyroid disease decreased the rates of negative obstetric outcomes in women with a TSH value greater than 2.0 mIU/litter and/or a high titre of thyroid antibodies. In view of the negative maternal and foetal outcomes of hypothyroidism, carefully monitored thyroid hormone treatment of TPO antibody positive pregnant patients might be a prudent measure.

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Thyroid function tests are the mainstay. Serum TSH elevation indicates primary hypothyroidism, and serum free T4 levels subclinical and overt hypothyroidism. Free hormone levels are estimated, as total hormone levels are elevated due to changes in TBG levels. “Trimester-specific” ranges are in vogue for TSH with an upper limit of 2.5 μiu/ml in the first trimester (due to the stimulatory effects of hCG) and 3 μiu/ml in the second and third trimesters.[19] Autoimmune origin is confirmed by measuring TPO and thyroglobulin (TG) antibodies.

Administration of levothyroxine is the treatment of choice for maternal hypothyroidism. Pregnant women need larger doses due to the rapid rise in TBG levels resulting from the physiological rise in oestrogen, the increased placental transport and metabolism of maternal T4 and the increased distribution volume of thyroid hormones. During pregnancy, the full replacement thyroxine dose is around 2–2.4 μg/kg / day. In severe hypothyroidism, for the first few days, a thyroxine dose twice the estimated final replacement daily dose may be given, to rapidly normalize the extra thyroidal thyroxine pool before reducing to the final replacement dose. Women who already on thyroxine prior to pregnancy usually need to increase their daily dosage, on an average, by 30-50% above preconception dosage. Dose of thyroxine also depends on the aetiology of hypothyroidism with disorders with very little residual tissue, like radioiodine ablation and extensive thyroid surgery requiring a greater increment in thyroxine dosage than women with Hashimoto's thyroiditis, who usually have some residual thyroid tissue.

Serum free T4 and TSH levels should be measured 1 month after the initiation of treatment. The thyroxine dose should be titrated to reach a serum TSH value less than 2.5 mIU/liter, while maintaining free T4 levels in the high normal range. Women should be followed up every 4–6 weeks with free T4 and TSH value, till delivery, to facilitate periodic adjustment of LT4 supplementation. If hypothyroidism has not been diagnosed until the end of the first trimester, offspring may display impairment in final intellectual and cognitive abilities, thus underscoring the importance of early diagnosis and treatment.

After delivery, most women should decrease thyroxine dosage received during pregnancy, over a period of approximately 4 wk postpartum. Post-partum, two patterns of thyroid dysfunction can be discerned: (i) postpartum thyroiditis characterized by transient hyperthyroidism or transient hyperthyroidism followed by transient or rarely permanent hypothyroidism, (ii) and a postpartum exacerbation of chronic Hashimoto's thyroiditis leading to transient or permanent hypothyroidism. The hyperthyroid phase of postpartum thyroiditis, is treated with a beta-adrenergic antagonist drugs. Transient hypothyroidism is treated with T4, which may be continued till six months and then tapered to determine if the hypothyroidism is permanent. Thyroid function tests should be monitored for at least 6 months after delivery. recent research has highlighted the adverse effects of mild to moderate maternal hypothyroidism on maternal health in addition to fetal cognitive development, bringing universal screening into sharp focus once again.

A recent study by Vaidya *et al*.,reported that screening only women considered “high risk” would miss 30% of women with overt or subclinical hypothyroidism , suggesting that universal screening is better than screening only high risk women. Another study by Negro *et al*. evaluated reduction in adverse pregnancy outcomes following treatment in those women identified by universal screening vs. targeted case finding for thyroid dysfunction in pregnancy. Universal screening, compared with case finding did not result in a decrease in adverse outcomes. Ostensibly, this study does not seem to be in favour of universal screening, but a closer examination reveals otherwise. This study divided women into two arms; universal screening arm, in which all the women were screened, (482 women with high risk and 1798 women with low risk) and the targeted case finding arm, in which only high-risk cases were investigated (454 women in high-risk group and 1828 women in

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the low-risk group). All the women identified to have hypothyroidism received levothyroxine replacement. Consequently, high risk women in both the universal screening and targeted case finding arms received treatment, while low risk women received treatment only in the universal screening arm. Low risk women in targeted case finding arm were not investigated and hence not treated.

In keeping with the predefined objective of the study, viz. "whether treatment of thyroid disease during pregnancy decreases the incidence of adverse outcomes and compare the ability of universal screening vs. case finding in detecting thyroid dysfunction", Negro *et al*., included outcomes of both the high risk and low risk women from both the arms, in the analysis of the study. This did not show any statistically significant reduction in adverse outcomes

However, comparison of only the 3600 "low-risk" patients across both the arms of the study reveals that rates of pregnancy-related adverse events were reduced by nearly 40% after detection and treatment, i.e., considerable benefit was derived by the low-risk women in the universal screening arm when compared to the low-risk women in the targeted case finding arm. This effect was large enough that approximately 40 low-risk women would require screening (and intervention) to prevent a single adverse pregnancy outcome, a number which is significant enough This once again indicates that universal screening followed by appropriate treatment of those detected to have hypothyroidism has an impact of reducing adverse pregnancy outcomes.

The "Controlled Antenatal Thyroid Screening Study," (CATS) by Lazarus *et al*., in the United Kingdom, is an ongoing 8-year prospective intervention trial seeks to determine whether universal screening of pregnant women (and levothyroxine treatment , when hypothyroid) prevents adverse outcomes. In this study, serum samples are obtained before 16 week s gestation, with half of the sera analyzed immediately for free T4 and TSH, and the other half frozen until delivery. Women with a free T4 below the 2.5th percentile and/or TSH above the 97.5th percentile would be given levothyroxine therapy. The main outcome measure is the development of the unborn child, measured at 3 yr of age. Once, the outcome data from this study filters in, it may perhaps give us a better understanding to the contentious issue of universal screening vs. targeted case finding. However, the recent spate of reports highlighting the advantages of universal screening and the propensity of targeted case finding to miss a sizeable number of cases, seem to give universal screening a definite edge over targeted case finding.

Congenital hypothyroidism, which occurs in approximately 1:2000 to 1:4000 newborns, is the most common treatable cause of mental retardation. There is an inverse relationship between the age at diagnosis and IQMost newborn babies with congenital hypothyroidism have few or no clinical manifestations of thyroid deficiency. The most common cause of congenital hypothyroidism is thyroid dysgenesis, followed by dyshormonogenesis, resistance to TSH, disorders in hormone transport, central hypothyroidism and transient congenital hypothyroidism

Screening of all newborns is now mandatory in the developed world and is catching on in most of the developing countries. Blood for screening is collected onto filter paper cards after heel prick, usually two to five days after delivery and sent to a centralized laboratory for testing. Two major screening strategies have evolved: (i) initial blood T4 assay, with follow-up TSH assay if the blood T4 value is below a certain cut-off (usually less than the 10th percentile); (ii) an initial blood TSH assay. Whatever may be the screening method, mandatory screening of all newborns, further evaluation where appropriate, and prompt initiation of treatment is absolutely essential.

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Recently, attention is being focused on utility of poor maternal iron status in predicting high TSH and low total T4 concentrations during pregnancy, especially in areas of borderline iodine deficiency. While causality has not been established, it is postulated that iron deficiency decreases the thyrotropic response to TRH, serum T3 and T4 levels, slows turnover of T3, and may reduce T3 nuclear binding Iron deficiency might cause impairment of the heme-dependent enzyme thyroid peroxidase, thereby limiting synthesis of thyroid hormones, which can lead to a reduction in circulating levels of total T3 and total T4 Iron repletion may reverse this hypothyroidism. More work is needed to elucidate a link between anemia, iodine, deficiency, autoimmune thyroid disease, and adverse outcomes in the mother and the foetus.

CONCLUSION

In conclusion, maternal hypothyroidism is a disorder with great potential to adversely affect maternal and foetal outcomes and is also associated with multiple other conditions which can affect maternal and foetal health. universal screening is better than screening only high risk women. If the condition is detected early, it is easy to treat, with very little detriment to the mother and the foetus. Hence, this condition needs early detection, prompt initiation of treatment, adequate follow-up and most importantly, sufficient education of the doctors and the patients regarding these objectives, the importance of this condition and the ease and advantages of prompt management.

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