

Clinical study of thyroid dysfunction in pregnant women and it's effect on maternal and fetal outcome

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Abstract

Background: Thyroid disorders constitute one of the most common endocrine disorders in pregnancy. Pregnancy is associated with profound modifications in the regulation of thyroid function. Women with thyroid dysfunction both overt and subclinical are at increased risk of pregnancy-related complications such as threatened abortion, preeclampsia, preterm labour, placental abruption and postpartum haemorrhage. Fetal complications include low birth weight, IUGR, neonatal hyperthyroidism, stillbirth and perinatal mortality. Due to paucity of information and studies showing the prevalence of thyroid dysfunction in pregnant women and its effect on the maternal and fetal outcomes in Indian population, this study is an effort to throw some light in this direction. **Methods:** This prospective study was conducted enrolling 200 pregnant women with thyroid dysfunction irrespective of their gestational age who came for antenatal check up. Recent TSH, fT3 and fT4 values were noted and whether the patient is on treatment or not was noted. The patients who were not on treatment were treated. These cases were followed up till the termination of pregnancy. TFT was repeated every 6-8 week or in each trimester and in cases of deranged TFT, drug dosage was titrated accordingly. At the end, obstetric and perinatal outcome of the pregnancy was noted. **Results:** In the study, subclinical hypothyroidism was associated with complications like PE(24%),AP(1%), anaemia(12.5%), abortion(4.8%), PPH(1.9%). Overt hypothyroidism was associated with complications like PE(39.3%),abruption(7.1%), anaemia(12.5%),abortion(17.9%) and PPH(1.9%). Overt hyperthyroidism was associated complications like PE(60%) and abortion(30%) and subclinical hyperthyroidism was associated with complications like PE(33.33%), PTD(33.33%) and respiratory distress(33.33%). **Conclusions:** Maternal thyroid dysfunction is associated with significant adverse effects on maternal and fetal outcome emphasizing the importance of routine antenatal thyroid screening in first trimester. **Key Words:** Thyroid dysfunction, Hypothyroidism ,Hyperthyroidism, Pregnancy

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INTRODUCTION

Thyroid disorders constitute one of the most common endocrine disorders in pregnancy. The thyroid undergoes physiological changes during pregnancy, such as moderate enlargement of the gland and increased vascularization. Pregnancy is associated with profound modifications in the regulation of thyroid function. These changes are the result of various factors like an increase of thyroxine-binding globulin(TBG) due to elevated estrogen and human chorionic gonadotrophin(hCG), increased renal losses of iodine due to increased glomerular filtration rate, modifications in the peripheral metabolism of maternal thyroid hormones and modification in iodine transfer to the placenta.

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Hyperthyroidism occurs in 0.1-0.4% of pregnant women. Whereas about 2-3% of pregnant women are hypothyroid, of whom 0.3-0.5% have overt hypothyroidism and 2-2.5% present subclinical hypothyroidism.¹ Uncontrolled hyperthyroidism and hypothyroidism are associated with adverse pregnancy outcomes. There is also a concern about the effect of overt maternal thyroid disease and even subclinical maternal thyroid disease on fetal development. Indeed subclinical hyperthyroidism is not associated with adverse outcomes. In addition, medications that affect the maternal thyroid gland can cross the placenta and affect the fetal thyroid. Women with thyroid dysfunction both overt and subclinical are at increased risk of pregnancy-related complications such as threatened abortion, preeclampsia, preterm labour, placental abruption and postpartum haemorrhage. Fetal complications include low birth weight, IUGR, fetal or neonatal hyperthyroidism and hyperbilirubinemia, still birth and perinatal mortality. The present study has been undertaken to know the obstetric and perinatal outcomes of pregnant women suffering from thyroid dysfunction.

METHODS

Pregnant women with thyroid dysfunction who came for ANC check up to Cheluvamba hospital attached to OBG department, MMC and RI, Mysuru irrespective of gestational age.

The study period was for 18 months from December 2015 to May 2017

Method of collection of Data:

Sample size: 200

In 2014, Total number of pregnant women with thyroid dysfunction coming for ANC check up to Cheluvamba hospital attached to OBG department, MMC and RI was 120, for 18 months it will be approximately equals to 180. Using online sample size calculator provided by www.surveysystem.com for proposed population of 180, with 95% of confidence interval and confidence level of 5%, the required sample size is 123. However, we have used the sample size of 200 for more valid results.

Sampling method: Convenient sampling

All pregnant women with thyroid dysfunction coming for ANC check up to Cheluvamba hospital attached to OBG department, MMC and RI, Mysuru during the study period irrespective of the gestational age were selected for the study.

Type of study: PROSPECTIVE STUDY

INCLUSION CRITERIA:

- All Pregnant women with thyroid disorder who came for ANC check up
- With singleton pregnancy

EXCLUSION CRITERIA:

- Multifetal gestation
- Medical disorders like diabetes, hypertension

METHOD OF STUDY:

SUBJECTS:

Pregnant women with thyroid dysfunction who are coming for ANC check up to Cheluvamba Hospital attached to OBG department, MMC and RI, Mysuru after signing the written informed consent for participation underwent examination as follows

1. Gestational age was estimated on the basis of last menstrual period and early obstetric scan.
2. Detailed history was taken regarding the symptoms, and signs of thyroid disorders, menstrual history, obstetric history, past history, medical history, family history, personal history.
3. Detailed examination with reference to pulse rate, BP, temperature, respiratory rate were noted. Local thyroid examination was done. CVS, CNS, RS, per abdomen and PV examination was done.
4. Recent TSH, fT3 and fT4 values were noted and whether the patient was on treatment or not was noted.
5. Based on the TSH, fT3 and fT4 values patients were grouped as hypothyroid or hyperthyroid.
6. The patients who were not on treatment were treated. For Hypothyroid patients-Thyroxine was started and for Hyperthyroid patients - Methimazole was started (PTU in first trimester)
7. Every 8 weeks TSH value was estimated and the dose of the drug titrated.

At the end, obstetric outcome and the perinatal outcome of the pregnancy was noted.

The following outcome variables in relation to thyroid disorders were studied:

Hyperthyroidism in pregnancy:

Maternal outcome variables include:

- Preeclampsia
- Heart failure

Fetal outcome variables includes:

- Preterm delivery
- Growth restriction
- Still birth

Hypothyroidism in pregnancy:

Maternal outcome variables include:

- Miscarriage
- Anaemia in pregnancy
- Pre-eclampsia (PE)
- Abruption placenta
- Postpartum haemorrhage (PPH)

Fetal outcome variables includes:

- Premature birth
- Low birthweight
- Increased neonatal respiratory distress.

Preeclampsia was defined as persistently elevated blood pressure (systolic ≥ 140 mm Hg and diastolic pressure ≥ 90 mm Hg on more than 2 occasions) with proteinuria. Preterm delivery was defined as delivery before 37 completed weeks of gestation after the period of viability. IUGR was defined as birth weight less than 10th percentile for gestational age. Still birth was defined as the birth of a new born after 28 completed week (1000g or more) when the baby does not breathe or show any sign of life after delivery. Abortion was defined as spontaneous termination of pregnancy before the period of viability. Abruptio placenta was defined as a form of antepartum haemorrhage where the bleeding occurs due to premature separation of normally situated placenta. Postpartum haemorrhage is defined as the blood loss of 500 ml or more from the genital tract following vaginal delivery or 1000 ml or more following caesarean section. Low birth weight was defined as weight < 2500g. Anaemia in pregnancy was defined as Hemoglobin concentration in the peripheral blood ≤ 11 g/100 ml. Neonatal respiratory distress was defined as presence of any 2 of the following features:

1. Respiratory rate > 60/min.
2. Subcostal/ intercostal recessions
3. Expiratory grunt/ groaning

**STATISTICAL METHODS APPLIED:
DESCRIPTIVE STATISTICS**

The Descriptive procedure displays univariate summary statistics for several variables in a single table and calculates standardized values (z scores). Variables can be ordered by the size of their means (in ascending or descending order), alphabetically, or by the order in which the researcher specifies.

Following descriptive statistics were employed in the present study- mean, Standard deviation, frequency and percentages

the statistical methods were carried out through the SPSS for Windows (version 20.0)

RESULTS

Out of 104 subclinical hypothyroid(s.hypo) pregnant women, 25(24%) of them had pre eclampsia(PE), 1(1%) had abruption, 13(12.5%) had anemia, 5(4.8%) of them had abortion and 2(1.9%) had PPH. Out of 28 overt (o.hypo) pregnant women, 11(39.3%) had PE, 2(7.1%) of them had abruption, 5(17.9%) had anemia, 5(17.9%) had abortion and 1(3.6%) of them had PPH. Out of 50 hypothyroid pregnant women in (eu.hypo) state, 7(14%) had PE, 4(8%) had anemia, 1(2%) of them had PPH, none of them had abruption and abortion. Out of 3 subclinical hyperthyroid(s.hyper) pregnant women, 1(33.3%) had PE. Out of 10 overt hyperthyroid(o.hyper) pregnant women, 6(60%) had PE and 3(30%) of them had abortion. Out of 5 hyperthyroid pregnant women in euthyroid(eu.hyper) state, none of them had any complications.

Table 1: Maternal complications in the study population

Maternal complications	S.hypo	O.hypo	Eu.hypo	S.hyper	O.hyper	Eu.hyper	P value
PE	25	11	7	1	6	0	0.012
Abruption	1	2	0	0	0	0	0.201
Anemia	13	5	4	0	0	0	0.511
Abortion	5	5	0	0	3	0	0.002
PPH	2	1	1	0	0	0	0.982

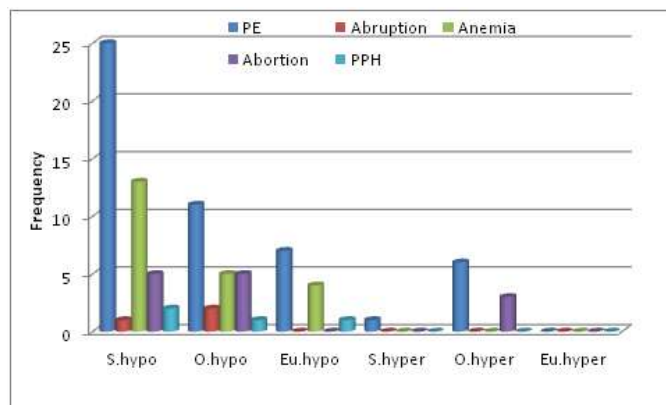


Figure 1: Maternal complications in the study population

Among subclinical hypothyroid pregnant women, 97 had live births, 9 were preterm babies, 14 were IUGR babies ,29 babies had respiratory distress and 2 were IUD. Among overt hypothyroid pregnant women,21 had livebirths, 3 were preterm babies, 3 were IUGR babies, 11 babies had respiratory distress and 2 were IUD. Among hypothyroid pregnant women in euthyroid state, 49 had livebirths, none of them had preterm delivery, 7 were IUGR babies, 5 babies had respiratory distress and 1 was IUD. Among subclinical hyperthyroid pregnant women, 3 had livebirths, 1was preterm baby and 1 baby had respiratory distress. Among overt hyperthyroid pregnant women,7 were livebirths, 2 were preterm babies,2 were IUGR babies and 1 baby had respiratory distress. Among hyperthyroid pregnant women in euthyroid state, 5 were livebirths and 1 baby had IUGR.

Table 2: Fetal outcome in the study population

Fetal outcomes	S.hypo	O.hypo	Eu.hypo	S.hyper	O.hyper	Eu.hyper
Live births	97	21	49	03	07	05
Preterm	09	03	00	01	02	00
IUGR	14	03	07	00	02	01
Respiratory distress	29	11	05	01	01	00
IUD	02	02	01	00	00	00

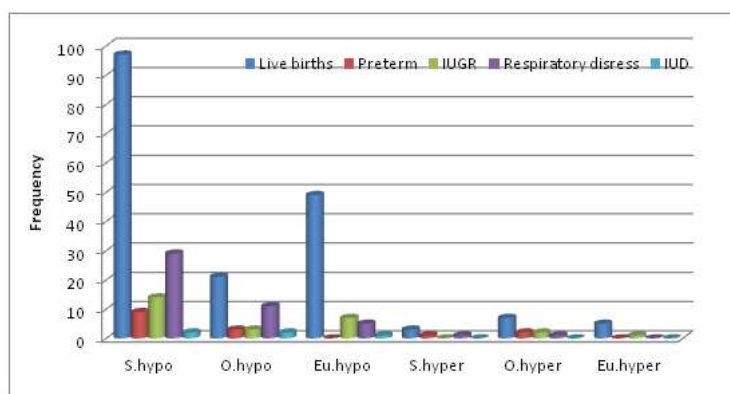


Fig-2: Fetal outcome in the study population

DISCUSSION

The present study was done in Cheluvamba hospital attached to OBG department, MMC and RI, Mysuru. A total of 200 pregnant women with thyroid dysfunction were included in the study. It was a prospective study. The main aim of the study was to know the impact of maternal thyroid dysfunction on maternal and fetal outcome. Thyroid disorders are common among pregnant women. Diagnosis of thyroid dysfunction is complicated by non-specific symptoms, the hypermetabolic state of pregnancy and normal physiological changes associated with thyroid gland and its function in pregnancy. If untreated, thyroid dysfunction may adversely affect the mother and fetus. In our study, subclinical hypothyroidism was associated with complications like PE(24%),AP (1%), anaemia (12.5%), AB (4.8%), PPH (1.9%), preterm(8.65%), IUGR(13.46%), respiratory distress(27.88%), IUD(1.92%). In a study done by

Ajmani *et al.*² the incidence of complications in cases of subclinical hypothyroidism were PE(22.3%), anaemia(14.1%), abortion(5.5%), PPH(5.5%),PTD(5.8%), IUGR(4.9%), respiratory distress(11.8%) and IUD(1.7%). Incidence of complications associated with subclinical hypothyroidism in our study were comparable to the study conducted by Ajmani *et al.* In a study conducted by Leung *et al.*³ the incidence of complications in cases of subclinical hypothyroidism were PE(7.6%),PTD(9%),LBW(9%). In a study done by Sahu MT *et al.*⁴ the complications like PE(9.8%), PTD(10.3%),IUGR(2.4%) and IUD(2.5%) were seen in cases subclinical hypothyroidism. In these 3 studies there was no incidence of abruptio placenta. In a study done by Sreelatha *et al.*⁵ the complications like PE(14.7%), anaemia(4.2%), abortion(2.1%), PPH(6.3%) and PTD(3.1%). In our study, the incidence of respiratory distress was more compared to other studies.

Table 3: Incidence of complications in subclinical hypothyroidism

Study	PE	AP	Anaemia	AB	PPH	PTD	IUGR	Respiratory distress	IUD
Our study	24%	1%	12.5%	4.8%	1.9%	8.65%	13.46%	27.88%	1.92%
Ajmani	22.3%	0	14.1%	5.5%	5.5%	5.8%	4.9%	11.8%	1.7%
Leung	7.6%	-	-	-	-	9%	-	-	-
Sahu MT	9.8%	-	-	-	-	10.3%	2.4%	-	2.5%
Sreelatha	14.7%	-	4.2%	2.1%	6.3%	3.1%	-	-	-

In our study, overt hypothyroidism was associated with complications like PE(39.3%), AP(7%), anaemia(17.9%), abortion(17.9%), PPH(3.6%), PTD(10.71%), IUGR(10.71%), RD(39.28%) and IUD(7.14%). In a study done by Ajmani *et al*, the complications like PE(16.6%), AP(16.6%), anaemia(8.3%),abortion(16.6%), PPH(8.3%), PTD(33.3%), IUGR(25%), RD(25%)and IUD(16.6%) were seen in cases of overt hypothyroidism. In a study done by Leung *et al*. the incidence of complications in overt hypothyroidism were like PE(22%) and IUD(4%). In a study done by Sahu M T *et al*. the complications like PE(20.7%),PTD(4.7%), IUGR(13.8%) and IUD(2.9%) were seen in overt hypothyroidism. In a study done by Thanuja *et al*.⁶ the incidence of complications like AP(33.4%) and abortion(66.7%) seen in overt hypothyroidism. In a study done by Ablovich *et al*.⁷ the complications like AP(19%) and IUD(3%) were seen in cases of overt hypothyroidism. The incidence of complications varied in different studies but some studies are comparable. In our study the incidence of PE and respiratory distress were high compared to other studies.

Table 4: Incidence of complications in Overt hypothyroidism

Study	PE	AP	Anaemia	Abortion	PPH	PTD	IUGR	Respiratory distress	IUD
Our study	39.3%	7%	17.9%	17.9%	3.6%	10.71%	10.71%	39.28%	7.14%
Ajmani	16.6%	16.6%	8.3%	16.6%	8.3%	33.3%	25%	25%	16.6%
Leung	22%	-	-	-	-	-	-	-	04%
Sahu MT	20.7%	-	-	-	-	4.7%	13.8%	-	2.9%
Thanuja	-	33.4%	-	66.7%	-	-	-	-	-
Ablovich	-	19%	-	-	-	-	-	-	3%

In our study subclinical hyperthyroidism was associated with complications like PE(33.33%), PTD(33.33%) and respiratory distress(33.33%). In a study conducted by Kriplani³ *et al* complications like PE(22%) and PTD(25%) were seen in subclinical hyperthyroidism. In a study done by Thanuja *et al*.⁶ complications like PE(50%) and IUGR(25%) were seen in subclinical hyperthyroidism. In a study done by Tuija Mannisto *et al*.⁸ subclinical hyperthyroidism was associated with complications like PE(3.5%) and Abruptio placenta(1%). In none of the study was associated with abortion and perinatal mortality. Incidence of RD was more in our study.

Table 5: Incidence of complications in subclinical hyperthyroidism

Study	PE	AP	AB	PTD	IUGR	RD	IUD
Our study	33.33%	-	-	33.33%	-	33.33	-
Kriplani	22%	-	-	25%	-	-	-
Thanuja	50%	-	-	-	25%	-	-
Tuija Mannisto	3.5%	1%	-	-	-	-	-

In our study, Overt hyperthyroidism was associated with complications like PE(60%), Abortion(30%), PTD(20%), IUGR(20%) and RD(10%). In a study done by Kriplani *et al*. complications like PE(22%), PTD(25%) and IUGR(13%) were seen in cases overt hyperthyroidism. In a study done by Thanuja *et al*. overt hyperthyroidism was associated with PE(33.4%), Abortion(50%) and PTD(16.67%). In our study incidence of PE was more compared to other studies. Incidence of abortion was more in the study conducted by Thanuja *et al*. In all ³ studies, incidence of PTD was comparable.

Table 6: Incidence of complications in overt hyperthyroidism

Study	PE	AP	AB	PTD	IUGR	RD	IUD
Our study	60%	-	30%	20%	20%	10%	-
Kriplani	22%	-	-	25%	13%	-	-
Thanuja	33.4%	-	50%	16.67%	-	-	-

CONCLUSION

Maternal thyroid dysfunction is associated with significant adverse effects on maternal and fetal outcome like PE(25%),Abruptio

placenta(1.5%),anaemia(11%),PTD(18.8%),PPH(2%), and NICU admission(42.5%) etc emphasizing the importance of routine antenatal thyroid screening in first trimester. This study re-emphasizes the need to control

thyroid dysfunction during pregnancy, by maintaining mothers thyroxine levels in the high normal range. This will avoid complications like abortion, preterm labour, preeclampsia, anaemia and low birth weight etc

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