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The profile of infants born to mothers with subclinical hypothyroidism in a tertiary care centre.

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Abstract:
Background: *Pregnancy is a stress test for thyroid gland resulting in hypothyroidism in women who were euthyroid before conception. This spectrum starts with subclinical hypothyroidism the effect of which on the fetal clinical profile is less studied.*
Objectives:
1. *To study the clinical profile of infants born to mothers who have subclinical hypothyroidism during pregnancy.*
2. *To study the association between thyroid hormone replacement in subclinical hypothyroid mothers and the birth weight of their infants.*

Methods: *A cross sectional study was conducted on the profile of 49 infants born to mothers with subclinical hypothyroidism during pregnancy. Anthropometric details of infant and clinical details of mothers are collected and analyzed.*
Results: *The mean birth weight of infants was 2.94 ±0.42Kg. Among the 49 infants studied 16.32% born with low birth weight. 6% of mothers had preterm delivery. Mean length: 49.02± 1.5cm. Mean head circumference: 33.74±1.0cm. Mean mid-arm circumference: 11.17 ±0.71cm. No statistically significant association was observed between thyroid hormone replacement treatment and birth weight of infants (p=.9146). 30.61% of infants born through caesarian section. 20.4% of mothers have previous history of abortions.*
Conclusion: *Maternal subclinical hypothyroidism has significant effect on fetal anthropometric parameters.*
Keywords: *Anthropometry, Subclinical Hypothyroidism*

I. Introduction

Pregnancy is a physiological process in which many changes occur in the normal endocrine physiology of human body. One of the commonest endocrine abnormalities related to pregnancy is thyroid dysfunction.. The incidence of maternal hypothyroidism is relatively high in our part of country. The spectrum of thyroid dysfunction ranges from subclinical hypothyroidism to overt hypothyroidism. The effect of maternal thyroid hormone on developing fetus is crucial for its physical and mental growth. Maternal hypothyroidism has been proven to be a risk factor for preterm delivery, low birth weight and inadequate neuro-cognitive development of the infant [1]. Besides that maternal hypothyroidism has been related to pregnancy related complication for the mother including abortion, gestational hypertension, preeclampsia, placental abruption and neonatal death [2].

The considerable fraction of pregnant women having thyroid dysfunction during pregnancy belongs to subclinical hypothyroidism. The biochemical definition of subclinical hypothyroidism is an elevated TSH levels with a normal free T4 levels. Due to the dynamic changes during pregnancy, use of trimester specific and assay specific TSH ranges are recommended. Where such reference ranges are not available, the following cut offs may be used; first trimester, <2.5 mIU/L; second trimester, <3 mIU/L; third trimester <3 mIU/L [3]. The effects of mild maternal hypothyroidism on developing fetus are less documented. It has been observed that subclinical hypothyroidism in pregnancy is related to increased incidence of preterm delivery and thus low birth weight of infants [4,5]. The effects of subclinical hypothyroidism in pregnancy on fetal anthropometric parameters are very less documented. In women with overt hypothyroidism (elevated TSH and low free T_4); thyroxin supplementation during pregnancy also has been associated with improved pregnancy outcomes [6]. Whereas, there is limited data available about the benefits of thyroid hormone replacement for subclinical hypothyroidism in pregnancy.

II. Aims and objectives

- To study the clinical profile of infants born to mothers who have subclinical hypothyroidism during pregnancy.
- To study the association between thyroid hormone replacement in subclinical hypothyroid mothers and the birth weight of their infants.

III. Methodology

3.1 Study type: Cross sectional study

3.2 Study population: All infants who were born to mothers with subclinical hypothyroidism in pregnancy, either vaginally or by elective Caesarean section during the study period of two consecutive months after April 2014 in a tertiary care centre.

3.3 Case Definition: A mother is defined to have subclinical hypothyroidism if the TSH level is found to be > 2.5 mIU/L in first trimester and >3 mIU/L in second and third trimester with no symptoms of hypothyroidism.

3.4 Selection criteria: All infants of mothers with Subclinical hypothyroidism, who have been born in the labour suite of this tertiary care centre, were included in the study after obtaining the informed consent.

3.4.1 Inclusion criteria:

All infants born either vaginally or by elective Caesarean in the labour suite of this tertiary care centre during two consecutive months after April 2014.

3.4.2 Exclusion criteria:

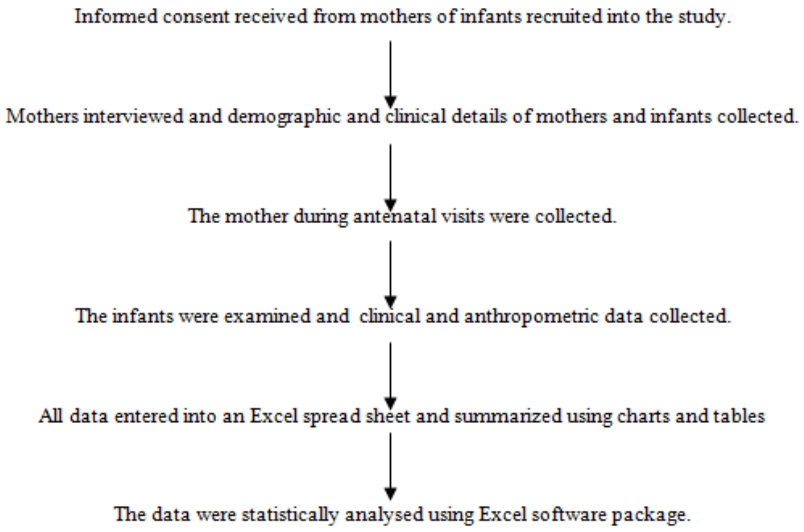
- Infants born to mothers who had previous thyroid surgery
- Infants born to mothers who have other co-morbidities such as gestational diabetes, pregnancy induced hypertension, preeclampsia, eclampsia, rheumatic heart diseases, collagen vascular disease, bronchial asthma, uncorrected anemia, TORCH infection during pregnancy.
- Hypothyroidism detected before pregnancy and receiving treatment.
- Overt hypothyroidism detected during or before pregnancy and on treatment (TSH >10mIU/L).

3.5 Study design: Written informed consent obtained from all mothers of infants recruited into the study. All infants born to parturient women who delivered vaginally or by elective Caesarian in the study setting during the study period of two consecutive months after April 2014 were surveyed.

3.5.1 Data about Mothers: Details of infant's mother such as demographical details, trimester in which the TSH analysis done and started on treatment with thyroxin, symptoms of hypothyroidism were collected.

3.5.2 Details of Infant: The infants were examined and anthropometric and clinical data of the infant such as body weight, height, chest circumference and gestational age were collected. The collected data analysed statistically using Microsoft Excel statistical package.

3.5.3 Study Flow Chart



3.6 Sample size: The sample size was 49 for the study to have a confidence interval of 95% and a variability of 10% for a prevalence of preterm delivery in subclinical hypothyroidism in pregnancy of 15% [7].

3.7 Ethical issues

The study was approved by the Institutional Ethics Committee on 15.01.2014. The details of the study were explained to all participants and written informed consent is obtained.

3.8 Confidentiality

Confidentiality of all data will be maintained. All the investigations that are done as part of the study are routine investigations in the hospital protocol of mothers with subclinical hypothyroidism and there will be no additional cost to the participant.

IV. Results

TABLE .1

Demographic data of subclinical hypothyroid mothers

Age(years)	Number of mothers (Percentage)
≤20	2(8.16)
21 -25	17(34.69)
26-30	25(51.02)
≥30	4(4.08)
Obstetric status(Gravida)	
Primi	27(55.10)
G2	16(32.65)
G3	5(10.20)
>G3	1(2.04)
Previous history of adverse pregnancy outcomes	
Abortions	10(20.40)
Neonatal death	1(2.04)

TABLE. 2 TSH assessment and treatment history of subclinical hypothyroid mothers.

Trimester in which TSH value checked	Number of mothers (Percentage)
First trimester	36(73.46)
Second trimester	10(20.40)
Third trimester	3(6.12)
Mean TSH levels (mIU /L)	3.649±1.30
Number of patients received treatment	12(24.48)
Timing of initiating treatment	
First trimester	6 (50.0)
Second trimester	5(41.66)
Third trimester	1(8.33)

TABLE .3 Details regarding delivery and demographic and clinical profiles of infants

Time of delivery	Number of mothers (Percentage)
Term delivery (37- 42 weeks)	46(93.87)
Preterm delivery(< 37 weeks)	3(6.12)
Post term delivery (≥42 weeks)	0
Mode of delivery	
Vaginal	34(69.38)
Caesarian section	15(30.61)
Gender of infants	
Male	24(48.97)
Female	25(51.02)
Number of low birth weight infants	8(16.32)
Mean birth weight of low birth weight infants(Kg)	2.234±0.20
History of Neonatal ICU admission	Number of infants 6(12.24)

TABLE .4 Anthropometric data of infants born to subclinical hypothyroid mothers

Parameters	Value
Birth weight (Kg)	2.94 ± 0.42
Length(cm)	49.02±1.59
Mid arm circumference(cm)	11.17±0.71
Head circumference(cm)	33.75±1.08

- No statistically significant association exists between age of pregnant women having subclinical hypothyroidism and mode of delivery (p = 0.907).
- No statistically significant association exists between thyroid hormone replacement for subclinical hypothyroidism in pregnancy and the birth weight of infants (p = 0.915).
- No statistically significant association exists between type of delivery and obstetric status of pregnant women with subclinical hypothyroidism (p = 0.317).

V. Discussion

The present study was aimed at studying the profile of infants born to mothers having subclinical hypothyroidism during pregnancy and the result obtained were discussed below.

5.1. Age pattern of the subclinical hypothyroid mothers.

According to the obtained age pattern of subclinical hypothyroid mothers, it is evident that most of them belong to an age group 26-30 years (51.02%). 34.69% belong to 20-25 years of age group. 4.08% and 8.16% mothers belong to <20 years and >30 years of age group. The reports suggest that other studies also obtained nearly the same findings (26.9 $\pm$ 5.9, 25.6$\pm$ 11.1) [4, 8]. No statistically significant association obtained between age of mothers and type of delivery (p= 0.977).

5.2 Obstetric status of the subclinical hypothyroid mothers.

55% of subjects were primi-gravida and 32% were second gravida. 10% of them belong to third gravida. Only <3% have had more than 3 pregnancies. Similar results were reported prior in the literatures [4].

5.3 previous histories of adverse pregnancy outcomes

20.4% of subjects had previous history of abortions and 2% had history of neonatal death.

5.4 TSH assessment and treatment history of subclinical hypothyroid mothers

36% of subjects underwent TSH assay in first trimester.10% in second trimester and 8% in third trimester respectively. In our study the mean TSH levels obtained were 3.65 $\pm$ 1.30 m IU / L. In another study the mean TSH levels obtained were 3.6 $\pm$ 11.1 m IU / L [8].

50% of treated patients started to receive treatment in first trimester.42% in second and 8% in third trimester respectively. But no statistically significant association has been observed between thyroid hormone replacement for subclinical hypothyroidism and birth weight of infants (p=0.9146).

5.5 pattern of delivery and demographic and clinical profiles of infants

In this study 69 % of subclinical hypothyroid mothers delivered vaginally, while 31% needed caesarian section. There is increased incidence of caesarian sections among subclinical hypothyroid mothers (25%) [4] .No statistically significant association obtained between obstetric status of subclinical hypothyroid mothers and type of delivery (p=0.11).

In this study 51% of infants born to subclinical hypothyroid mothers were females and 49% were males. In our study 6% of infants born to mothers with subclinical hypothyroidism were preterm infants, which is similar to other studies (4%, p = .011) [4].

5.6Anthropometric data of infants born to subclinical hypothyroid mothers

On assessment of anthropometric parameters the mean body weights of infants were 2.94 $\pm$ .42Kg. In another study the mean birth weight of infants was 3.317 $\pm$ .599 Kg [4]. In our study the mean length of the infants are 49.02 $\pm$ 1.58 cm , mean head circumference 33.75 $\pm$1.07 cm and mean mid arm circumference 11.17 $\pm$ 0.71 cm.

Among 49 infants studied 8 (16.32%) infants were low birth weight infants (2.234±0.20Kg).

In our study 4% of infants were admitted in Neonatal ICU which is similar to other reports (4%, p = 0.019) [4].

VI. Conclusion

This study enabled us to realize that subclinical hypothyroidism, being the mild variety of thyroid dysfunction, is common among primi gravid and early young age group. It can be concluded that it could be cause for pregnancy losses, increased caesarian sections and preterm labor. Assessment of anthropometric data of infants revealed it has little effect on fetal birth weight and other parameters. But observed a n increased prevalence of neonatal ICU admission among participant infants.

The main limitations of the study were the smaller sample size. Further researches are needed for a proper understanding of morbidity caused by mild thyroid dysfunction in pregnancy.

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