



## RESEARCH ARTICLE

### PREVALENCE OF SUBCLINICAL AND OVERT HYPOTHYROIDISM IN PREGNANCY AT NORTH INDIAN TERTIARY CARE CENTER

**1Meenakshi, 1,\*Prabhat and 2Sahu, D.**

**1**Department of Biochemistry, Lady Hardinge Medical College, New Delhi

**2**Department of Biochemistry, King George Medical College, Lucknow

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\*Corresponding author: Prabhat

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#### ABSTRACT

**Background:** Thyroid disorders are among the common endocrine problems in pregnant women. It is now well established that not only overt, but subclinical thyroid dysfunction also has adverse effects on maternal and fetal outcome. There are very few data from India about the prevalence of thyroid dysfunction in pregnancy. **Aims and objectives:** This study aims to find prevalence of thyroid dysfunction in pregnancy and its impact on obstetrical outcome in Indian population. The study has also an objective of finding the occurrence of subclinical hypothyroidism and overt hypothyroidism. **Materials and Methods:** 1055 pregnant women in first and second trimester were registered. Detailed history and examination was done. Apart from routine obstetrical investigations, thyroid stimulating hormone(TSH) level estimation was done. If TSH level was deranged then free T4 and T3 levels estimation were done. **Results:** Prevalence of thyroid dysfunction was high in this study, with subclinical hypothyroidism in 13.2 %, hypothyroidism in 20.7%and overt hypothyroidism in 1.4% women in a north Indian tertiary care center. **Conclusions:** Prevalence of thyroid disorders, especially hypothyroidism (20.7%) and subclinical hypothyroidism (13.2%) was high.

## INTRODUCTION

Subclinical hypothyroidism is an abnormally high thyroid-stimulating hormone (TSH) level with normal free thyroxine level without symptoms of hypothyroidism (Davis, 1988). Subclinical hypothyroidism during pregnancy has been reported to be associated with adverse pregnancy outcomes and impaired fetal neurodevelopment, such as gestational diabetes, preeclampsia, preterm labor, placental abruption (Leung, 1993; Haddow et al., 1999; Pop et al., 1999), increased cesarean section rates for fetal distress (Pop, 1995), spontaneous abortion (Glinoer, 2010), and low intelligence quotient (IQ) score of the offspring (Sapin, 2004). In addition, Negro et al. (1999) showed that the supplementation of thyroid hormone in pregnant women with subclinical hypothyroidism improved pregnancy outcomes. Following these results, Thung et al. (2009), The Spanish Society of Endocrinology and Nutrition (Glinoer, 1998), and Dosiou et al. (Goodwin, 1992) recommended maternal serum screening of thyroid-stimulating hormone in early pregnancy. In addition, the Endocrine Society recommended replacement of levothyroxine in pregnant women with subclinical hypothyroidism (Davis et al., 1989). Because of dynamic changes of human chorionic gonadotropin (hCG) and thyroxine-binding globulin, which affects hypothalamic-pituitary-thyroid axis, the concentrations

of TSH and free thyroxine (fT4) change during pregnancy (Millar, 1994; Kriplani, 1994; Momotani et al., 1987; Casey, 2005). Based on these reports, the 2017 American Thyroid Association (ATA) guideline recommended the trimester-specific criteria of TSH concentration for the diagnosis of subclinical hypothyroidism (Reference ranges: First trimester, 2.5-4  $\mu$ IU/ml; Second trimester, 2.5-4.5  $\mu$ IU/ml; Third trimester, 2.5-4.5  $\mu$ IU/ml (Goodwin, 1992). When pregnancy overlaps maternal endocrine imbalance, undesirable consequences for both mother and fetus may appear. It is acknowledged that hypothyroidism in pregnancy is associated with an increased risk of abortion, habitual abortion, premature delivery, intrauterine fetal death, fetal retardation and fetal congenital anomalies, congenital hypothyroidism, postpartum bleeding, anemia, post-partum depression and cardiac dysfunction, which leads to increased maternal morbidity, perinatal morbidity and mortality (Haddow et al., 1999; Pop et al., 1999; Pop et al., 1995).

## MATERIALS AND METHODS

**Study design:** In this cross-sectional study, singleton pregnant women who were tested for serum TSH during the first trimester of pregnancy and delivered at Lady Hardinge Medical College and Hospitals, New Delhi, India between

September 2017 and September 2017 were enrolled. Women with known thyroid disease were excluded.

Pregnant women with multiple pregnancies, miscarriage, stillborn, or those with underlying medical diseases, such as pregestational diabetes or chronic hypertension, were also excluded. The median TSH, T4 and T3 values were obtained in pregnant women at 12-14 weeks and patients were segregated as euthyroid, hypothyroid, overt hypothyroid and hyperthyroid. As per the latest 2017 American Thyroid Association criteria hypothyroidism was classified using a cutoff TSH level of 4.0  $\mu\text{IU}/\text{ml}$ . Moreover, subclinical hypothyroidism was considered at a TSH level of 2.5-4.0  $\mu\text{IU}/\text{ml}$  with elevated free T4 levels. Overt hypothyroidism was considered at normal T4 levels and elevated TSH level. Hyperthyroidism was defined at TSH level of less than 0.1  $\mu\text{IU}/\text{ml}$ .

**Measurement of TSH, T4 and T3:** Serum TSH, T4 and T3 for adults was measured by Chemiluminescence on Access 2 Immunoassay System (Beckman Coulter, California, United States). Functional sensitivity of TSH was 0.008  $\mu\text{IU}/\text{ml}$ , and the laboratory reference range for adult is 0.55-4.78  $\mu\text{IU}/\text{ml}$  for our laboratory. Serum samples of neonates for same parameters were analysed by electroChemiluminescence at Cobas e411 (Roche diagnostics, Risch-Rotkreuz, Switzerland)

**Statistical analysis:** Statistical analysis was performed by SPSS software (version 20.0, Chicago, IL, USA), using the Mann-Whitney U-test, Fisher's exact test, or chi-square test for trends, as indicated. Correlation analysis between parameters were done and coefficient and p values were obtained using medcalc version 8.0. The result was considered statistically significant when the P value was less than 0.05.

**Ethics statement:** This cross sectional study was approved by the institutional review board of Lady Hardinge Medical College and Hospitals, New Delhi, India.

## RESULTS

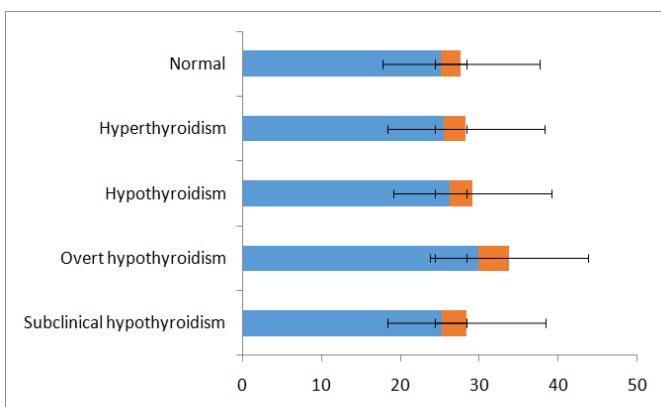
The baseline characteristics of the study population are given in Table 1. The mean age of the study population was  $25.6 \pm 2.43$  years with a mean gestational age of  $12 \pm 1.1$  weeks. Body Mass index of the study population group was on an average 25.6 years. Mean gestational age at study was 12 weeks.

**Table 1. Demographic characteristics of the study population (n=1055)**

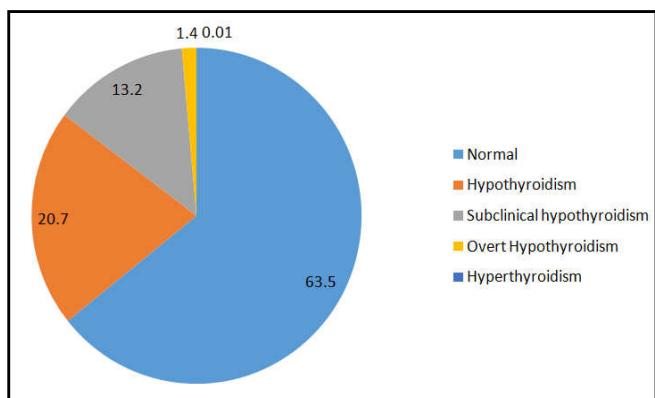
1.	Age (years)	$25.6 \pm 2.43$
2.	BMI( $\text{kg}/\text{m}^2$ )	$23.9 \pm 3.1$
3.	Gestational age(weeks)	$12 \pm 1.1$
4.	Total Cholesterol( $\text{mg}/\text{dl}$ )	$190 \pm 26$
5.	Hb( $\text{gm}/\text{dl}$ )	$10.1 \pm 1.2$

Out of 1055 pregnant women studied over a 1-year time span, 140 (13.2%) were subclinical hypothyroid (Group-1), 15 (1.4%) were overtly hypothyroid (Group-2), 220 (20.7%) were hypothyroid (Group-3) and 10 (0.01%) were hyperthyroid (Group-4). 670 (63.5%) subjects were found to be euthyroid (Group-5). Overt hypothyroidism group were the oldest at an average age of  $29.9 \pm 3.8$  years and had maximum thyroid stimulating hormone (TSH) levels  $13.51 \pm 3.44 \mu\text{IU}/\text{ml}$ . Mean age of population with normal thyroid levels were 25.07 years. Average TSH of subclinical hypothyroidism group was  $3.24 \mu\text{IU}/\text{ml}$ , while that of hypothyroidism group was  $5.38 \mu\text{IU}/\text{ml}$ . maximum TSH levels were seen in overt hypothyroidism

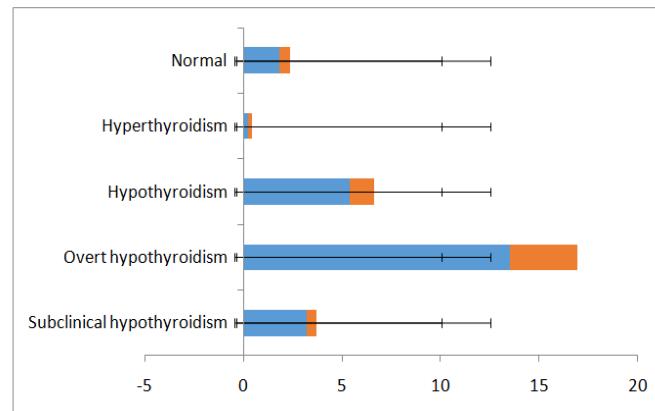
group at  $13.51 \mu\text{IU}/\text{ml}$ , whereas minimum levels were found in hyperthyroidism group at  $0.266 \mu\text{IU}/\text{ml}$ .



**Figure 1. Mean $\pm$ SD of age distribution of various thyroid disorders during first and second trimester of Pregnancy**



**Figure 2. Prevalence of various thyroid disorders in population of first and second trimester of Pregnant women**



**Figure 3. Mean $\pm$ SD of TSH concentrations in thyroid disorders during first and second trimester of Pregnancy**

## DISCUSSION

Pregnancy brings many physiological changes that affect the thyroid environment, including increased plasma volume and increased renal clearance (8). The cross-reactivity of hCG to the TSH receptor and the increase of thyroid hormone carrier (thyroxine-binding globulin) also affect the levels of TSH and free T4 in normal pregnancy. Moreover, the most dynamic increase of TSH concentrations is observed during the first trimester due to multifarious hormonal and biochemical alterations in mother's body (7).

**Table 2. Prevalence and levels of thyroid abnormalities in pregnancy**

	Normal		Age (years)	T3(pg/ml)	T4(ng/dl)	TSH( $\mu$ IU/ml)
Group-1	Subclinical hypothyroidism	140 (13.2%)	25.2±3.13	2.96±0.35	1.78±0.41	3.24±0.49
Group-2	Overt hypothyroidism	15 (1.4%)	29.9±3.8	3.08±0.40	0.7±0.25	13.51±3.44
Group-3	Hypothyroidism	220 (20.7%)	26.3±2.8	2.99±0.40	0.67±0.23	5.38±1.27
Group-4	Hyperthyroidism	10 (0.01%)	25.44±2.87	3.55±0.55	0.85±0.26	0.266±0.20
Group-5	Normal	670 (63.5%)	25.07±2.67	3.05±0.45	0.62±0.14	1.83±0.54

Moreover, American Thyroid Association (ATA) has recently changed the criteria of hypothyroidism by raising the TSH cutoff levels to  $4\mu$ IU/ml. Indeed, the diagnosis rate of subclinical hypothyroidism changed according to the latest ATA guidelines. Change in TSH levels has been found in first and second trimesters of pregnancy has been found at various regions of world based on ethnic and lifestyle changes. Thyroid hormones profile has been documented to be slightly different at various regions of the world. We obtained normal reference values of TSH concentrations in first trimester among women of Delhi.

In addition, it is well known that there is a slight but significant difference in TSH concentration among ethnic groups (7), and Asians along with black women were observed to have approximately 0.4 mIU/L lower TSH values in comparison with white women (Millar, 1994). Few studies have been done among South Asian pregnant women reporting increased risk of thyroid dysfunction [Lee, 2009]. It was, therefore, important to conduct the present study because the findings of other studies may not apply to an Indian population. Overt hypothyroidism group had an average age of  $29.9\pm3.8$  years and had maximum thyroid stimulating hormone (TSH) levels  $13.51\pm3.44 \mu$ IU/ml. Mean age of population with normal thyroid levels were 25.07 years and TSH levels were  $1.83 \mu$ IU/ml. Average TSH values of women with subclinical hypothyroidism group was  $3.24 \mu$ IU/ml, while that of hypothyroidism women group was  $5.38 \mu$ IU/ml. Minimum levels were found in hyperthyroidism group at 0.266 with an average age of 25.44 years.

We found a very high prevalence of hypothyroidism (20.7%) and subclinical hypothyroidism (13.2%) among urban Indian population. We also found that incidence of hypothyroidism was much common among higher age groups. The prevalence of hypothyroidism has been reported from different countries very recently (Goodwin, 1992; Davis, 1989; Millar, 1994). On analysis, results of this study are consistent with recently published data from India and other countries. Previous studies conducted in Delhi reported a 14.3% prevalence of hypothyroidism during the first trimester (Kriplani, 1994). There are at least two small-scale published studies from the South, one from Chennai, and another from Hyderabad. Rao *et al.* included 163 non-pregnant women with recurrent pregnancy loss in a gestational age up to 12 weeks (2006) in Hyderabad (Momotani, 1987). Similarly, in a community-based large-scale study involving over 500,000 pregnant women from the USA showed a 15.5% prevalence of hypothyroidism (Casey, 2005). Our study shows a high prevalence of thyroid dysfunction, especially overt and subclinical hypothyroidism among Indian pregnant women with associated adverse perinatal outcome. Based on the results of the present study, we, therefore, suggest for a decrease threshold for screening and detection of thyroid dysfunction among Indian pregnant women attending routine antenatal clinic and to be potentially aware of associated maternal and fetal complications.

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