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Original Research Article

A Observational Study on Effect of Subclinical Hypothyroidism in Pregnant Women in Our Population.

Pratibha[1], Radhika C[2], Shwetha S[3]

[1]Senior Resident, Department of Obstetrics, ESIC Kalaburagi
[2]Assistant Professor, Department of Obstetrics, ESIC Kalaburagi
[3]Senior Resident, Department of Obstetrics, ESIC Kalaburagi

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Corresponding author: Dr. Pratibha
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Abstract

Introduction: Thyroid dysfunction is second most common endocrine disorder affecting women of reproductive age group in pregnancy after Diabetes Mellitus. Pregnancy has a profound impact on the thyroid gland and its function.

Materials and Methods: This study was conducted in Department of Obstetrics and Gynaecology, CSS. All the antenatal patients attending OPD of this hospital fulfilling eligibility criteria of this study and giving consent were subjected to study.

Results: Out of the total 879 pregnant women during the period of study 116 pregnant women had subclinical hypothyroidism. Thus, as per the study the prevalence of subclinical hypothyroidism in pregnancy was 13.2%. SCH has significant effects on fetal and maternal health. Prevelence of presence Anti TPO antibodies in SCH mothers is 29% and prevalence of postnatal hypothyroidism in SCH mothers is 6.3%.

Conclusion: Incidence of SCH is high in pregnancy so universal screening should be done during preconceptional period and in early pregnancy period.

Keywords: Pregnancy, Hypothyroid, Diabetes Mellitus

Introduction

Thyroid dysfunction is second most common endocrine disorder affecting women of reproductive age group in pregnancy after Diabetes Mellitus. Pregnancy has a profound impact on the thyroid gland and its function. During pregnancy, the thyroid gland increases in size by 10% in iodine replete countries but by 20% to 40% in areas of iodine deficiency. Production of the thyroid hormones, thyroxine (T4), and Triiodothyronine (T3), increases by nearly 50%, in conjunction with a separate 50% increase in the daily iodine requirement due to increase in renal iodine excretion. There is an increase in thyroxine binding proteins and thyroid stimulatory effects of hCG (human chorionic gonadotropin). All of these factors influence thyroid function tests in the pregnant patient. The healthy thyroid adapts to these alterations through changes in thyroid hormone metabolism, iodine uptake, and the regulation of the hypothalamic-pituitary-thyroid axis [1]. Thyroid disorder is more common in pregnancy due to inadequate adaptation with above changes. Women with adequate iodine intake before and during pregnancy have adequate intrathyroidal iodine stores and have no difficulty in

adapting to the increased demand for thyroid hormone during gestation. In these women, total-body iodine level remains stable throughout pregnancy [2]. However, in areas of mild to moderate iodine deficiency, total-body iodine stores, as reflected by urinary iodine values, decline gradually from the first to the third trimester of pregnancy [3]. Subclinical hypothyroidism (SCH) in pregnancy is defined as a serum thyroid-stimulating hormone (TSH) concentration higher than the upper limit of the pregnancy-related reference range associated with a normal serum thyroxine (T4) and serum tri-iodothyronine (T3) level concentration without any symptoms. In pregnancy, overt hypothyroidism is seen in 0.2% cases and subclinical hypothyroidism (SCH) is reported to have a prevalence of 1-2% of all pregnancies [4,5]. The prevalence of hypothyroidism in pregnancy is around 2.5% according to the western literature. There are a few reports of prevalence of hypothyroidism during pregnancy from India with prevalence rates ranging from 4.8% to 11% and SCH is as high as 13.5% women [4,6,7]. In the majority of SCH, the cause is autoimmune thyroiditis but may also be due to iodine deficiency. Furthermore, most of the pregnant women are thyroid peroxidase antibody (TPO Ab) or thyroglobulin antibody (Tg Ab) positive. Increasingly, anti TPO Ab positivity adversely modulates the impact of maternal thyroid status (especially hypothyroidism) on the pregnancy and the developing fetus. Thyroid antibody positivity increases the risk of thyroid dysfunction following delivery and during the postpartum period. In children SCH (serum TSH concentration >5.5–10 mU/l) normalizes in >70% and persists in most of the remaining patients over the subsequent 5 years, but rarely worsens. There is a lack of studies examining the impact of SCH on the neuropsychological development of children under the age of 3 years. In older children, the evidence for an association between SCH and impaired neuropsychological development is inconsistent. Good quality studies examining the effect of treatment of SCH in children are lacking. During the last two decades advances in our understanding of thyroid physiology in pregnancy have led to the appreciation of the adverse effects of SCH on mother like anemia, abortion, preeclampsia, abruption placenta and preterm labour and the fetal complications like prematurity, low birth weight, still birth and perinatal death. There is an increase in the incidence of NICU admissions and respiratory distress syndrome. Also, Maternal hypothyroidism in the 1st trimester may be harmful for fetal brain development and leads to mental retardation and cretinism which includes impairment of mental and physical growth and development and has a negative impact on most organ system. Despite the known complications and adverse events due to thyroid abnormalities, there is ongoing debate regarding the need for universal screening for thyroid dysfunction during pregnancy. Current guidelines differ between aggressive case finding approach versus testing only symptomatic women or those with a personal history of thyroid disease or other associated medical condition. But now there is a unanimous consensus about the use of serum TSH measurement concerning the test to be applied for diagnosis of thyroid dysfunction. This test is widely reproducible, reliable, and inexpensive. Evaluation of test results require trimester specific reference ranges of TSH level in hypothyroidism [8].

Materials and Methods

Study area: This study was conducted in Department of Obstetrics and

Gynaecology, CSS. All the antenatal patients attending OPD of this hospital fulfilling eligibility criteria of this study and giving consent were subjected to study.

Study type: prospective comparative observational study

Study period: (April 2018 to July 2019)

Sample size: 879 mothers for calculation of SCH prevalence. 100 cases and 100 controls for comparative study.

Inclusion criteria:

1. Subclinical hypothyroidism detected for the first time in first trimester of pregnancy.
2. Singleton pregnancy
3. TSH cutoff in 1st trimester- >2.5 mIU/L to 10 mIU/L
4. Normal T3 and T4 level

Exclusion criteria:

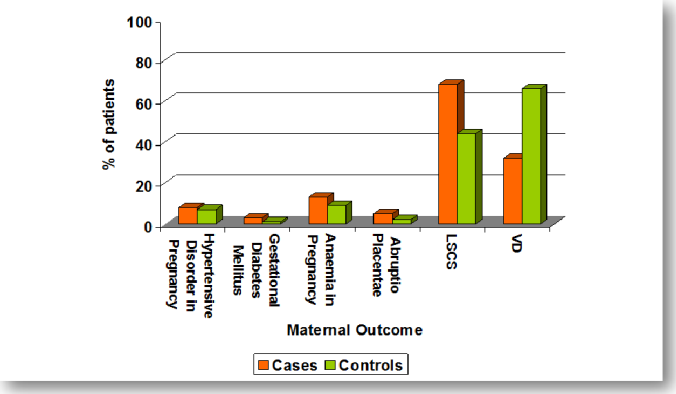
1. Multiple pregnancy
2. Patients presenting with overt hypothyroidism
3. Pre-existing thyroid disorder
4. H/O Preeclampsia in previous pregnancy
5. Chronic hypertension
6. H/O GDM or T2DM
7. Bad Obstetric History
8. Past history of thyroid radiation exposure
9. History of any thyroid surgery/ treated or untreated thyroid swelling/thyroid nodule

Results

Statistical Analysis

Statistical Analysis was performed with help of Epi Info (TM) 7.2.2.2 EPI INFO is a trademark of the Centers for Disease Control and Prevention (CDC). Descriptive statistical analysis was performed to calculate the means with corresponding standard deviations (s.d.). Test of proportion was used to find the Standard Normal Deviate (Z) to compare the difference proportions and Chi-square (χ^2) test was performed to find the associations. t-test was used to compare the means of the two groups. Fishers Exact test was used for in case of Chi-sqaure test was not applicable. Odds Ratio (OR) with 95% confidence interval (CI) had been calculated to find the risk factors. $p<0.05$ was taken to be statistically significant.

Out of the total 879 pregnant women during the period of study pregnant women had subclinical hypothyroidism. Thus, as per the study the prevalence of subclinical hypothyroidism in pregnancy was 13.2%. Out of the 116 patients with subclinical hypothyroidism 100 patients were randomly selected to be included in the study. Also out of the 763 patients with euthyroid 100 patients were randomly selected to be included in the study. Thus the total number of patients in the study was 200.



Comparison of maternal complications of the pregnant women with SCH and with euthyroid mothers

Table 1: Comparison of maternal complications of the pregnant women with SCH and with euthyroid mothers

Maternal outcomes	Status of thyroid of the mothers				z-value	p- value
	Sub-clinical Hypothyroidism (cases) (n=100)		Euthyroid (Controls) (n=100)			
	Number	%	Number	%		
Hypertensive disorder in pregnancy	8	8.0	7	7.0	0.26	0.78 NS
Gestational diabetes Mellitus	3	3.0	1	1.0	1.01	0.31 NS
Anaemia in Pregnancy	13	13.0	9	9.0	0.90	0.36 NS
Abruptio Placentae	5	5.0	2	2.0	1.15	0.25 NS
MOD						
LSCS	68	68.0	44	44.0	3.41	< 0.001 S
VD	32	32.0	66	66.0	4.80	< 0.001 S

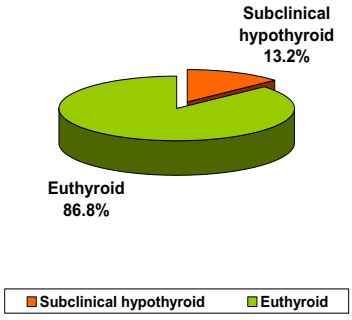
Table 2: Comparison of fetal complications of the pregnant women with SCH and with euthyroid mothers

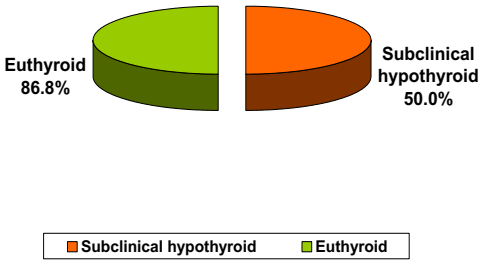
Fetal Outcomes	Status of thyroid of the mothers				z-value	p- value
	Sub-clinical Hypothyroidism (cases) (n=100)		Euthyroid (Controls) (n=100)			
	Number	%	Number	%		
Preterm delivery	13	13.0	8	8.0	1.15	0.25 NS
LBW	22	22.0	16	16.0	1.08	0.28 NS
NICU Admission	15	15.0	11	11.0	0.84	0.40 NS
APGAR Score at 5 mins	2	2.0	1	1.0	0.58	0.56 NS
Neonatal Hypo/ Hyperthyroidism	0	0.0	0	0.0	0.01	0.99 NS
Neonatal Hyperbilirubinaemia	16	16.0	10	10.0	1.26	0.21 NS
Miscarriage	9	9.0	5	5.0	1.10	0.26 NS

Table 3: Distribution of the patients in two groups

Group	Number of patients	%
Subclinical hypothyroid	116	13.2%
Euthyroid	763	86.8%
Total	879	100.0%

Out of the total 879 pregnant women during the period of study pregnant women had subclinical hypothyroidism. Thus, as per the study the prevalence of subclinical hypothyroidism in pregnancy was 13.2%.Out of the 116 patients with subclinical hypothyroidism 100 patients were randomly selected to be included in the study. Also out of the 763 patients with euthyroid 100 patients were randomly selected to be included in the study. Thus the total number of patients in the study was 200.



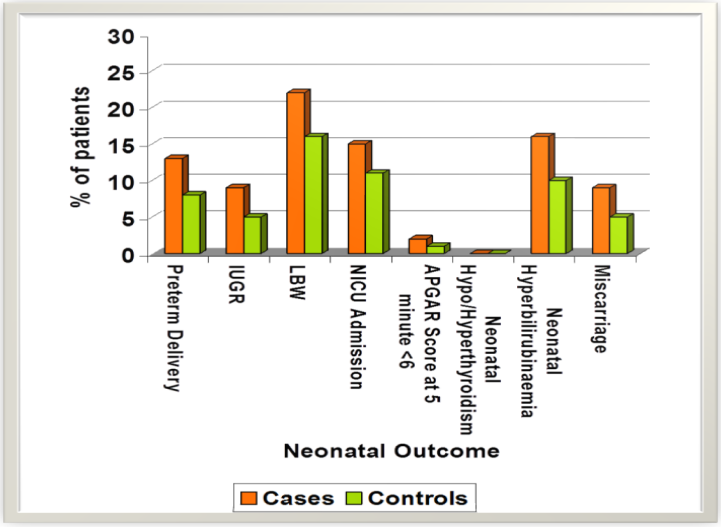


Neonatal outcome

Table 4: Distribution of patients according to their thyroid function test

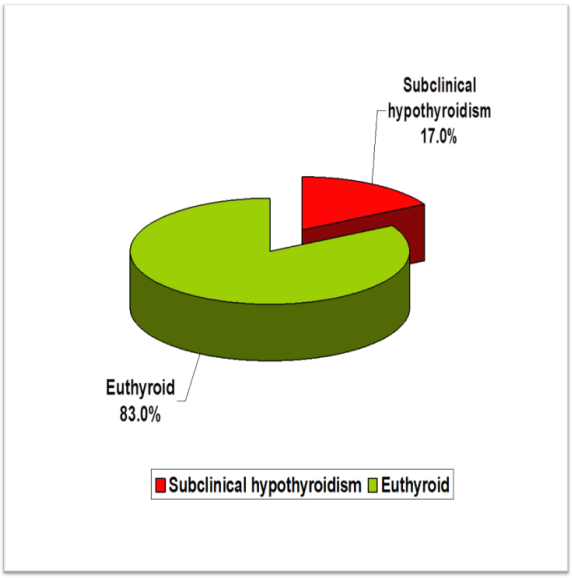
Diagnosis	Number	%
Subclinical hypothyroid	100	50.0%
Euthyroid	100	50.0%
Total	200	100.0%

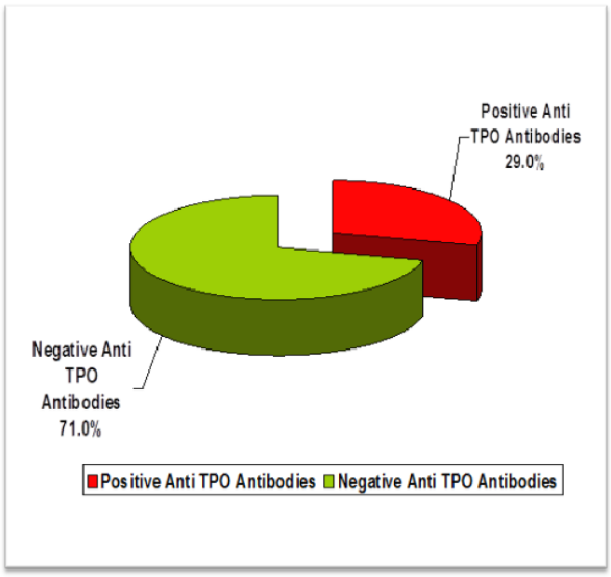
In the study 100 (50.0%) of the patients were having Subclinical hypothyroid and rest 100 (50.0%) of the patients were having euthyroid. Thus the patients in the two groups were in the ratio 1:1.

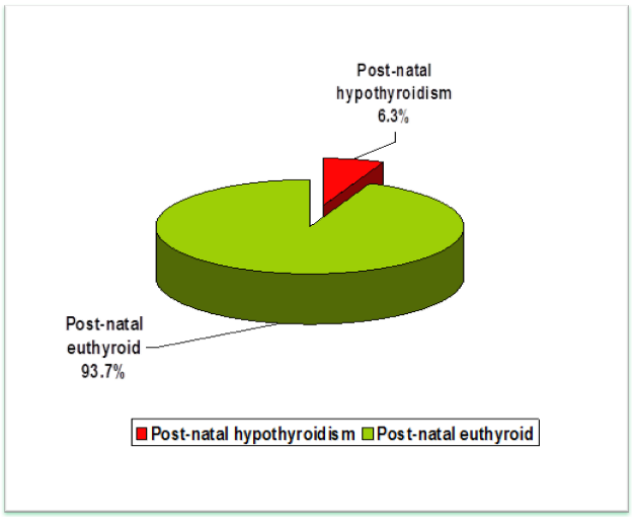


Prevalence of SCH:

Out of the total 588 pregnant women during the period of study 100 pregnant women had subclinical hypothyroidism. Thus as per the study the prevalence of subclinical hypothyroidism in pregnancy was 17.0%.







Prevalence of presence Anti-TPO Antibodies in SCH mothers:

Again out of the 100 pregnant women with subclinical hypothyroidism 29 cases were with positive Anti TPO Antibodies and so the prevalence of positive Anti TPO Antibodies among the pregnant women with subclinical hypothyroidism was 29.0%.

Prevalence of postnatal hypothyroidism in SCH mothers:

During follow-up at 6 month 63 mothers under study attended OPD and out the 63

Discussion

Our study presents the first data on the prevalence followed by foeto-maternal outcome in SCH women covering a

cases 4 cases had hypothyroidism. Thus the prevalence of post-natal hypothyroidism in antenatal subclinical hypothyroidism cases was 6.3%.

S-Statistically Significant

NS-Statistically not Significant

t-test showed that mean level of TSH of the patients with Subclinical hypothyroid was significantly higher than that of the patients with Euthyroid ($p<0.0001$).

But there is no significant difference between the mean level of FT3 and FT4 of the patients of the two groups ($p=0.18$).

population from eastern India. Most of the studies on hypothyroidism among pregnant women are from our western counterpart, which showed a prevalence

ranging from 0.23-3.9% for SCH and 0.3-1% for OH [9,10]. All these studies vary in their definition of hypothyroidism and sample size. Besides, there are differences in the iodine intake of the population screened. Few studies have been done among South Asian pregnant women reporting increased risk of thyroid dysfunction [11]. This study had been started with 954 pregnant women attending our ANC, as this is a tertiary care teaching institution many patients come from outstation area among them 879 patients register for study, for them serum TSH was done and Ft3, Ft4 and anti TPO antibodies done in patients with raised TSH level and prevalence of subclinical hypothyroidism calculated. The prevalence of SCH in our study population was 13.2 % (116) and euthyroid 86.8% (763). Dhanwal et al [12], Sreelata Et Al [13] and Ankita et al [14] study showed the prevalence of 14.3%, 14.7% and 12.5% respectively, which is comparable to our study. Prevalence of SCH and OH is likely to be higher in iodine deficiency regions [15,16]. The united states of America, United Kingdom are relatively iodine sufficient countries, there is adequate iodine supplementation and even pregnant population has sufficient iodine intake [15,16,17,18]. On the other hand, the situation of Indian pregnant women is different. Although Marwaha et al have reported that India has become iodine sufficient after two decades of salt iodisation, there is no normative data for thyroid function for healthy pregnant women of this country [19]. In this review of nine studies on the assessment of iodine nutrition of pregnant women in India, Yadav et al, identified significant iodine deficiency among pregnant Indian women [20]. According to the review, the household level coverage of adequately iodised salt consumption in pregnant women ranged from 59.5% to 95%. However, even a 95% household level coverage of adequately iodised salt may not lead to iodine sufficient in pregnant women [21]. This is because the current salt iodisation guidelines (15 ppm of iodine at consumer level) is designed to deliver only 150 micro gram/ L of iodine per day, whereas the dietary requirement of pregnant women are much greater (250 microgram/L). The current available data in India of pregnant women shows that India is iodine deficient as per the World Health Organisation/ United Nations International Childrens Emergency Fund Criterion [20]. This is probably the reason for the high prevalence of hypothyroidism observed in the present study. Among registered patients 100 patients of SCH (study group) and 100 patients of euthyroid (control group) are selected by computer generated randomised method for further study of comparison of fetomaternal outcomes of both groups. Among the patient with thyroid dysfunction, subclinical hypothyroidism was the most common thyroid disorder. In the present study, the mean BMI was 26.47±3.95 Kg/m2 of subclinical hypothyroid, 27.11±3.80 Kg/m2 of euthyroid patients, which was statistically not significant. According to the gravida and parity, primigravida was high in our study population (56% control group and 61% in study group) followed by multigravida (44% control group and 39%% in study group).and results are comparable with study Sreelatha et al 53% were primigravida in newly detected SCH and 46% euthyroid. it is quite similar to our study [22]. The mean TSH level in cases of subclinical hypothyroidism and euthyroid was 4.31±1.38 m IU/ ml and 1.51±0.59 m IU /ml respectively, mean level of TSH of the patients with Subclinical hypothyroid was significantly higher than that of the patients with Euthyroid ($p<0.0001$). comparable mean of Ft3 and Ft4 in both groups are comparable and statistically not significant. As per thyroid profile inference done within first trimester of gestation, patients of study group and control group are followed till delivery

with replacement dose of levothyroxine. In cases where any complications have developed, managed accordingly, then their obstetrical and perinatal outcomes are noted. TSH level has significantly declined during 2nd and 3rd trimester of pregnancy after levothyroxine supplementation (mean dose 60.86±21.62). Hypertension is one of the most important health problems related to both hypothyroidism and hyperthyroidism (1, 34). In our study the prevalence of preeclampsia was 12% in SCH group and 3% in euthyroid group pregnant women which is 3 times higher than euthyroid group and statistically significant which is comparable with study Wilson KL et al [24] (10.9%), Leung et al [23] (15%), Antika Tiwari et al (14.7%) [14]. In present study prevalence of GDM in SCH and euthyroid group was 3% and 2% respectively, which was statistically not significant. Similar results have been reported by Tudel et al study (4.9%) [25]. Cleary Goldman et al [26], who did not find any association between GDM and SCH (3.0% in euthyroid, 2.6% and 1.7% in SCH in first and second trimester). On the contrary, Casey et al [27] have reported a higher incidence of GDM in SCH. The study linked the high incidence with increased maternal age and body weight, because in their study group women with SCH were older and heavier than control group. [28]

Conclusion

Incidence of SCH is high in pregnancy so universal screening should be done during preconceptional period and in early pregnancy period. SCH has adverse effects on fetomaternal outcomes so early detection of cases with levothyroxine treatment should be initiated. Postnatal followup of mothers with SCH during antenatal period to be done as incidence of Postnatal thyroiditis is high

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