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Analysis of Feto-Maternal Outcome in Patients with Hypothyroidism in Pregnancy

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Original Research Article

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Abstract: Thyroid disorders are the second most common endocrinological disorders in pregnancy next to diabetes mellitus. Despite all the evidence available regarding the adverse feto-maternal outcome in women with thyroid dysfunction, universal screening for thyroid dysfunction is not accepted by all the authorities. The current study is designed to study the prevalence and feto-maternal outcome in women with hypothyroidism in a tertiary care centre catering population from 7 North-East Indian states and compare it with other regions of India. 100 pregnant women with hypothyroidism were followed up through-out pregnancy and their feto-maternal outcomes were compared with 100 euthyroid women. The maternal outcomes studied were: ante-partum factors (anemia, pre-eclampsia, abortions, IUGR, IUFD), Intra-partum events (progress of labor, liquor stain during labor, mode of delivery and indication of instrumental/operative delivery) and post-partum complications. Neonatal outcomes studied were birth weight, Apgar score(1',5'), NICU admission, jaundice requiring treatment, respiratory distress, sepsis, hypoglycemia, hypothermia, and early neonatal death. The prevalence of hypothyroidism in this study was 6.0%. (SCH-4.21%, OH- 1.79%) Comparison of pre-term labor with hypothyroidism shows statistical significance (p valu- 0.01). Hypertensive disorder of pregnancy was significantly higher among cases than controls(p value-0.02). Higher incidence of low birth-weight babies among cases than controls(32.5% vs. 15.5%) can be attributed to prematurity. We emphasize on universal screening of hypothyroidism in pregnancy and categorizing them as high risk pregnancy. With early diagnosis and prompt treatment of this condition feto-maternal outcome can be improved. Follow-up with S.TSH levels every 4 weeks through-out pregnancy is also mandatory to keep up the feto-maternal outcome.

Keywords: Thyroid disorders, respiratory distress, sepsis, hypoglycemia, hypothermia

INTRODUCTION

Thyroid disorders are the second most common endocrinological disorders in pregnancy next to diabetes mellitus. The symptoms can be overlooked because some mimic the hormonal changes of a normal pregnancy, such as tiredness and weight gain. Thyroid dysfunction among women belonging to reproductive age group is regarded as a threat to fertility. Adverse feto-maternal outcome in these women include miscarriage, preterm labour, still births, hypertensive disorders of pregnancy, placental abruption, low birth weight, congenital anomalies and impaired neuro-psychological development in the infant [1,2].

Pregnancy by itself causes alteration in thyroid physiology which results in several changes in thyroid function tests. There is a three-fold increased requirement of thyroid hormones in pregnancy which can be easily achieved by a properly functioning thyroid gland. Women with pre-existing hypothyroidism lack

the functional reserve to increase thyroxine and as a result require 25-47% increase in levothyroxine dose during pregnancy [3].

India is one of the major endemic regions of goiter in the world. The overall prevalence of hypothyroidism in adults was 10.95% in a cross-sectional, multi-centre, epidemiological study conducted in eight major cities of India. [4] Prevalence of hypothyroidism in population-based study done in Cochin, India on 971 adult subjects was 3.9%. The prevalence of subclinical hypothyroidism was also high in this study, the value being 9.4% [5].

Despite all the evidence available regarding the adverse feto-maternal outcome in women with thyroid dysfunction, universal screening for thyroid dysfunction is not accepted by all the authorities.

Indian Thyroid Society (ITS) recommends screening of TSH levels in all pregnant women at the time of their first visit, ideally during pre-pregnancy evaluation or as soon as pregnancy is confirmed. The American College of Obstetricians and Gynecologists recommends thyroid testing in pregnant women with a history or symptoms of thyroid disease but states that there are "insufficient data to warrant routine screening of asymptomatic pregnant women for hypothyroidism".

The current study is designed to study the prevalence and feto-maternal outcome in women with hypothyroidism in a tertiary care centre catering population from 7 North-East Indian states and compare it with other regions of India. The study will also guide us towards a definitive approach in managing these women and the information may throw some light on the acceptance of the need for screening pregnant women for thyroid dysfunction.

MATERIALS AND METHODS

This analytical cross sectional study was conducted at the Department of Obstetrics & Gynaecology, NEIGRIHMS, Shillong for a period of 18 months. All pregnant women were recruited from the antenatal OPD of NEIGRIHMS, SHILLONG.

Cases

All booked pregnant women with hypothyroidism admitted in Obstetrics and Gynaecology ward/labor room, NEIGRIHMS, Shillong.

Controls

Every 3rd booked euthyroid pregnant women admitted in Obstetrics and Gynaecology ward/labor room, NEIGRIHMS, Shillong.

Sample size

200 (cases and controls)

Inclusion criteria

- All pregnant women with hypothyroidism as cases.

Exclusion criteria

Pregnant women with:

- Overt diabetes
- Chronic hypertension
- Obesity
- Uterine anomaly
- Multiple pregnancy
- Previous H/O preterm deliveries
- Known case of Hyperthyroidism(treated/untreated)

Parameters studied

- Age, parity
- Gestational age at delivery
- Duration of thyroid dysfunction and treatment
- Thyroid profile at first diagnosis and thyroid profile after every 4 wks(for hypothyroid women).
- Obstetric complications: abortion, preterm labour, IUGR, APH, gestational hypertension, preeclampsia, IUD, fetal presentation at term,
- Mode of delivery.
- Neonatal outcome: birth weight, APGAR, NICU admission and its cause, jaundice requiring treatment, TSH at day-3 of life(72+/- 12hrs)

All the parameters concerning feto-maternal outcome were collected for all the 100 cases and 100 controls. Both maternal and neonatal outcome were compared between hypothyroid versus euthyroid women. Appropriate statistical measurement like mean, median, relative risk and comparison between the groups using Fischer's exact test were derived using SPSS version 22 (Statistical Package for the Social Sciences) statistics software.

RESULTS AND OBSERVATIONS

In the present study, 151 out of 2503 pregnant women screened had hypothyroidism. Thus, the prevalence of hypothyroidism in this study was 6.0%. The prevalence of subclinical hypothyroidism, overt hypothyroidism was 4.21% and 1.79% respectively. Figure 1 shows percentage distribution in total registered ante-natal women during study period.

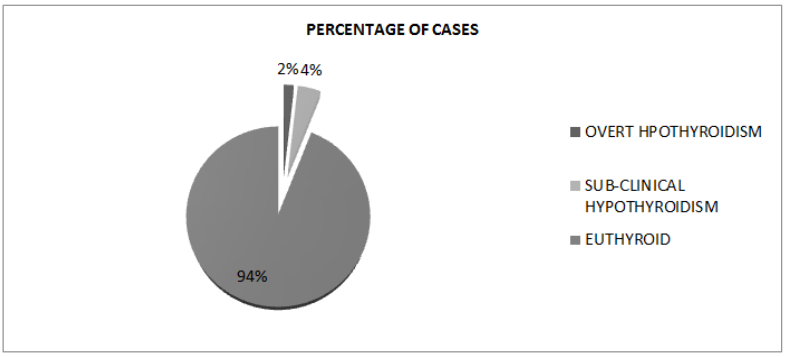

Fig-1: Showing percentage distribution in total registered ante-natal women during study period

Age distribution

The mean age of pregnant women with hypothyroidism was 28.19+/-5.112yrs and median age of 29yrs. The mean age of pregnant women who were euthyroid was 26.56+/-5.170yrs and the median age was 26.5yrs. The age distribution among the study population has been shown in table 2.

Table-2: Showing age distribution

Age(yrs)	Number of cases (%) (n=100)	Number of control (%) (n=100)
15-20	7(7)	11(11)
21-25	26(26)	35(35)
26-30	32(32)	35(35)
31-35	27(27)	14(14)
36-40	8(8)	5(5)

Parity in study population

Table 2a and figure 2a shows the parity of women in the study population. Most women in the study population were multi-parous, 57% among cases and 55% among controls. Most patients were Gravida-2 among both cases and controls.

Table-3a: Parity of patients in study population

Parity	Number of cases (%) (n=100)	Number of controls (%) (n=100)
Primigravida	33 (33)	36 (36)
Multi-gravida	57 (57)	55 (55)
Grand multi-gravida	10 (10)	9 (9)

Gestational age at delivery

In present study, mean gestational age at delivery among cases was 35.53wks±7.732wks and among controls it was 37wks+/-6.827 wks. Comparison of pre-term labor with hypothyroidism shows statistical significance. Relative risk of 1.612(95% CI-1.208 to 2.151,p value-0.01). Among the cases, 28.5% of overt hypothyroid patients had pre-term labor & 18.3% of sub-clinical hypothyroid women had pre-term labor.

Fig-3: shows gestational age at delivery for cases and controls population.

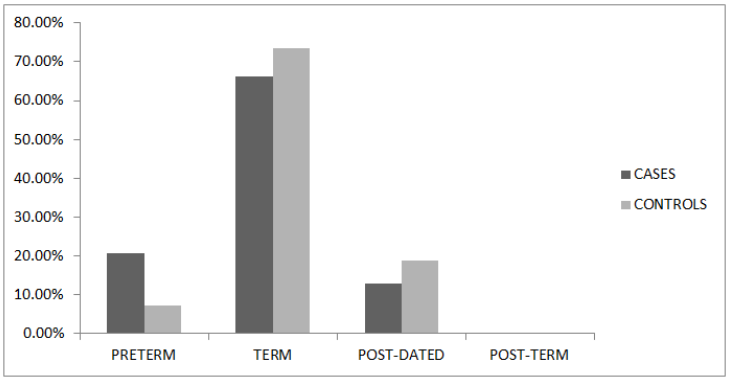

Fig-3: Gestational age at delivery

Hemoglobin levels in study population

In present study, 34% of the cases were anemic whereas 29% of the controls were anemic. Comparison between Hb levels of cases and controls showed no statistical significance with p value of 0.524.

Abortions in present pregnancy

18 out 0f 100 had abortions among cases and 8 out of 100 had abortions among controls. Comparison between spontaneous abortions between cases and controls showed no statistical significance, p value of 0.1528.

Ante-natal complications

In present study, most common ante-natal complication among cases was Preterm labor (20.6%) followed by Hypertensive disorder of pregnancy (15.1%). Hypertensive disorder of pregnancy complicated 15.1% of pregnancy among cases and 5.2% of pregnancies among controls. On comparison, statistical significance found between cases and controls developing hypertensive disorder of pregnancy. Relative risk was 1.58(95% CI -1.159 to 2.173, p value-0.02).

Table-9a: Ante-natal complications in cases & control group

Ante-natal complications	Number of Cases (%) (n=92)	Number of controls (%) (n=95)	p value
Preterm labor	19(20.6)	7(7.3)	0.018
PPROM,PROM	4(4.3)	0(0)	0.060
Post-dated	9(9.7)	10(10.5)	1.000
GHTN	12(13.0)	3(3.1)	0.0295
Pre-eclampsia	2(2.1)	2(2.1)	
Oligohydramnios	6(6.5)	6(6.3)	1.000
Polyhydroamnios	1(1.0)	0(0)	0.4920
Placenta previa	2(2.1)	5(5.2)	0.4446
Cholestasis of pregnancy	3(3.2)	1(1.0)	0.3630
GDM	6(6.5)	2(2.1)	0.1647
IUGR	2(2.1)	1(1.0)	0.6170
IUFD	1(1.0)	2(2.1)	1.000

Mode of delivery

Table 4 shows modes of delivery among case and control group. The indication of LSCS as fetal distress has no statistical difference among cases and control group, p value being 0.6753.

Table-4: Mode of delivery in case and control population

Mode of delivery			Number of cases(%) (n=92)	Number of control (%) (n=95)	p value
Vaginal delivery	Spontaneous		35(38.4)	43(44.7)	0.3767
	Assisted breech		2(2.1)	0(0)	0.2381
	Instrumental	Ventouse	10(10.8)	6(6.25)	0.3025
		Forceps	0(0)	2(2.08)	0.4976
LSCS	Emergency		31(33.6)	33(34.3)	1.000
	Elective		14(15.1)	12(12.5)	0.6745

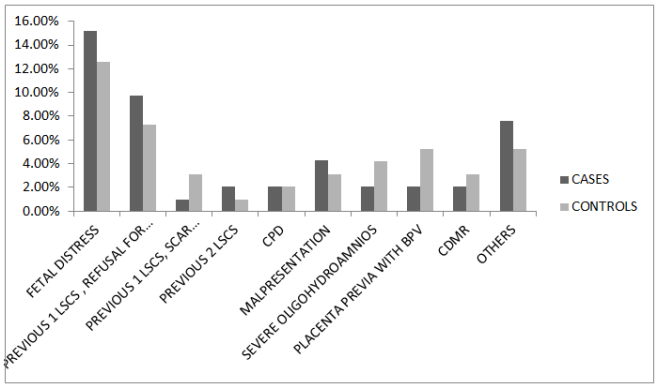

Fig-12b: Indication of LSCS among case and study population

Post-partum complications

Most common post-partum complication in both groups was post-partum hemorrhage, cases (5.4%) and controls (5.2%). On comparing occurrence of post-partum complications among cases and controls, no statistical significance was found, p value 0.6087.

Birth weight

In present study, average birth weight among case and control groups was 2746±644gms and 2927±528gms respectively. On comparing birth weights of babies born to hypothyroid women and euthyroid women statistical significance was found, Relative risk-1.476(95% CI-1.211 to 4.871, p value- 0.01)

Apgar score

Majority of the babies among both groups had Apgar of 8(1'),9 (5'). On comparing low Apgar of babies at 5' among the two groups, no statistical significance was found, p value 1.000.

Neonatal complications

Among cases, 19.5% had neonatal jaundice and 21.7% had NICU admission Among controls, 16.8% had neonatal jaundice and 15.7% had NICU admission.

On comparing development of jaundice requiring treatment among cases and controls there was no statistical significance, p value was 0.7054. On comparing NICU admissions of babies among cases and controls there was no statistical significance, P value- 0.3494.

Serum TSH Value in pregnant women

The mean of TSH level in first trimester among pregnant women with hypothyroidism was 5.188±2.40microIU/ml and among thyroid patients was 1.505±0.618microIU/ml.

Serum TSH in newborns

The mean of TSH level in newborn of hypothyroid women at 72 hrs of birth was 8.91±3.663microIU/ml.

DISCUSSION

The prevalence of hypothyroidism in pregnancy is under-rated due to poor ante-natal health care and inconsistency in the recommendations regarding screening. "Study on prevalence of hypothyroidism in women of reproductive age in Meghalaya, North-Eastern India", by Kharkhongar *et al*. recorded a prevalence of 3.70% hypothyroidism in pregnant women in the age group 15-25 years [6]. In study conducted by Gayathri *et al*. in South-India pregnant women found prevalence of subclinical hypothyroidism to be 2.8% [7]. In another study by Sahu *et al*. prevalence of subclinical hypothyroidism was 6.47% and overt hypothyroidism was 4.58% women [8].

Singh *et al*. conducted a study in Sub-Mountain State of Manipur and found very high prevalence of hypothyroid among pregnant women 23%(subclinical-4.5%, overt-18%) using S.TSH>3microIU/ml as cut-off [9]. The lesser prevalence of hypothyroidism in our study might be attributed to the low sample size, shorter study duration and also to the different population characteristics. However, the value is comparable to that found in study by Kharkhongar *et al*. in the state of Meghalaya.

Saraladevi *et al*. in their study, found prevalence of thyroid disorder to be 11.6% with which was high when compared to other regions in India and in other parts of Asia. Subclinical hypothyroidism and overt hypothyroidism was 6.4% and 2.8% respectively [10]. In recent study published by Dhanwal *et al*. 13.13% of pregnant women had hypothyroidism using a cutoff TSH level of 4.5μIU/ml. The prevalence was much higher using the American Thyroid Association criteria [11].

In present study, out of 29 cases with overt hypothyroidism, maximum women fell under the age group 21-25 (34.4%). Out of 71 cases of sub-clinical hypothyroidism, maximum women belonged to age group 26-30 (33.8%). This shows that in present study sub-clinical hypothyroidism is more prevalent in higher age group women as compared to overt hypothyroidism.

However, in study conducted by Ajmani *et al*. it was noted that overt hypothyroid women had higher maternal age as compared to women in the other groups(sub-clinical hypothyroidism/ sub-clinical hyperthyroidism/ overt hyperthyroidism). The current trend of older women becoming pregnant might be the reason for increase in prevalence of thyroid dysfunction in the older age group [12].

In present study, pre-term delivery was significantly higher among cases than controls. On reviewing the literature, in study by Casey *et al*., they found that the risk of pre-term delivery (defined as delivery at or before 34 weeks of gestation) was almost 2-fold higher in women with subclinical hypothyroidism (relative risk, 1.8, 95% confidence interval 1.1–2.9) [13]. In contrast, Cleary-Goldman *et al*. assessed maternal thyroid function in 10,990 pregnancies at 10–13 weeks and reported that the rate of delivery before 37 weeks in 240 women with subclinical hypothyroidism was not significantly different than in euthyroid pregnancies (5.6% compared with 7.2%) [14]. Saraladevi et *al*. recorded incidence of 7.81 % preterm delivery among women with sub-

clinical hypothyroidism and 10.71% among those with overt hypothyroidism [10].

In our study, 34% of the cases were anemic. However, no statistical significance was found between anemia among hypothyroid and euthyroid women.Previous study by Davis *et al*. found anemia in 31% of cases which is similar to our finding [15]. Saraladevi *et al*. concluded that 4.68% among sub-clinical hypothyroid & 7.14% among overt hypothyroid cases had spontaneous abortions, which is lower than that found in our study [10].

In present study none of the women with hypothyroidism developed IUGR. However, Sahu *et al*. found that there was significant association between IUGR and overt hypothyroidism (p value-0.04) [8]. Ajmani *et al*. IUGR was found in 25% vs. 8.4% vs. 4.9% among sub-clinical, overt and euthyroid pregnant women respectively [12]
In the present study, there was only 1(1%) IUFD among cases and 2(2%) among controls.

Studies by Casey BM *et al*. [13] and Lopamundra *et al*. [16] couldn't find any association between fetal demise and hypothyroidism. On the contrary, Sahu *et al*. found that overt hypothyroids were prone intrauterine demise ($P = 0.0004$) as compared to control [8]. Also study by Anjmani *et al*. found prevalence of IUFD of fetal death as 16.6% among overt hypothyroid patients vs. 1.7 % among euthyroid patients [12].

The difference in findings can be attributed to the lower sample size and better ante-natal care given to the patients. In index study, rate of LSCS was similar in both groups and there was no association between fetal distress as indication of LSCS. Contrary to our findings, Nirmala *et al*. found that rate of caesarean section (51.3%) were higher among cases of hypothyroid women [17]. Also, Sahu *et al*. found that lower segment Cesarean section rate for fetal distress was significantly higher among subclinical hypothyroid women ($P = 0.04$) as compared to euthyroid women [8].

Most common post-partum complication in both groups was post-partum hemorrhage, cases (5.4%) and controls (5.2%). On reviewing the literature, we found that in study by Davis *et al*. (1988) postpartum hemorrhage was found in 19% of hypothyroid cases [15]. And, Nirmala *et al*. found postpartum hemorrhage (12.8%) were higher among cases that controls [17].

On comparing birth weights of babies born to hypothyroid women and euthyroid women statistical significance was found, p value 0.0171 suggesting that hypothyroidism is associated with Low-birth weight. Out of 30 cases with low birth weight, 26(36.6%) were sub-clinical hypothyroid whereas 4(19.0%) were overt hypothyroid women.

Davis *et al*. reflected frequent low birth weight (31%) among hypothyroid women [15]. Ajmani *et al*. found prevalence of LBW babies in overt hypothyroidism, sub-clinical hypothyroidism, euthyroidism, as 50% vs. 25% vs. 12.11 % respectively [12]. Whereas, Saraladevi *et al*. found percentage of low birth weight as 4.68% among SCH women and 10.7% among OH women [10].

Contrary to all the above studies, Cleary-Goldman *et al*. in their study found that Subclinical hypothyroidism was not associated with birth weight [14]. Tudosa R *et al*. found lower Apgar score (<8) in babies of pregnant women who continued to be hypothyroid until the due term [18]. However, in our study, low Apgar was found equally in babies of both groups.

Among Cases of overt hypothyroidism 51.7% showed inadequate response(TSH below trimester specific values) with thyroxine supplementation however among sub-clinical hypothyroid patients only 25.3% showed inadequate response. The complications experienced by cases during the pregnancy in our study might be because of inadequate response to treatment. However, even in adequately treated hypothyroid women there are significantly higher risks of obstetric complications as seen by Nirmala *et al*. [17] and Lopamudra *et al*. [16] in their studies.

Only 1% of the neonate developed neonatal hypothyroidism among cases and none among the controls.

Hulya *et al*. stated that the infants of hypothyroid mothers had higher recall rate in newborn TSH screening and transient thyroid dysfunction in the first 8 weeks of life [19]. However, in our study none of the babies except one needed repeat TSH testing.

CONCLUSION

Based on the present study, we can conclude that universal screening of hypothyroidism in pregnancy should be recommended especially in a country like India, where there are many cases of undiagnosed thyroid disorders. Moreover, even adequate thyroxine replacement in hypothyroid women can still carry the risk of developing obstetric complications. With this background, we emphasize on universal screening of hypothyroidism in pregnancy and categorizing them as high risk pregnancy. With early diagnosis and prompt treatment of this condition feto-maternal outcome can be improved. It needs to be mentioned here that follow-up with S.TSH levels every

4 weeks through-out pregnancy is also mandatory to keep up the feto-maternal outcome

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