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ORIGINAL RESEARCH

Pregnancy Outcome in Thyroid Disorder -A Clinical Study

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ABSTRACT

Background: The objectives is to Screening of all the antenatal pregnant women for thyroid dysfunction, To study the maternal and fetal noutcome in pregnancy thyroid dysfunction, To provide adequate treatment and there by reduce adverse outcome, Follow up of cases six weeks post partum.

Materials and Methods: Prospective, observational study. 110 patients were included. The study was conducted at Department of Obstetrics and Gynecology (OBG), Modern Govt MaternityHopsital, Petlaburz attached to Osmania Medical College, Hyderabad, Telangana, India during the period from 1st December 2019 to 30th June 2021.Mothers attending for ante-natal check-up and having either a detected or documented thyroid dysfunction. An Institutional Ethics Committee approval was obtained. Written informed consent was obtained from all the study participants. The mothers during their first visit were included for detailed history, clinical examination and blood investigations as follows.

Results: No age related influence in the presence of thyroid dysfunction, there was no statistical significance. it was observed that 68% of abortions were in primigravida, it was found that with increase in gravida abortion rate was less. the mode od delivery had no significant variations in both hypo/hyperthyroidism. it was noted that subclinical hypothyrid and overt hypothroid cases resulted in more preterm deliveries than hyperthyroid patients.the study showed no significance difference in newborn thyroxine levels among thyroid dysfunction groups.

Conclusion: The study showed that thyroid dysfunction is more among the pregnant women. Hypothyroidism is the major thyroid dysfunction among the antenatal women. The women with thyroid dysfunction had more incidents of adverse outcomes of pregnancy like increased abortion rates, caesarean deliveries on the mothers and preterm babies and lbw on the newborn.

Keywords: Pregnancy, Hypothyroidism, Hyperthyroidism, Low Birth Weight.

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INTRODUCTION

Among endocrine disorder in pregnancy thyroid dysfunction is the second most common. Pregnancy increases the demand on maternal thyroid gland. Thyroid dysfunction has an adverse maternal and fetal effects. Anatomically, the thyroid gland undergoes moderate enlargement which is caused by glandular hyperplasia and increased vascularity during pregnancy. Mean thyroid volume increased from 12 ml in first trimester to 15 ml at delivery. Total volume of is inversely proportional to serum thyrotropin concentration, (so any goiter should be investigated) normal pregnancy does not cause significant thyromegaly. Several

alterations in thyroid physiology and function during pregnancy. In 1st trimester–TBG increase, reach their zenith at about 20wks and stabilize at double baseline value for the remainder of the pregnancy.

Increased TBG–higher hepatic synthesis due to estrogen and lower metabolism rate of TBG sialylation and glycosylation and reduced renal clearance Effect of increased TBG due to increased binding of T4 to TBG so Total serum T3 and T4are increased. Biologically active free T4are slightly increased and peak along with hCG. Total T4 sharply increasing between6 and 9 wks and reaches plateau at 18 wks. Thyroid disorders are considered to be one of the major endocrine disorders reported in pregnancy. The physiology of thyroid plays a vital part during pregnancy.[1,2] In general, thyroid hormones possess an intense variation in the life span. It is often related with that of many severe health effects.[3,4] Thyroid disorders are the most important scenario seen in women of childbearing age group.[5] Pregnancy is the most significant reproductive part in every woman's life yet it has an intense effect which can be reversible affecting the function of thyroid gland.[3] Therefore Pregnancy hence observed as a blend of a set of incidents which occurs to alter the thyroidal function.[6] If there exists any insufficient adjustments to these modifications may end in thyroid dysfunction.[7]

Cut off values for TSH in pregnancy:

Non pregnant TSH reference range are unreliable in pregnancy due to physiological changes of thyroid- suppressive effect of increasing thyroxin and increased TSH excretion, TSH is kept at its lowest minimal level or can even go below normal range.

Trimester	TSH(miu/dl)	fT4(ng/dl)
1 trimester	0.1-2.5	0.8-1.2
2 trimester	0.2-3	0.6-1.0
3 trimester	0.3-3	0.5-0.8

Analyzing the function of Thyroid gland during pregnancy:

Due to the overlapping of symptoms reported by the normal pregnant women with proper thyroid with that of the pregnant women with thyroid dysfunction the clinical identification is usually not direct. Due to the alteration in the physiology of thyroid, it now becomes evident that normal ranges that are used during the gestational period for thyroid hormones are very crucial.

Thus Thyroid dysfunction is predicted by the serum Thyroid Stimulation Hormone (TSH) which is the first clinical indicator. Therefore TSH acts as the best clinical indicator of thyroid function. Hence now a day there is a dependable trimester specific (or gestation specific) normal reference levels for Thyroid Stimulation Hormone are available.

Additional tests may include:

Free T4 estimate: Measuring the levels of FT4 is by estimating the quantity of biologically active hormone which is accessible to the woman who is pregnant also the fetus, and is not affected by the concentration of binding proteins. Many of them consider that estimation of free T4 is very helpful comparative to that of TSH in pregnant women.[34] The fetus is more dependable on the thyroxin which is synthesized by the mother during the 1st trimester. Therefore a small unobserved malfunction in the thyroid gland of the mother, will therefore do not threaten the course of the pregnancy, but it can cause adverse effects in the fetus psychomotor development system.[35]

Aims and Objectives

1. Screening of all the antenatal pregnant women for thyroid dysfunction.

2. To study the maternal and fetal outcome in pregnancy with thyroid dysfunction.
3. To provide adequate treatment and thereby reduce adverse outcome.
4. Follow up of cases 6wks postpartum

MATERIALS & METHODS

Type of study: Prospective, observational study

Study area: Department of Obstetrics and Gynecology (OBG), ModernGovt Maternity Hopsital, Petlaburz attached to Osmania Medical College, Hyderabad, Telangana, India.

Study period: 1st December 2019 to 30th June 2021

Study population: Mothers attending to the OBG OPD for ante-natal check-up during the study period and having either a detected or documented thyroid dysfunction.

Inclusion Criteria

1. Primigravida/Multigravida.
2. Multiple pregnancies.
3. 12 to 18 weeks of pregnancy who attended the antenatal clinic.
4. Pregnant females with history of hypothyroidism.
5. Pregnant females with history of Hyperthyroidism.

Exclusion criteria

Pregnant mothers with history of:

1. Diabetes Mellitus
2. Collagen Vascular diseases
3. Coronary heart disease
4. Chronic Kidney disease

Methodology: The study was conducted in the Department of Obstetrics and Gynaecology during 1st December 2019 to 30th June 2021 including 110 pregnant mothers who have either a documented or newly detected thyroid dysfunction as per the inclusion criteria. An Institutional Ethics Committee (IEC) approval was obtained prior to the start of the study. Written informed consent was obtained from all the study participants. The mothers during their first visit were included for detailed history, clinical examination and blood investigations as follows.

History and Examination:

A detailed history was taken regarding the symptoms of thyroid disorders such as past history and family history of thyroid disorders, menstrual history, obstetric history and any significant or relevant medical/ surgical history was obtained.

The mothers were then subjected to thorough clinical examination which included general physical examination including pulse rate, blood pressure and local examination of thyroid gland for diffuse or nodular swelling or any structural anomaly. Signs of thyroid dysfunction including clinical features of hypothyroidism and hyperthyroidism were elicited. Abdominal /Obstetric examination was done to correlate the duration of gestation with ultrasonogram for confirmation of gestation period.

Blood investigations

All the participants were asked to undergo routine blood investigations pertaining to the ante-natal visit. Thyoid investigations including T3, T4, TSH levels were estimated using Chemiluminiscent assay system. If at all there was a discrepancy in the above serum level estimations, a free T3, T4 estimation was done. All tests of the panel werebased on the ELFA (Enzyme Linked Fluorescent Assay) technique. The reference normal limits for all the

thyroid parameters were based on recommendations by American Thyroid Association- 2011. [40]
The reference range for three trimesters is as follows: 1st trimester 0.1- 2.5 μIU/ml
2nd trimester 0.2- 3.5 μIU/ml
3rd trimester 0.3- 3.5 μIU/ml
Laboratory specific reference range for FT3 and FT4 are as follows: FT3 4-8.3 pmol/l
FT4 9-20 pmol/l

Follow-up:
The enrolled participants were followed-up during every ante-natal check-up. The outcomes of pregnancy were documented at the end of the gestation period during delivery. The following attributes were followed up and recorded for each of the participants:
1. Type of delivery: Caesarean/ elective/ Instrumental
2. Birth weight of the child
3. Gender of the newborn
4. Gestational Maturity: Preterm/ term/ post-dated

Statistical analysis
Descriptive data for frequencies are presented as percentages and proportions. Chi square ($\chi 2$) test was applied to see significant differences and associations of various parameters with categories. Student independent t test and one way ANOVA test were applied wherever comparison of two or more means was necessary. For all tests a „p" value of 0.05 or less was considered for statistical significance. Data entry was done in Excel 2010 and analysis was done in SPSS version 20.1.

RESULTS
The prospective study was conducted by following-up 100 pregnant women attending to the ante-natal clinic, Obstetrics and Gynaecology OPD and labour ward. The mean age of the study participants was 26.57± 3.97 years. The age distribution is given in [Table 1].
Most of the study participants were in the age group of the 20 -30 years (88%) and elderly gravid women were only (12%).

Table 1: Age distribution of the study participants (n=110)

Age categories	Frequency	Percentage
20-25 years	45	45
26-30 years	43	43
31-35 years	10	10
>35 years	2	2
Total	100	100

Table 2: Gravida status of the study participants (n=100)

Gravida	Frequency	Percentage
Primi	40	40
2	31	31
3	21	21
4	6	6
5	2	2
Total	100	100

In our study thyroid disorders was more in primigravidas (n=40, 40%) than in second gravid (n=31, 31%) and was least in multigravida mothers (of G4 and GS).

Table 3: Abortions among the study participants

Abortions	Frequency	Percentage
0	68	68
1	21	21
2	8	8
3	3	3
Total	100	100

In our study, it was observed that 68%of abortions were in primigravida and 21% in second gravida and it was found that with increasing gravida the abortion rate was less.

Table 4: Types of thyroid dysfunction (TD) among the study participants (n=100)

Thyroid dysfunction	Frequency	Percentage
Clinical hypothyroidism	80	80
Clinical hyperthyroidism	6	6
Sub-clinical hypothyroidism	14	14
Total	100	100

Out of 100 participants, the clinically overt hypothyroidism were 80, accounting for 80% and subclinical hypothyroidism 14(14%) than hyperthyroidism 6 (6%).

Table 5: Mean TSH and T4 levels among the study participants with various TD

Thyroid dysfunction	TSH (Mean ± SD) µIU/ml	T4 (Mean ± SD) pmol/L
Clinical hypothyroidism	5.54 +2.4	9.39 +3.8
Clinical hyperthyroidism	0.89 +0.3	12.8 +5.3
Sub-clinical hypothyroidism	2.12 +0.8	12.61 + 2.5
ANOVA (F- value)	46.8	8.5
p-value	<0.001	<0.001

There was significant ($p<0.001$) difference of serum TSH and T4 levels among the three thyroid dysfunction groups.

Table 6: Thyroid dysfunction among various age categories (n=100)

Age categories	Thyroid dysfunction			
	Hyperthyroid	Hypothyroid	Subclinical hypothyroid	Total
20-25 years	1	31	12	44
26-30 years	5	31	6	42
31-35 years	0	12	1	13
>35 years	0	1	0	1
Total	6	75	19	100

There was no significant variation in the incidence of thyroid dysfunction among the various age categories. The younger age groups comparatively had increased incidence of hyperthyroidism compared to the higher age groups.

Table 7: Thyroid dysfunction and parity status (n=110)

Gravida	Thyroid dysfunction			
	Hyperthyroid	Hypothyroid	Subclinical hypothyroid	Total
1	1	31	12	44
2	1	25	7	33
3	1	11	3	15
4	1	5	0	6
5	1	1	0	2
Total	6	75	19	100

In our study there was no significant variation in the incidence of thyroid dysfunction among the different parity groups. Primigravida and second gravida comparatively had higher incidence of thyroid dysfunction compared to higher parity groups.

Table 8: Thyroid dysfunction and incidence of abortions (n=100)

Abortions	Thyroid dysfunction			
	Hyperthyroid	Hypothyroid	Subclinical hypothyroid	Total
0	2	52	14	68
1	2	16	4	22
2	0	6	2	8
3	1	1	0	2
Total	6	75	19	100

It was observed that in our study there was significant variation in the incidence 4/6, 68%) of abortion among hyprthyroid and among the hypothyroid groups Subthyroid cases comparatively had more (16/22, 22%) abortions than to overt hypothyroids (2/6, 19%).

Table 9: Type of deliveries encountered in various thyroid dysfunction (n=100)

Type of delivery	Thyroid dysfunction			
	Hyperthyroid	Hypothyroid	Subclinical hypothyroid	Total
1.Normal vaginal	2	8	8	18
a.Withencirclage	0	4	0	4
2.Caesarean	3	49	6	58
a.Elective	0	3	1	4
b.Emergency	3	7	3	13
3.Vaccum	1	4	1	6
Total	6	75	19	100

The mode of delivery had no significant variations in both hypo or hyperthyroid groups However hypothyroid cases had more caesarean deliveries (49/75, 65.33%) compared to the hyperthyroids (3/6, 50%).

Table 10: Gestational term of delivery in various thyroid dysfunction (n=110)

Gestational term	Thyroid dysfunction			
	Hyperthyroid	Hypothyroid	Subclinical hypothyroid	Total
Term	5	60	13	68
Preterm	1	14	3	18
Miscarriage	0	1	3	4
Total	6	75	19	100

The important observation noted in our study which was statistically significant was the gestational maturity period among the thyroid dysfunction groups. It was noted that Subclinical hypothyroid (15.7%) and overt hypothyroid cases (18.6%) resulted in more preterm deliveries than that of hyperthyroid patients (16%).

Table 11: Gender of the baby born to the TD pregnant mothers (n=110)

Gender	Thyroid dysfunction			
	Hyperthyroid	Hypothyroid	Subclinical hypothyroid	Total
Male	6	37	11	54
Female	0	38	8	46
Total	6	75	19	100

There was a significant variation in the gender of child born to the thyroid dysfunction group mothers. It was observed that all hyperthyroid mothers had male babies but eqal proportion of males and females in hypothyroid mothers.

Table 12: Birth weight of the newborn child of the study participants (n=110)

Thyroid dysfunction	Birth weight (Mean ± SD) kg
Clinical hypothyroidism	2.61 + 0.45
Clinical hyperthyroidism	2.59+ 0.49
Sub-clinical hypothyroidism	2.69 + 0.49
ANOVA (F- value)	0.09
p-value	0.93, Not significant

The P value not significant as shown in the table in newborn birth weight among the various thyroid dysfunction groups.

Table 13: Neonatal T4 levels of the newborn child of the study participants (n=110)

Thyroid dysfunction	Neonatal T4 (Mean ± SD)
Clinical hypothyroidism	17.27 + 1.54
Clinical hyperthyroidism	16.9 + 1.09
Sub-clinical hypothyroidism	17.33 + 1.34
Total	17.26 + 1.47
ANOVA (F- value)	0.37
p-value	0.54, Not significant

Also the study showed no significant difference in newborn thyroxin levels among the various thyroid dysfunction groups.

DISCUSSION

The prospective study was conducted at the department of Obstetrics and Gynaecology by including 100 women who suffered some form of thyroid dysfunction hypothyroidism or hyperthyroidism or sub-clinical modes of both extremes. The study participants were selected by screening for various other metabolic abnormalities like diabetes, chronic kidney disease and endocrine dysfunctions which can be major confounders in depicting the outcomes of pregnancy.

Age and Parity

The present study documented that the mean age of the study participants was 26.57± 3.97 years. There was higher representation from the 20 -30 years age group (88%) whereas there

was less representation of elderly gravid women in the study sample (12%). There was no age-related influence in the presence of thyroid dysfunction which was shown by chi-square test showing no statistical significance in the occurrence of thyroid dysfunction in various age groups. The magnitude of hypothyroidism was more in all younger age groups than the older ages but the difference was not statistically significant.

In the study done by Ajmani et al,[8] on the prevalence of overt and subclinical thyroid dysfunction among pregnant women and its effect on maternal and fetal outcome, it was documented that mean age (in years) among the euthyroid subjects was 24.56±3.733 years and 24.51±4.71 years, 27.16±5.23 26±1 years and 30.5±0.70 years in subjects with subclinical hypothyroidism,overt hypothyroidism, subclinical hyperthyroidism and overt hyperthyroidism, respectively which was similar to the results obtained in our study.

There was similar study by Rooplekha Chauhan et al.[9] who found that there is no significant difference between the groups as the mean age in euthyroid; subclinical hypothyroid and overt hypothyroid group was 25±2.7, 25±3.2 and 25±5.6 years, respectively.

In the present study, majority of the study subjects were primigravidas (n=40, 40%) and second gravid (n=31, 31%). There was significantly lower representation of multigravid mothers in the study. There was more chance incidence of abortions as the gravid status of the mothers increased from Primigravida to Multigravida. There was incidence of atleast one abortion in 21% (n=21) of the included participants.

In a study done by Dhara Singh Meenaet al.[10] it was reported that 32% subjects with thyroid dysfunction were primigravida, 26% were gravida 2, 19% of subjects were gravida 3 and 23% were gravida 4.

Enough literature is not available to enunciate the differences in incidence of abortions as per gravida but the literature documents a correlation of increased abortions as the age increased along with the parity. This may due to the fact that higher the age more chances of pregnancy related complications.

Sapana Shah et al.[11] in their study documented that 40.7% of subjects with hypothyroidism were primigravida and 59.3% subjects were multigravida. In our study we found that 31% (n=31) of hypothyroids were gravida 1 which was lesser compared to the above-mentioned study. This may be because of the age differences of participants included in that study which differed from our study.

Thus the age distribution and parity status showed no great differences when comparing the present study results with that of the previous studies.

Type of thyroid dysfunction and biochemical levels:

The study classified the thyroid dysfunction into clinical and sub-clinical, hypothyroidism and hypothyroidism respectively. Accordingly, among the mothers with thyroid dysfunction (n=100), the proportion of mothers with clinical hypothyroidism was 41.3% (n=75), Clinical hyperthyroidism was 16% (n=6) and Sub- clinical hypothyroidism was 31.5% (n=19). The study did not report any case of sub- clinical hyperthyroidism.

Nidhi Chauhan et al.[12] in their study found that 0.67% had subclinical hyperthyroidism, 87.67% of the subjects were euthyroid, and 0.33% had overt hyperthyroidism, whereas 2% had subclinical hypothyroidism, 9.33% had overt hypothyroidism. This was different from our study which showed higher magnitude of overt hypothyroidism and no case of hyperthyroidism.

Rodrigo Moreno-Reyes et al,[13] in their study also found that 3.6% had subclinical hyperthyroidism which was higher than the proportions recorded in other studies. They also recorded that 88.7% of the subjects were euthyroid, 6.8% had subclinical hypothyroidism and 0.4% had overt hypothyroidism which was comparatively lesser than previous studies. There was no hyperthyroidism reported in a study done by FakhrolmoloukYassaee et al,[14] that

95.35% of the subjects were euthyroid, 4.15% had subclinical hypothyroidism, 0.5% had overt hypothyroidism.
Thus the presence of various thyroid dysfunctions had similarities to previous literature.

Mean TSH and T4 levels in various thyroid dysfunctions

The mean TSH levels in the present study showed significant ($p<0.001$) differences among the various groups of thyroid dysfunctions. The mean TSH levels in the overt hypothyroidism group was 5.54 ± 2.4 (iIU/ml, overt hypothyroidism was 0.89 ± 0.3 (iIU/ml and Sub-clinical hypothyroidism 2.12 ± 0.8 ^lIU/ml. (ANOVA (F- value)= 46.8, $p<0.001$)
Yet another study by Baveja et al,[15] the mean TSH level in euthyroid subjects was 1.58 [iIU/ml, among subclinical hypothyroid subjects it was 3.95[iIU/ml, in overt hypothyroid subjects was 7.62[iIU/ml and in hyperthyroid subjects was 0.06 [iIU/ml. This was different from the present study which showed higher mean TSH levels among the various thyroid dysfunction groups. Those with sub-clinical hypothyroidism had normal TSH levels (2.12 ± 0.8(iIU/ml) in the present study whereas it was higher in the study done by Neelam Aggarwal et al,[16] where the Mean TSH level in euthyroid subjects were 2.81±1.7 [iIU/ml and in subclinical hypothyroid subjects it was 6.81±1.1 [iIU/ml.
The results recorded in a study done by PanditVinodhBandela et al,[17] showed that Mean TSH level in euthyroid subjects was 2.30±1.24 [iIU/ml, in subclinical hypothyroid subjects it was 8.15±23 [iIU/ml, in overt hypothyroid subjects it was 69.43±13.65 [iIU/ml and in hyperthyroid subjects it was 0.07±0.10 iIU/ml. This study results showed TSH levels in overt hypothyroids were very high dissimilar to our study. Thyroid dysfunction and mode of delivery:
The present study found that, among the subjects with thyroid dysfunction (n=100), there was a higher rate of caesarean section deliveries (58%) compared to normal vaginal (18%) and instrumental (4%) deliveries. There was also comparatively higher rate of Hypothyroid cases going for caesarean deliveries (49/75, 65.33%) compared to the hyperthyroid mothers (3/6, 50%). The difference was not statistically significant though. ($p=0.15$). Among those who went for caesarean delivery (n=58) majority were emergency caesarean sections (n=54) than elective LSCS.
Similarly, AjmaniSangitaNangia et al,[18] in their study found that 79.3% of euthyroid, 78 % of subclinical hypothyroid, 41.6 % of overt hypothyroid, 100 % of subclinical hyperthyroid and 50 % of overt hyperthyroid subjects had normal vaginal delivery. No significant increase was seen in the subclinical hypothyroid and hyperthyroid groups. Whereas, the rate of caesarean section was significantly higher in patients with overt hypothyroidism (41.6 vs. 17.1 %, $p = 0.0031$) as compared to the euthyroid controls. Our study did not include euthyroid subjects and so such comparison was not in the scope of the present study.

Thyroid dysfunction and the gestational term outcome of pregnancy:

The present study showed that preterm deliveries were significantly ($p=0.02$) more common in Subclinical Hypothyroid (15.7%) and overt hypothyroid cases (18.6%) compared to the hyperthyroid patients (16%). There was an increased incidence of miscarriages in the Subclinical Hypothyroid (11%) and overt hypothyroid cases (1%) compared to nil miscarriages in hyperthyroid subjects.
In the study by Upadhyaya TL et al,[19] in their study found that 19.35% of subjects with subclinical hypothyroidism and 38.46% of subjects with overt hypothyroidism had preterm deliveries. This was higher compared to the proportions recorded in our study. The fact that only hypothyroidism is associated with gestational term related problems and no such association has been identified in hyperthyroidism was clearly affirmed in this study also.

Neelam Aggarwal et al,[16] in their study found that 16% of subjects with subclinical hypothyroidism had preterm deliveries. The incidence of preterm labor and preeclampsia was similar in both groups (P =>0.05). This study showed incidence of preterm deliveries lesser than that of the present study. The reasons which can be attributed are the influence of thyroid hormones on the placental and uterine environment which needs further postulation.

Thyroid dysfunction and fetal weight

In the present study, the average weight of the newborn was 2.61 ± 0.45 kg delivered for the mothers with overt hypothyroidism, 2.59 ± 0.49 kg for overt hyperthyroidism and 2.69 ± 0.49 kg for Sub-clinical hypothyroidism.

In the earlier by Baveja et al,[15] study21.7% of subjects with subclinical hypothyroidism, 9.7 % subjects with overt hypothyroidism and 22.2% subjects with hyperthyroidism have EFW between 2.1 to 2.5 kg.

CONCLUSION

The study clearly showed that thyroid dysfunction is more among the pregnant women. Hypothyroidism is the major thyroid dysfunction among the antenatal women. The women with thyroid dysfunction had more incidents of adverse outcomes of pregnancy like increased abortion rates, caesarean deliveries on the mothers and preterm babies and low birth weight on the newborn.

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