



STUDY OF PREVALENCE OF SUBCLINICAL HYPOTHYROIDISM AMONG PREGNANT WOMEN.

KEYWORDS

hypothyroidism, preterm, eltroxine, oligohydramnios, iugr.

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ABSTRACT

Objective: To study of prevalence of subclinical hypothyroidism (SCH) among pregnant women and analyse the fetomaternal effects.

Materials and methods: This study was made on 217 antenatal patients at GOVT ISO & KGH, MADRAS MEDICAL COLLEGE- CHENNAI , a prospective study.

Results: The prevalence of subclinical hypothyroidism was 12% in this study:

1. 11.5% of patients had moderate to severe anaemia.
2. 6.55% of babies have low APGAR (less than 7), 8.93% of babies had intra uterine growth retardation, 10.71% of babies had respiratory distress syndrome.
3. 11.5% had gestational hypertension, 9.5% had preeclampsia, 0.9% patients had eclampsia, 4% had abruption of placenta, 8.2% had oligohydramnios, and 9.2% had post partum haemorrhage.
4. There was no perinatal or maternal deaths in the study.

Conclusion: Even though the total number of maternal and perinatal complications is less, the results were in concordant with those reported in larger studies thereby validating the same.

INTRODUCTION:

During a normal pregnancy thyroid hormone production increases by 50% and play an important role in the development and function of both the foetus and the placenta. Subclinical hypothyroidism (SCH) is the commonest form of hypothyroidism in pregnancy. SCH is present, when the thyroid-stimulating hormone (TSH) is high but the thyroxine (T4) level is in the normal or low normal range and during pregnancy results in impaired neurodevelopment in offspring , preterm delivery, pre-eclampsia and postpartum thyroiditis.

Study by Mannisto et al showed that mothers with high TSH and are positive for thyroid antibodies had higher perinatal morbidity and mortality . Nambiar et al and Sahu et al in their study had reported a prevalence rate ranging from 4.8% to 11%. It seems that prevalence of hypothyroidism is more in Asian countries like India compared with the West

The strength of evidence relating maternal hypothyroidism to low IQ in children suggests strongly that screening thyroid function in early gestation with l -thyroxine intervention in appropriate women would be beneficial.

The reference range for normal values of thyrotropin (TSH) is established. The ATA 2011 and the ES 2012 guidelines recommend that normal TSH reference range should be 0.1-2.5 mIU/L, 0.2-3.0 mIU/L, and 0.3-3.5 mIU/L in the first, second, and third trimesters of pregnancy, respectively (values differ with different geographic region and ethnic origin).

The decision on whether to treat subclinical hypothyroidism diagnosed during pregnancy is controversial. The ATA 2011 and the ES 2012 guidelines, but not the American College of Obstetricians and Gynaecologists guidelines, recommend initiating levothyroxine therapy in these patients Guidelines from AACE, the Society of Maternal-Foetal Medicine, the American College of Obstetrics and Gynaecology, the Cochrane Collaboration, and the ATA all endorse a case finding strategy. Those who are in favour of universal screening

cite the increased prevalence of hypothyroidism subclinical during pregnancy, the inexpensive nature of the treatment, the wide availability of an inexpensive screening test, and the cost.

AIM OF THE STUDY

1. To access the prevalence of Subclinical Hypothyroidism in antenatal mothers.
2. To access the maternal outcomes of antenatal mothers with subclinical Hypothyroidism
3. To access the perinatal outcomes in children born to mothers with subclinical Hypothyroidism.

MATERIAL AND METHODS:

STUDY DESIGN

This is a prospective observational study which was conducted in the Institute of Social Obstetrics, Kasthurba Gandhi Hospital, Chennai. The study was approved by the ethical committee of the institution.

STUDY PERIOD

The study was conducted in the Institute of Social Obstetrics For a period of 12 months

STUDY POPULATION

The study was conducted in antenatal women who attended the outpatient clinic and were admitted in the ward at ISO & KGH Chennai during the above mentioned period. A total of 217 patients were included in the study who satisfied the inclusion and exclusion criteria.

INCLUSION CRITERIA:

- a) Age 18-35 years
- b) First visit to KGH
- c) Singleton pregnant women
- d) Patients who attend antenatal OP
- e) Patients who were admitted in antenatal ward.
- f) Patient whose thyroid status was not known.

EXCLUSION CRITERIA:

- a) Age < 18 Years, > 35 years
- b) Multiple pregnancy
- c) Patients who are already diagnosed as hyperthyroidism or hypothyroidism
- d) Patients who were on thyroxine, propylthiouracil, etc
- e) Hypoalbuminemia, Nephrotic syndrome
- f) Goitre
- g) History of type I diabetes

DEFINITION OF COMPLICATIONS:

Preeclampsia was diagnosed when a pregnant woman develops both of the followings: 1) systolic blood pressure > 140 mm Hg and/or diastolic blood pressure > 90 mm Hg at two separate visits with at least six hour interval in a previously normotensive woman; and 2) proteinuria ≥ 0.3 g/24 hours. Eclampsia defined as those with features of preeclampsia and associated seizures without any past history of seizure disorder. Low birth weight was defined as birth weight less than 2.5 kilogram. IUGR was defined as birth weight ≤ 10th percentile for its gestational age. Preterm delivery was defined as the delivery before the end of 37th week of gestational age. Neonates admitted for more than 72 hrs in NICU were considered hospitalized in NICU. APGAR score was determined by evaluating the newborn on five simple criteria on a scale from zero to two and summing up the five values. The resulting Apgar score ranges from zero to ten. The five criteria are appearance, pulse, grimace, activity, and respiration. The first min and five minute APGAR were calculated.

METHODOLOGY:

1. DATA COLLECTION

Antenatal mothers who were hospitalized for the first time in Institute of social Obstetrics, Kasthurba Gandhi Hospital, Chennai were selected for the study. After explaining in detail regarding the study, a written informed consent was obtained. Then a proper detailed history was obtained from the antenatal mothers including cold intolerance, asthenia, drowsiness, constipation, dry skin, hoarseness of voice etc pertaining to hypothyroidism. Questions were specifically asked about personal and family history (in first and second degree relatives) of thyroid disorders; personal and family history of other autoimmune diseases; and current and past treatment with antithyroid drugs, T4, radioiodine, or thyroid surgery. Duration of gestation was calculated from last menstrual period and verified by ultrasonography. A detailed examination of the patient is carried out including pallor, icterus, pedal edema, blood pressure, pulse, examination of the cardiovascular, respiratory, neurological systems, and per abdomen and per vaginal findings were recorded.

All women had a blood sample obtained at the first visit. Under sterile precautions 4ml of blood obtained as an early morning fasting sample and was sent for free T3, free T4, and TSH analysis. Serum TSH and FT4 were measured using a third-generation electrochemiluminescence immunoassay.

Patients who were admitted for delivery and were seen for the first time in our hospital without prior thyroid status were included in the study and were followed up after delivery. The maternal and foetal outcomes of those patients were recorded.

DATA ANALYSIS

To classify as subclinical hypothyroidism, serum TSH <2.5mIU/l was taken as cut off in first trimester and TSH > 3 mIU/ml in the second and third trimester with normal free T4 levels.

Pregnant women who are diagnosed as having subclinical hypothyroidism will be referred to endocrinology department for further management were they received l-thyroxine. All Pregnant women enrolled in the study were ensured routine standard antenatal care.

STATISTICAL ANALYSIS:

Analysis was done using SPSS 18 (SPSS Inc., Chicago, IL, USA). Differences in demographic and clinical characteristics were analyzed in a descriptive way. Data were mentioned as mean ± SD or median. P value < 0.05 was considered as statistically significant.

RESULTS:

Association of Subclinical hypothyroidism with maternal and perinatal outcomes

Subclinical hypothyroidism was significantly associated with gestational hypertension. 9.95% of Euthyroid patients was associated with blood pressure >140/90mmHg whereas 23% of subclinical hypothyroidism patients had high blood pressure.

Table: association between TSH levels and blood pressure

	TSH Score					
	< 3		> 3		TOTAL	
	Number	Percent age	Number	Percent age	Number	Percent age
< 140/90	172	90.05	20	76.92	192	88.48
≥ 140/90	19	9.95	6	23.08	25	11.52
Total	191	100	26	100	217	100
Chi-square	3.87					
p-value	0.05					
Significant	Significant					

11 patients (5.76%) of euthyroid patients had pre eclampsia whereas 19.23% of subclinical hypothyroid patients had pre eclampsia.

Table: Association between TSH and OLIGOHYDRAMNIOS

Oligohydramnios	TSH Score					
	< 3		> 3		TOTAL	
	Number	Percent age	Number	Percent age	Number	Percent age
TRUE	11	5.76	7	26.92	18	8.29
FALSE	180	94.24	19	73.08	199	91.71
Total	191	100	26	100	217	100
Chi-square	13.48					
p-value	0.000					
Significant	Significant					

5.76% of euthyroid patient have oligohydramnios while 26.9% of subclinical hypothyroid patients had oligohydramnios. The association is statistically significant. (Chi square 13.48; p value <0.0001)

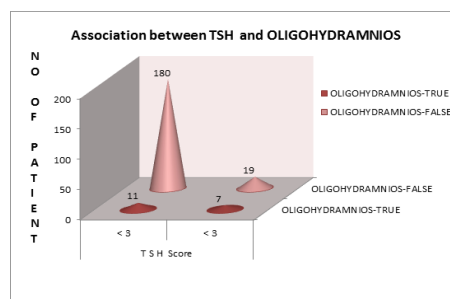


Figure: Association between TSH and OLIGOHYDRAMNIOS

Table: Association between TSH and BIRTH WEIGHT

	TSH Score					
	< 3		> 3		TOTAL	
	Number	Percent age	Number	Percent age	Number	Percent age
1.50 - 1.79	3	1.99	1	5.88	4	2.38
1.80 - 1.99	5	3.31	3	17.65	8	4.76
2.00 - 2.19	16	10.60	2	11.76	18	10.71
2.20 - 2.49	43	28.48	6	35.29	49	29.17

≥2.50	84	55.63	5	29.41	89	52.98
Total	151	100	17	100	168	100
Chi-square	9.81					
p-value	0.04					
Significant	Significant					

Among euthyroid patients 1.99%, 3.31%, 10.6%, 28.4%, 55.63% had their birth weight between 1.5 – 1.79kg, 1.8 – 1.99, 2 – 2.19, 2.2 – 2.49, >2.5 kg respectively. In Subclinical hypothyroid patients 5.88%, 17.65%, 11.76%, 35.29%, 29.41% had their birth weight between 1.5 – 1.79kg, 1.8 – 1.99, 2 – 2.19, 2.2 – 2.49, >2.5 kg respectively. The association between hypothyroidism and low birth weight is statistically significant. (Chi square value 9.81; p value 0.04)

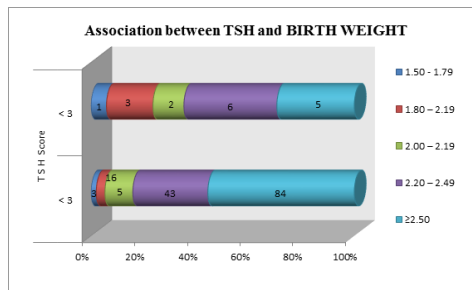


Figure: Association between TSH and BIRTH WEIGHT

4% of euthyroid patients have their APGAR less than 7 while comparing patients with subclinical hypothyroidism where it is 18.75%. The difference is statistically not significant (chi square 8.24; p value 0.08)

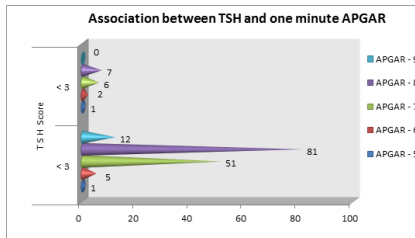


Figure: Association between TSH and one minute APGAR

Table: Association between TSH and IUGR

	T S H Score					
	< 3		< 3		TOTAL	
	Number	Percent age	Number	Percent age	Number	Percent age
TRUE	11	5.76	4	15.38	15	6.91
FALSE	180	94.24	22	84.62	202	93.09
Total	191	100	26	100	217	100
Chi-square	3.30					
p-value	0.07					
Significant	Not Significant					

5.76% of euthyroid patients had IUGR while 15.38% of subclinical patients had IUGR babies, and the difference was statistically not significant (chi square 3.30; p value 0.07)

Table: Association between TSH and Preterm births.

preterm	T S H Score					
	< 3		< 3		TOTAL	
	Numbe r	Percent age	Numbe r	Percent age	Numbe r	Percent age
TRUE	19	9.95	6	23.08	25	11.52
FALSE	172	90.05	20	76.92	192	88.48
Total	191	100	26	100	217	100

Chi-square	3.87
p-value	0.05
Significant	Significant

9.95% of euthyroid patients had pre term deliveries compared to 23% of subclinical hypothyroid patients, and difference is statistically significant (chi square 3.87; p value 0.05).

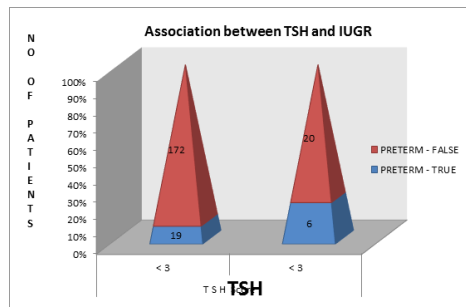


Figure: Association between TSH and IUGR

Table: Association of PRETERM birth and other parameters

Variable		PRETERM				Chi-square	P-value
		TRUE		FALSE			
		NO	%	NO	%		
IUGR	TRUE	4	16.00	11	5.73	3.63	0.06
RDS	TRUE	7	28.00	11	5.73	14.42	0.000
PPH	TRUE	6	24.00	17	8.85	5.36	0.02
APGAR	5	2	8.00	0	0.00	28.00	0.000
	6	2	8.00	5	3.55		
	7	16	64.00	41	29.08		
	8	5	20.00	83	58.87		
	9	0	00.00	12	8.51		

Among preterm deliveries 16% had IUGR (chi square 3.63; p value 0.06), 28% had RDS(chi square 14.42; p value <0.0001), 24% had post partum haemorrhage (chi square 5.36; p value <0.0001), 16% had APGAR less than 7 (chi square 28; p value <0.0001). All these associations are statistically significant except IUGR.

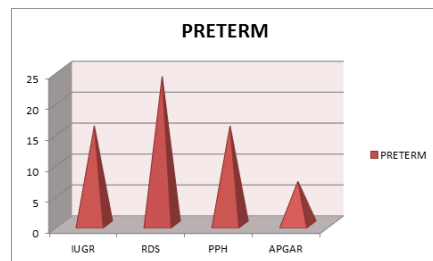


Figure: Association of PRETERM birth and other parameters

Among patients with oligohydramnios 43% had low birth weight (chi square 34.79; p value >0.0001), 50% had IUGR (chi square 3.63; p value 0.06), 72.2% had RDS (chi square 105; p value <0.0001), 38.8% had post partum haemorrhage (chi square 16.58; p value <0.0001), 23.52% had APGAR less than 7 (chi square 28.62; p value <0.0001). All these associations are statistically significant

DISCUSSION:

Thyroid disease has multiple deleterious impacts on pregnancy, the postpartum, and the developing foetus. The prevalence of subclinical hypothyroidism in antenatal mothers was 12%, Dhanwal et al (2013) in his study in North India showed that, there is a high prevalence of hypothyroidism (14.3%), majority of it being subclinical in pregnant women during first trimester, thereby necessitating routine screening.

65% of antenatal mothers were primigravida and 65% were admitted at term.. The reason for huge number of patients evaluated at Term is probably because of the Institute in which the study was conducted was a tertiary referral centre in Tamil Nadu

Only 15% of the pregnant women had their Hb greater than 11gm% and 11.5% of women had severe anaemia with Hb less than 7. Toteja et al showed the prevalence of anaemia to be 85% with 13% of patients having severe anaemia needing blood transfusion.

Subclinical hypothyroidism was significantly associated with gestational hypertension. 23% of subclinical hypothyroidism patients had high blood pressure and 19.23% had pre eclampsia. A total of only 2 eclampsia patients were present in the study, one had subclinical hypothyroidism and one patient is euthyroid(Mannisto et al study)

A total of seven patients had **abruption of placenta**, of which the incidence is 1.57% in euthyroid and 15% in subclinical hypothyroid patients. The difference is statistically significant (Casey et al, in the study of 25,756 women)

5.76% of euthyroid patient have **oligohydramnios** while 26.9% of subclinical hypothyroid patients had oligohydramnios. Among euthyroid patients 1.99%, 3.31%, 10.6%, 28.4%, 55.63% had their birth weight between 1.5 – 1.79kg, 1.8 – 1.99, 2 – 2.19, 2.2 – 2.49, >2.5 kg respectively. In Subclinical hypothyroid patients 5.88%, 17.65%, 11.76%, 35.29%, 29.41% had their birth weight between 1.5 – 1.79kg, 1.8 – 1.99, 2 – 2.19, 2.2 – 2.49, >2.5 kg respectively. The association between hypothyroidism and **low birth weight** is statistically significant

4% of euthyroid patients have their **APGAR** less than 7 while comparing patients with subclinical hypothyroidism where it is 18.75%. The difference is statistically not significant (chi square 8.24; p value 0.08). 5.76% of euthyroid patients had **IUGR** while 15.38% of subclinical patients had IUGR babies

9.95% of euthyroid patients had **preterm deliveries** compared to 23% of subclinical hypothyroid patients. 9.42% of patients in euthyroid group had **post partum haemorrhage**, compared with 19.23% in subclinical hypothyroidism. Among the babies born to mothers in the euthyroidism group 7.33% had **respiratory distress syndrome**, 7.33% had **NICU admission**, compared with 15.38% in the subclinical hypothyroidism group. The difference was not statistically significant There was one intra uterine death in both euthyroid and subclinical hypothyroid group,

Among **preterm deliveries** 16% had IUGR ,28% had RDS, 24% had post partum haemorrhage ,16% had APGAR less than 7. All these associations are statistically significant except IUGR. The association of hypothyroidism and preterm delivery might be due to secondary confounding factors such as maternal BMI, age, and preeclampsia.

Among patients with **Oligohydramnios** 43% had low birth weight; 50% had IUGR 72.2% had RDS ,38.8% had post partum haemorrhage 23.52% had APGAR less than All these associations are statistically significant.

Having said that this study was done in a larger population, and the patients belong to various economic strata and various geographic locations thereby representing a mixed group of sample population. Hence the prevalence reported closely represents those in general population. Even though the total number of maternal and perinatal complications is less, the results were in concordant with those reported in larger studies thereby validating the same. Since it is a prospective observational study the results are more reliable compared with a cross sectional study.

Subclinical hypothyroidism has been associated with multiple negative outcomes, including pregnancy loss, preterm delivery, gestational diabetes, and impaired neurologic development in the offspring. Universal screening of all pregnant women to detect and treat hypothyroidism is recommended.

However, the incidence and impact of hypothyroidism and the ability of treatment to prevent associated adverse events is sufficient to justify universal screening for thyroid disease. In support of this position, a cost effective analysis showed that universal screening with the goal of identifying and treating hypothyroidism is cost effective Because universal screening would also identify patients with subclinical hypothyroidism, these patients should be treated as indicated in current guidelines unless ongoing and future studies prove otherwise.

CONCLUSION

- The prevalence of subclinical hypothyroidism was 12% in this study
- 11.5% of patients had gestational hypertension and 11.52% had severe anaemia.
- 6.55% of babies have low APGAR (less than 7), 8.93% of babies had intra uterine growth retardation, 10.71% of babies had respiratory distress syndrome.
- 0.9% patients had eclampsia, 9.5% had pre eclampsia, 4% had abruption of placenta, 8.2% had oligohydramnios, and 9.2% had post partum haemorrhage.
- Subclinical hypothyroidism was significantly associated with Gestational hypertension, preeclampsia, Abruption of placenta, oligohydramnios, low birth weight, and preterm deliveries.

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