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Original Research Article

An analytical cross sectional study on hypothyroidism in pregnancy, its maternal and fetal outcome

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ABSTRACT

Background: Hypothyroidism is associated with maternal and fetal complications. This study aims to evaluate the prevalence, maternal and fetal outcome in hypothyroidism. Objective of this study was to determine whether thyroid function test can be recommended as a universal or selective screening in pregnancy.

Methods: An analytical cross-sectional study with internal comparison carried out at Govt. Kilpauk Medical College & Hospital from September 2017 to July 2018 for antenatal mothers in third trimester. Serum TSH and freeT3, T4 in case of abnormal TSH were measured, grouped into subclinical and overt hypothyroidism and were treated with Levothyroxine. Six-week follow-up with TSH, pregnancy complications were observed.

Results: 932 pregnant mothers were followed up. Prevalence of hypothyroidism was 10.5% (n = 98). Among the hypothyroid 62.24% (n = 61) had subclinical and 37.76% (n = 37) had overt hypothyroidism. The prevalence of anaemia was 35% in overt and 15% in subclinical hypothyroid group (p = 0.019). Preeclampsia is reported in 49% of overt and 16% of subclinical hypothyroid group (p = <0.001), statistically significant. Eclampsia was noted in 1 (1.64%) overt hypothyroid patient. Abruptio placenta was observed in 1 subclinical and 4 overt hypothyroid patients (5.1%). The incidence of preterm labour in this study subjects was 38% in overt and 20% in subclinical hypothyroid group (p = 0.048). The incidence of LBW fetus was 41% in overt hypothyroid and 21% in subclinical hypothyroid group (p = 0.041). The incidence of complication in this study was 41% in subclinical and 78% in overt hypothyroid group (p = <0.001).

Conclusions: Early screening, adequate treatment and follow up will bring down maternal and fetal complications in hypothyroidism.

Keywords: Overt hypothyroidism, Subclinical hypothyroidism

INTRODUCTION

Thyroid disorders constitute one of the most common endocrine disorders encountered in pregnancy as well as the reproductive life of a woman. Clinical hypothyroidism is associated with various pregnancy

complications such as abortions, pre-eclampsia, anaemia, placental abnormalities and postpartum hemorrhage.

Also, the offspring of these mothers can have complications such as premature birth, low birth weight, IUGR and increased neonatal respiratory distress,

congenital hypothyroidism and impaired cognitive function.¹

If authors are able to identify such problems early in the pregnancy or just before conception, authors will be able to prevent any adverse effects encountered in the mother and the fetus. It is also extremely important to titrate the dose of thyroid medications in a pregnant woman who is already a known case of hypothyroidism.

This study aimed to determine the prevalence of hypothyroidism in pregnancy and its association with various maternal and fetal outcomes in the population belonging to Central Chennai. Authors also would like to discuss regarding the recommendations of whether universal or high-risk screening to the populations.

Aims and objectives of this study were

- To assess the prevalence of hypothyroidism in pregnant women.
- To analyse the maternal and foetal outcome of pregnancies complicated by hypothyroidism.
- To determine whether thyroid function test can be recommended as a universal screening or high-risk screening test for the pregnant mothers.

METHODS

An analytical cross-sectional study with internal comparison conducted from September 2017 to July 2018 at antenatal OPD and labor ward casualty in the department of obstetrics and gynecology, Govt. Kilpauk Medical College and Hospital, Chennai.

Inclusion criteria

- All women with singleton pregnancy in third trimester previously unscreened for thyroid status
- Known hypothyroid prior to pregnancy or newly diagnosed hypothyroid during pregnancy
- Willing to deliver in this hospital.

Exclusion criteria

- Women with multiple gestation
- Women with chronic hypertension
- Women with overt diabetes mellitus
- Women with any autoimmune disorders
- Women those who are not willing to deliver in this hospital.

Study involved 932 antenatal eligible women who were not screened for hypo thyroidism earlier presenting in third trimester after obtaining the consent. Institutional ethical committee approval obtained.

The fasting TSH was measured by ELISA method (Table 1). Abnormal serum TSH required estimation of fT3 and fT4 (Table 2).

Table 1: Trimester-specific reference values for TSH.

Trimester	TSH value
1 st trimester	0.1-2.5 mIU/l
2 nd trimester	0.2-3 mIU/l
3 rd trimester	0.3-3 mIU/l

Table 2: Trimester-specific reference values for fT3, fT4.

Trimester	fT3 (pg/mL)	fT4 (ng/dL)
1 st trimester	2.11-3.83	0.70-2.00
2 nd trimester	1.96-3.38	0.50-1.60
3 rd trimester	1.96-3.38	0.50-1.60

Based on these values and the previous history, participants were grouped into subclinical and overt hypothyroidism. The patients were treated with L-thyroxine as per the National guidelines for screening of hypothyroidism during pregnancy.²

The women were followed every 6 weeks with TSH, till delivery and the details were recorded regarding the complications and the mode of delivery. Target TSH level should be < 3 mIU/L in the third trimester.²

The new born baby details were also obtained from the neonatologist at the time of delivery. These women after delivery in post-partum period were suggested to start pre-pregnancy dose of Levothyroxine or the same dose depending on the time of onset of the disease and advised to review in endocrinology department with serum TSH levels after 4-6 weeks.

Statistical analysis

Descriptive statistics was done for all data and were described in terms of mean values and percentages. Suitable statistical tests of comparison were done. Continuous variables were evaluated using unpaired t-test. Categorical variables were evaluated with the Chi-Square test and Fisher Exact test. Statistical significance was taken as p < 0.05. The data was analysed using SPSS version 16 and Microsoft Excel 2007.

RESULTS

Prevalence of hypothyroidism

Out of 932 pregnant antenatal mothers screened, hypothyroidism prevalence is found to be 10.5% (n = 98), subclinical hypothyroidism is 6.55% (n = 61) and overt hypothyroidism is 3.975% (n = 37) in this study (Table 3).

Study groups

In this study group, 62.24% were subclinical hypothyroid, 37.76% were overt hypothyroid (Table 4).

Age distribution

Most of the subclinical group subjects were in 21-25 years age group (49.18%) with a mean age of 25.28 years. In overt group, majority too were in 21-25 years age group (59.46%) with a mean age of 24.92 years. (p =

0.590), statistically non-significant association between age distribution and study groups (Table 5).

Table 3: Prevalence of hypothyroidism.

Prevalence of hypothyroidism	Number	%
Euthyroid	834	89.48
Subclinical hypothyroidism	61	6.55
Overt hypothyroidism	37	3.97
Total	932	100

Table 4: study groups.

Study groups	Laboratory criteria	Number	%
Subclinical group	Upper value of TSH level > 3 mIU/L and free T4 is normal	61	62.24
Overt group	Upper value of TSH level > 3 mIU/L and free T4 is below normal	37	37.76
Total		98	100.00

Table 5: Age groups.

Age groups	Subclinical	%	Overt	%	Total	%
≤ 20 years	4	6.56	2	5.41	6	6.12
21-25 years	30	49.18	22	59.46	52	53.06
26-30 years	21	34.43	9	24.32	30	30.61
> 30 years	6	9.84	4	10.81	10	10.20
Total	61	100.00	37	100.00	98	100.00
Age distribution	Subclinical		Overt		Total	
Mean	25.28		24.92		25.14	
SD	3.19		3.20		3.18	

p value unpaired t-test 0.590.

Table 6: Gestational age.

Gestational age	Subclinical	%	Overt	%	Total	%
28 weeks	19	31.15	9	24.32	28	28.57
29 weeks	12	19.67	11	29.73	23	23.47
30 weeks	15	24.59	9	24.32	24	24.49
31 weeks	15	24.59	8	21.62	23	23.47
Total	61	100.00	37	100.00	98	100.00

p value Chi squared test 0.932.

Table 7: Obstetrics score status.

Obstetric score status	Subclinical	%	Overt	%	Total	%
Primi gravida	27	44.26	15	40.54	42	42.86
Second gravida	19	31.15	15	40.54	34	34.69
Third gravida	15	24.59	7	18.92	22	22.45
Total	61	100.00	37	100.00	98	100.00

p value Chi squared test 0.610.

Gestational age

Most of the subclinical group subjects were around 28weeks of gestation (31.15%) and most of the overt group subjects were 29 weeks of gestation (29.73%) (p = 0.0932). The data subjected to chi squared test reveals the existence of statistically non-significant association (p > 0.05) (Table 6).

Obstetrics score

Most of the subclinical group subjects were primi gravida (44.26%) and in overt group majority were equally distributed in primi and second gravida (40.54%) (Table 7). There was a statistically non-significant association between obstetric score status and study groups (p = 0.610, p > 0.05)

Table 8: Anaemia status.

Anaemia status	Subclinical	%	Overt	%	Total	%
No	52	85.25	24	64.86	76	77.55
Yes	9	14.75	13	35.14	22	22.45
Total	61	100.00	37	100.00	98	100.00

p value Chi squared test 0.019.

Table 9: Pre-eclampsia status.

Pre-eclampsia status	Subclinical	%	Overt	%	Total	%
No	51	83.61	19	51.35	70	71.43
Yes	10	16.39	18	48.65	28	28.57
Total	61	100.00	37	100.00	98	100.00

p value Chi squared test < 0.001.

Table 10: Eclampsia status.

Eclampsia status	Subclinical	%	Overt	%	Total	%
No	61	100.00	36	97.30	97	98.98
Yes	0	0.00	1	2.70	1	1.02
Total	61	100.00	37	100.00	98	100.00

p value Fishers Exact test 0.378.

Anaemia

The prevalence of anaemia was 35% in the overt hypothyroid and 15% in the subclinical hypothyroid group, statistically significant association between anaemia status and study groups (p = 0.019, p < 0.05) (Table 8).

Preeclampsia

Preeclampsia is reported in 49% of the overt hypothyroid and 16% of the subclinical hypothyroid group (p = < 0.001) showing statistically significant association (Table 9).

Table 11: Abruptio placentae status.

Abruptio placentae status	Subclinical	%	Overt	%	Total	%
No	60	98.36	33	89.19	93	94.90
Yes	1	1.64	4	10.81	5	5.10
Total	61	100.00	37	100.00	98	100.00

p value Fishers Exact test 0.066.

Table 12: Preterm labour status.

Preterm labour status	Subclinical	%	Overt	%	Total	%
No	49	80.33	23	62.16	72	73.47
Yes	12	19.67	14	37.84	26	26.53
Total	61	100.00	37	100.00	98	100.00

p value Chi squared test 0.048.

Table 13: GDM.

Gestational diabetes mellitus status	Subclinical	%	Overt	%	Total	%
No	54	88.52	34	91.89	88	89.80
Yes	7	11.48	3	8.11	10	10.20
Total	61	100.00	37	100.00	98	100.00

p value Fishers Exact test 0.738

Eclampsia

No case of eclampsia was reported in subclinical group and 1 case was reported in overt group (1.02%) (Table 10).

Abruptio placentae

No statistically significant association was observed between the subclinical group subjects and the overt group subjects (p = 0.066) (Table 11).

Preterm labour

The incidence of preterm labour was 38% in the overt hypothyroid and 20% in the subclinical hypothyroid group (Table 12), statistically significant association between preterm labour status and study groups ($p = 0.048, p < 0.05$).

GDM

There was no statistically significant association between the GDM status and the study groups as incidence being 11.8% in subclinical group and 8.11% in overt group ($p = 0.738$) (Table 13).

Table 14: PROM.

Prelabour rupture of membranes status	Subclinical	%	Overt	%	Total	%
No	51	83.61	32	86.49	83	84.69
Yes	10	16.39	5	13.51	15	15.31
Total	61	100.00	37	100.00	98	100.00

p value Chi squared test 0.701.

Table 15: Mode of delivery.

Mode of delivery	Subclinical	%	Overt	%	Total	%
Vaginal	34	55.74	24	64.86	58	59.18
LSCS	27	44.26	13	35.14	40	40.82
Total	61	100.00	37	100.00	98	100.00

p value Chi squared test 0.373.

Table 16: Treatment status.

Treatment status	Subclinical	%	Overt	%	Total	%
Adequate	35	57.38	25	67.57	60	61.22
Inadequate	26	42.62	12	32.43	38	38.78
Total	61	100.00	37	100.00	98	100.00

p value 0.316.

Table 17: Preterm status.

Preterm status	Subclinical	%	Overt	%	Total	%
No	50	81.97	24	64.86	74	75.51
Yes	11	18.03	13	35.14	24	24.49
Total	61	100.00	37	100.00	98	100.00

p value Chi squared test 0.046.

Table 18: Low birth weight status.

Low birth weight status	Subclinical	%	Overt	%	Total	%
No	48	78.69	22	59.46	70	71.43
Yes	13	21.31	15	40.54	28	28.57
Total	61	100.00	37	100.00	98	100.00

p value Chi squared test 0.041.

Table 19: IUGR status.

IUGR status	Subclinical	%	Overt	%	Total	%
No	53	86.89	27	72.97	80	81.63
Yes	8	13.11	10	27.03	18	18.37
Total	61	100.00	37	100.00	98	100.00

p value Chi squared test 0.085.

Table 20: Complication status.

Complication status	Subclinical	%	Overt	%	Total	%
No	36	59.02	8	21.62	44	44.90
Yes	25	40.98	29	78.38	54	55.10
Total	61	100.00	37	100.00	98	100.00

p value Chi squared test < 0.001.

PROM

Most of the subclinical group subjects had no PROM (83.61%) and same picture was seen in overt group too (86.49%) (p = 0.701, statistically non-significant) (Table 14).

Mode of delivery

A total 44.26% of subclinical group subjects had LSCS and 35.14% of overt group subjects had LSCS (p = 0.373, statistically non-significant) (Table 15).

Treatment status

All the patients who were on levothyroxine treatment were subjected to repeat TSH values and grouped into adequately treated and inadequately treated. In overt group, majority had adequate treatment 67.57%. The incidence of adequate treatment in this study subjects was 67.57% in the overt hypothyroid and 57.38% in the subclinical hypothyroid group (p = 0.316) (Table 16).

Preterm babies

The incidence of premature foetus in this study subjects was 35% in the overt hypothyroid and 18% in the subclinical hypothyroid group statistically significant association between premature foetus status and study groups (p = 0.046, p < 0.05) (Table 17).

Low birth weight

The incidence of LBW foetus in this study subjects was 41% in the overt hypothyroid and 21% in the subclinical hypothyroid group (p = 0.041), statistically significant association between LBW foetus status and study groups (p < 0.05), (Table 18).

IUGR

There was no statistically significant association between IUGR status and study groups (p > 0.05), (Table 19).

Complications

The incidence of complication in this study subjects was 41% in the subclinical hypothyroid and 78% in the overt hypothyroid group (p = <0.001), showing statistically significant association between complication status and study groups (p < 0.05), (Table 20).

Treatment versus complication status

This Table 21 shows 11 out of 12 inadequately treated overt hypothyroid mothers and 17 out of 26 inadequately treated subclinical hypothyroid mothers developed complications. 18 out of 25 adequately treated overt hypothyroid patients and 8 out of 35 developed complications in this study.

Table 21: Treatment versus complications.

Treatment status versus complication status		Complications	%	No complications	%
Subclinical	Adequate	8	14.81	27	61.36
	Inadequate	17	31.48	9	20.45
Overt	Adequate	18	33.33	7	15.91
	Inadequate	11	20.37	1	2.27
Total		54	100.00	44	100.00

DISCUSSION

Thyroid disorders are the second commonest endocrine disorders next to diabetes mellitus in pregnancy. Thyroid dysfunction has a great impact on the maternal, fetal and neonatal outcomes.

This study was conducted in Govt Kilpauk Medical College and hospital, Chennai between September 2017 to July 2018. In my study, authors have compared the maternal and fetal outcomes between overt hypothyroidism and subclinical hypothyroidism.

Out of 932 pregnant women screened in the third trimester, 98 were found to be hypothyroid. Of which, 61 were found to be subclinical hypothyroid and 37 were found to be overt hypothyroid. The prevalence of hypothyroidism in my study is 10.5%, with subclinical

hypothyroidism being 6.6% and overt hypothyroidism being 3.8%.

Authors have compared this study outcome with similar other studies (Table 22, 23).

This study is comparable with a study conducted by Ajmani et al, who reported prevalence of hypothyroidism to be 12%.³

Pokhanna et al in his study reported a prevalence of hypothyroidism to be 13%, of which 3% had overt and 10% had subclinical hypothyroidism.⁴ Dhanwal et al stated prevalence of 14.3% when the cut off for upper limit of TSH was at 4.5 IU/L.⁵

Asian countries have reported a higher prevalence rate of hypothyroidism when compared to Western countries

with variation ranging from 2.55% in the West to 11% in India. This may be attributed to inadequate intake of iodine in diet, presence of goitrogenous substances in this diet and micronutrient deficiency of iron and selenium.⁶ In this study, majority were in the 21-25 years on both the

groups (49.1% versus 59.4%) and primi gravidas were 44.2% versus 40.5%. Gupta et al, in his study, 85% were in the age group of 20-30 years in subclinical group and 71.15% were in overt group and primi gravidas were 43.75% and 40.38% respectively.⁷

Table 22: Comparison of this study with similar studies in subclinical hypothyroidism.

Comparison	This study	Gupta et al ⁷	Ajmani et al ³	Pokhanna et al ⁴	Saraladevi et al ⁹
Prevalence	6.5%	3.7%	9%	10%	6.4%
Preeclampsia	16.39%	13.75%	22.3%	30%	9.3%
Anaemia	14.75%	38.75%	14.15%	13.3%	-
Eclampsia	0%	-	-	-	-
Abruption	1.64%	1.25%	-	3.3%	1.56%
GDM	11.48%	-	-	3.3%	-
Preterm labor	19.67%	13.75%	-	-	7.8%
PROM	16.39%	-	-	-	-
LSCS	44.26%	36.25%	16.6%	15.25%	-
Preterm babies	18.03%	12.75%	5.8%	30%	7.8%
LBW	21.31%	11.25%	12.11%	30%	4.68%
IUGR	13.11%	16.25%	4.9%	10%	6.25%

Table 23: Comparison of this study with similar studies in overt hypothyroidism.

Comparison	This study	Gupta et al ⁷	Ajmani et al ³	Pokhanna et al ⁴	Saraladevi et al ⁹
Prevalence	3.97%	2.45%	3%	3%	2.8%
Preeclampsia	48.65%	19.23%	16.6%	22.2%	14.28%
Anaemia	35.14%	23.07%	8.3%	11.1%	-
Eclampsia	2.7%	-	-	-	-
Abruption	10.81%	-	16.6%	22.2%	3.57%
GDM	8.11%	-	8.3%	11.1%	-
Preterm labor	37.84%	36.54%	-	-	10.71%
PROM	13.51%	-	-	-	-
LSCS	35.14%	51.92%	41.6%	55.5%	-
Preterm babies	35.14%	36.52%	33.3%	44.4%	10.71%
LBW	40.54%	19.23%	50%	66.6%	10.71%
IUGR	27.03%	19.23%	25%	33.3%	10.71%

Anaemia is identified in 9% of subclinical group and 13% in overt group in this study. There was a statistically significant difference in anaemia status between the two groups (14.75 versus 35.14%, p value 0.019). This is comparable with studies by Gupta et al, Agarwal U et al.^{7,8} Ajmani et al, and Pokhanna et al, reported no significant increase in anemia in both the groups.^{3,4}

This study did not notice any significant risk of GDM in both the groups (p value 0.738) which is comparable with Pokhanna et al, Ajmani et al.^{3,4} Karakosta et al reported a significant association between elevated TSH and presence of thyroid antibodies with GDM.¹⁰ Goldman C et al, reported a significant increase in the risk of GDM in overt hypothyroidism.¹¹

This study demonstrated a significant increase in the development of hypertensive disorders of pregnancy in

overt hypothyroid (48.6%) compared to subclinical hypothyroid (16.3) (p value 0.001).

Study have reported a significantly higher incidence of preeclampsia when compared to other studies.^{3,4,7,9} Ajmani et al reported pre-eclampsia to be the most common maternal complication in his study.³

Other studies have not discussed regarding the incidence of eclampsia but authors encountered a single case of eclampsia which may or may not be related to hypothyroidism (p value 0.378).

Study did not find any significant difference in the development of abruption among the two groups (p value 0.066). Other studies have demonstrated significant increase in incidence of abruption with inadequately treated overt hypothyroidism.^{4,3,9}

This study demonstrated an increased incidence of preterm labour (37.84%) and preterm birth (35.14%) in overt hypothyroid group compared to subclinical group (19.67%, 18.03%) respectively with a statistically significant association between the two groups (p value 0.048). This is consistent with studies by done by Gupta et al, Ajmani et al, Pokhanna et al.^{3,4,7}

This study showed no statistically significant association between the two groups with regard to prelabour rupture of membranes (p value 0.701).

This study showed that most of them after treatment attained the normal TSH values. 42.62% in the subclinical group and 32.43% in the overt group were inadequately treated. Inadequate treatment may be due to poor compliance of the patient or may be due to inadequate dose titration.

Studies conducted by a Gupta et al, Ajmani et al, Sharma Partha et al reported a significantly higher rate of a caesarean section in overt hypothyroid patients.^{3,7,12} In this study, there was no statistically significant difference in the mode of delivery when compared between the two groups (p value 0.373).

Coming to the neonatal outcomes, this study did not find any statistically significant association in the incidence of IUGR between the two groups (p value 0.085).

Study did not encounter any still birth, IUD and congenital malformations in this study in either groups. Pokhanna et al, Sahu et al, Abalovich et al, Saraladevi et al reported still births in overt hypothyroid group.^{4,9,13,14}

As per this observations, the incidence of LBW babies were 41% in the overt hypothyroid and 21% in the subclinical hypothyroid group (p = 0.046). The data subjected to chi squared test reveals the existence of statistically significant association between premature foetus status and study groups (p < 0.05). Leung et al demonstrated a higher incidence of LBW babies secondary to premature delivery or gestational hypertension in both overt and subclinical hypothyroidism.¹⁵

On the whole, the incidence of maternal and fetal outcomes in this study is comparable with others (Table 22, 23).^{3,4,7,9} The incidence of complications is higher in overt hypothyroid when compared to subclinical group in this study which is statistically significant (p value < 0.001). Sahu et al in his study found that incidence of gestational hypertension, gestational diabetes, foetal growth restriction, intrauterine demise and neonatal complications were significantly higher in the overt group.¹³

In this study authors found that most of the inadequately treated patients have developed complications. But higher rate of complications was also observed in the adequately

treated group. The possible explanation could be the timing of initiation of treatment. In this study, authors started the treatment from third trimester.

Placenta requires adequate amount of thyroid hormone for its normal development. Evidence showed that preeclampsia, placental abruption and preterm labour may be causatively linked to faulty early placentation. Higher rate of prevalence and complications may be attributed to the lack of initiation of treatment for subclinical hypothyroidism and an inadequate dose titration during the pregnancy.

As per the latest guidelines by endocrine society, it is advisable to delay the pregnancy in the hypothyroid patients until the appropriate TSH levels are attained. Also, pre-conceptional dose adjustment needs to be considered to attain TSH levels less than 2.5 μ IU/l before planning for conception.¹ Several studies propose that the prognosis is better in subclinical hypothyroidism when compared to overt due to normal levels of T4.¹

CONCLUSION

This study conclude that the course of the disease depends partly on the degree of hypothyroidism and partly on the treatment acquired.

Timely identification, early initiation of the treatment and close monitoring regarding the dose titration plays a vital role in preventing the development of maternal and fetal complications. The prevalence and complications being high in this study and as per Indian Thyroid Society guidelines, it's better to recommend screening of TSH levels in all the pregnant women at their first visit ideally during the pre-pregnancy evaluation or as early as the pregnancy is confirmed.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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