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RESEARCH ARTICLE

"High Prevalence of Thyroid Dysfunction Amongs Pregnant Women in Ahmedabad City, Gujarat, India"

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Abstract

Background: Thyroid dysfunction is the most frequent endocrine disorder in pregnant women. Maintaining a pregnant woman in a euthyroid state is a challenge for the thyroid gland during gestation. Thyroid disease in pregnancy can affect the health of the mother as well as the child before and after delivery. The deleterious effects of thyroid dysfunction can also extend beyond pregnancy.

Aims and Objectives: To determine the current prevalence of thyroid dysfunction in normal pregnant women and to study the potential adverse outcomes of thyroid dysfunction on mother and fetus.

Materials and Methods: The present study was conducted between January 2013 to December 2014. A total of 350 patients from antenatal clinics or maternity home of Ahmedabad city were included in the study. Apart from routine procedure, serum TSH level was estimated in all the patients enrolled in this study. In patients with deranged TSH level, Free T4 and anti-TPO antibody tests were also done.

Results: Out of total 350 patients, 58 (16.57 %) had deranged thyroid function. Hypothyroidism was detected in 46 (13.54 %) patients, out of which 26 (7.43 %) patients had overt hypothyroidism and 20 (5.71 %) patients had subclinical hypothyroidism. Hyperthyroidism was detected in 12 (3.43 %) patients, out of which 5 (1.43 %) patients had overt hyperthyroidism and 7 (2.0 %) patients had subclinical hyperthyroidism in our study. Anti-TPO antibody was found positive in 26 (56.5 %) hypothyroid patients.

Conclusion: Increased maternal age was associated with higher incidence of thyroid dysfunction. Chances of fetal distress as well as fetal loss were much greater in the pregnant women with hypothyroidism compared with those from the euthyroid group.

To screen pregnant women for serum TSH concentrations in the first trimester of pregnancy was cost saving compared with no screening.

INTRODUCTION

Thyroid dysfunction is the most frequent endocrine disorder in pregnant women.[1] Thyroid disease in pregnancy can affect the health of the mother as well as the child before and after delivery. Thyroid disorders are prevalent in women

of child-bearing age and for this reason commonly present as an intercurrent disease in pregnancy and the puerperium.[2] Uncorrected thyroid dysfunction in pregnancy has adverse effects on fetal and maternal well-being. The deleterious effects of thyroid dysfunction can also extend beyond pregnancy and delivery to affect neurointellectual development in the early life of the child. Demand for thyroid hormones is increased during pregnancy which may cause a previously unnoticed thyroid disorder to worsen. Still, the overall lack of evidence precludes a recommendation for universal screening for thyroid disorder in all pregnant women.[3]

Fetal thyroxine is wholly obtained from maternal sources in early pregnancy since the fetal thyroid gland only becomes functional in the second trimester of gestation. As thyroxine is essential for fetal neurodevelopment it is critical that maternal delivery of thyroxine to the fetus is ensured early in gestation. In pregnancy, iodide losses through the urine and the feto-placental unit contribute to a state of relative iodine deficiency.[4] Thus, pregnant women require additional iodine intake. A daily iodine intake of 250 µg is recommended in pregnancy but this is not always achieved even in iodine sufficient parts of the world.[5]

Maintaining a pregnant woman in a euthyroid state is a challenge for the thyroid gland during gestation because of an increased thyroid hormone demand and decreased iodine availability due to iodine transfer to the fetus and intensified iodine urinary losses induced by the increased renal glomerular filtration.[6,7]

Women with thyroid dysfunction both overt and subclinicalare at increased risk of pregnancy-related complicationssuch as threatened abortion, preeclampsia, pretermlabor, placental abruption, and postpartum hemorrhage.Fetal complications include low-birth-weight babies, first trimesterspontaneous abortions, preterm delivery, fetal orneonatal hyperthyroidism, intrauterine growth retardation,
high rates of still birth and neonatal deaths, neonatalhyperbilirubinemia, higher incidence of neonatal hypothyroidism,and increased perinatal mortality.[8,9,10]

Thyroid disorders are frequently observed during pregnancy and are more frequent in case of mild iodine deficiency (MID). Pregnancy induces fundamental changes in thyroid function and iodine metabolism leading to thyroid stimulation. The main metabolic modifications include (1) a marked rise in estrogen and human chorionic gonadotrophin concentration leading to a more than doubling of serum thyroxin binding globulin levels; (2) an increase in iodide renal clearance due to increased glomerular filtration rate; (3) a transfer of iodide to the fetal compartment;
and finally;(4) a direct, albeit transient, stimulation of the thyroid by human chorionic gonadotropin near the end of the first trimester of gestation.[11,12,13]

To prevent some potential adverse outcomesassociated with maternal thyroid disorders and theobvious benefits of treatment, some expert panels havesuggested routine thyroid function screening in allpregnant women.[14,15]

The prevalence of overt hyperthyroidism complicating pregnancy has been reported to range between 0.4 and 1.7 % [16]and an estimated 2–3 % of women are hypothyroid during pregnancy.[17,18] Overt hyperthyroidism occurs in 0.4–1.7 % of pregnant women.[19]

MATERIALS AND METHODS:

The present study was conductedbetween January 2013to December 2014. The study was conducted after getting permission from the institutional ethical committee.A total of 350 patients from antenatal clinics or maternity homes of Ahmedabad citywereincluded in the study. All healthy pregnant women without any known medical disorder, between 13 and 28 weeks of gestation, were included in the study.Patients with multifetal gestation, known thyroid and othermetabolic disorders like diabetes, hypertension, having past historyof miscarriage or missed abortion and who were not interested for this studywere excluded from the study.

Apartfrom routine procedure like informed consent, detailed history and examination, serum TSH level was estimated inall the patients enrolled in this study. In patients withderanged TSH level, Free T4 and anti-TPO antibody tests were also done. TSH and Free T4 were assayed by electro-chemiluminescence immunoassay (ECLIA) method using an automated clinical chemistry analyzer (Elecsys 2010; Roche Diagnostics). TPO antibody assaywas done using the Enzyme Linked ImmunoSorbantAssay (ELISA)microwell kit.The reference range used in the study was based onguidelines of the American thyroid association 2011[20] forthe diagnosis and management of thyroid disease during pregnancy and postpartum.

According to the guidelines, iftrimester-specific reference ranges for TSH are not availablein the laboratory, the following reference ranges arerecommended: first trimester, 0.1–2.5 μIU/ml; second trimester,0.2–3.0 μIU/ml; and third trimester, 0.3–3.0 μIU/ml. [20]

The patients with deranged thyroid dysfunction weretreated and followed up till the termination of pregnancy.Those with abnormal tests were put on treatment, andthyroid function tests were repeated every 6 weeks duringpregnancy and drug dosages were adjusted accordingly.Patients were followed up throughout pregnancy andmonitored.The maternal outcome and fetal outcome were noted.

RESULTS:

The patients were divided into the following groupsaccording to thyroid function test results:Group A: Euthyroid, defined as normal TSH(0.2–3.0 μIU/l). Group B: Subclinical hypothyroid, definedas high TSH (> 3.0 μIU/l) in the presence of normal levelsof Free T4 (0.8–2.0 ng/dl). Group C: Overt hypothyroid,defined as high TSH (> 3.0 μIU/l) with low Free T4(< 0.8 ng/dl). Group D: Subclinical hyperthyroid, defined aslow serum TSH (< 0.2 μIU/l) concentration with normalFree T4 (0.8–2.0 ng/dl). Group E: Overt hyperthyroid,defined as with high Free T4 (> 2.0 ng/dl) with decreasedTSH (< 0.2 μIU/l).

Out of total 350 patients, 58 (16.57 %) had deranged thyroidfunction, making the prevalence of thyroid dysfunction16.57 %. Hypothyroidism was detected in 46(13.54 %) patients, out of which 26(7.43 %) patients had overt hypothyroidism and 20 (5.71 %) patients hadsubclinical hypothyroidism. Hyperthyroidismwas detected in 12 (3.43 %) patients, out of which 5 (1.43 %) patients had overthyperthyroidism and 7(2.0 %) patients had subclinical hyperthyroidismin our study. Anti-TPO antibody was done inpatients with deranged TSH levels. Anti-TPO antibody wasfound positive in 26(56.5 %) hypothyroid patients. No anti-TPO antibody was found in hyperthyroid patients.

TABLE: 1 : Obstetrical variable in the antenatal period

Group	Mean Age in Years	Mean BMI in kg/m^2
A	23.8 ± 3.26	23.1 ± 1.2
B	24.6 ± 3.18	24.8 ± 1.4
C	25.1 ± 3.82	25.6 ± 1.8
D	26.3 ± 2.74	21.3 ± 1.2
E	28.8 ± 1.10	20.4 ± 0.8

(BMI = Body Mass Index, Obesity is defined as a BMI ≥30 kg/m^2.[21]
Table 1 show maternal demographic characters. Maternal age was comparatively high in the overt hypothyroid and overt hyperthyroid groups than normal euthyroid group. In present study, the mean BMI was 23.1 ± 1.2 for euthyroid patients, 24.8 ± 1.4 for subclinical hypothyroid, 25.6 ± 1.8 for overt hypothyroid, 21.3 ± 1.2 for subclinical hyperthyroid, and 20.4 ± 0.8 for overt hyperthyroid. Obese women had higher serum TSH concentration and were more prone to hypothyroidism than normal-weight women. The data on hypothyroidismwere more conclusive than in hyperthyroidism asthe sample size in the hyperthyroidism group was smalland the disease is comparatively infrequent.

TABLE: 2 : Maternal complications in the study

Types of Complications	Group A n=292	Group B n=20	Group C n=26	Group D n=7	Group E n=5	Total n=350
Anemia	32 (11.0%)	7 (35.0%)	3 (11.5%)	1 (14.3%)	0	43 (12.3%)

Pre-eclampsia	19 (6.5%)	2 (10.0%)	3 (11.5%)	0	1 (20.0%)	25 (7.1%)
Abruption	3 (1.0%)	0	1 (3.8%)	0	0	4 (1.1%)
GDM	3 (1.0%)	1 (5.0%)	3 (11.5%)	0	0	7 (2.0%)
PPH	23 (7.9%)	3 (15.0%)	2 (7.7%)	1 (14.3%)	1 (20.0%)	30 (8.6%)
Total	80 (27.4%)	13 (65.0%)	12 (46.0%)	2 (28.6%)	2 (40.0%)	104 (31.1%)

(GDM=Gestational Diabetes Mallitus, PPH=Post PartamHaemorrhage)

Table 2 shows the different types of maternal complications like anemia, pre-eclampsia, placental abruption, GDM and PPH in differentgroups. Adverse maternal effects in overt hypothyroidismincluded preeclampsia (11.5 vs. 6.5 %) and GDM (11.5 vs. 1.0 %). No significantincrease in anemia (11.5 vs. 11.0 %), placental abruption (3.8 vs. 1.0 %), and postpartum hemorrhage (7.7 vs. 7.9 %) was seen in the overt hypothyroid group. Subclinicalhypothyroidism was significantly associated with anemia (35.0 vs. 11.0 %), postpartum hemorrhage (15.0 vs 7.9%) and gestational diabetes mellitus (5.0 vs. 1.0 %), as compared tothe euthyroid patients. No significant increase in preeclampsia (10.0 vs. 6.5 %) and placental abruption (0 vs. 1.0 %) was seen in thesubclinical hypothyroid patients.There were no maternal deaths in any of the groups.

TABLE: 3 :Foetaloutcomes in the study

Types of Complications	Group A n=292	Group B n=20	Group C n=26	Group D n=7	Group E n=5	Total n=350
Pre-term	18 (6.2%)	5 (25.0%)	7 (26.9%)	1 (14.3%)	0	31 (8.8%)
IUGR	10 (3.5%)	2 (10.0%)	1 (3.8%)	0	0	13 (3.7%)
LBW	46 (15.6%)	6 (30.0%)	10 (38.5%)	1 (14.3%)	0	63 (18.0%)
Abortion	5 (1.8%)	2 (10.0%)	3 (11.5%)	0	0	10 (2.9%)
Still Birth	3 (1.0%)	0	1 (3.8%)	0	0	4 (1.1%)
Total	82 (28.1%)	15 (75.0%)	22 (84.5%)	2 (28.6%)	0	121 (34.5%)

(IUGR=Intrauterine growth retardation, LBW=Low birth weight)

Table 3 shows different types of fetal outcomes like preterm, IUGR, LBW, abortion and still birth in different groups.Adverse fetal outcomes in overt hypothyroidism includedspontaneous abortion (11.5 vs. 1.8 %), pretermbirth (26.9 vs. 6.2 %) and low birth weight (38.5 vs 15.6 %) ascompared to the euthyroid women. No significant increase in intrauterine growth retardation (3.8 vs 3.5 %) and fetal death (3.8 vs. 1.0 %)was seen in the overt hypothyroid group.Adverse fetal outcomes in subclinicalhypothyroidism included spontaneous abortion (10.0 vs 1.8 %), preterm delivery (25.0 vs 6.2 %), low birth weight(30.0 vs 15.6 %), and intrauterine growth retardation (10.0 vs 3.5 %) as compared to the euthyroid women. Preterm birthwas found to be statistically significant.

TABLE: 4 : Neonatal Outcomes in the study (Only live births in each group included)

Types of Complications	Group A n=284	Group B n=18	Group C n=22	Group D n=7	Group E n=5	Total n=336
Hyperbilirubinemia	18 (6.3%)	2 (11.1%)	4 (18.2%)	1 (14.3%)	0	25 (7.4%)
ARDS	13 (4.6%)	1 (5.6%)	2 (9.1%)	0	0	16 (4.7%)
Septicemia	8 (2.8%)	1 (5.6%)	1 (4.5%)	0	0	10 (3.0%)
Others	3 (1.1%)	0	1 (4.5%)	0	0	4 (1.2%)
Neonatal Death	2 (0.7%)	0	1 (4.5%)	0	0	3 (0.9%)
Total	44 (15.5%)	4 (22.3%)	9 (40.8%)	1 (14.3%)	0	58 (17.2%)

(ARDS=acute respiratory distress syndrome)

Table 4 shows different types of neonatal outcomes like hyperbilirubinemia, ARDS, septicemia and early neonatal death. Adverse neonatal outcomes in overt hypothyroidism included hyperbilirubinemia (18.2 vs. 6.3 %), ARDS (9.1 vs. 4.6 %) and early neonatal death (4.5 vs 0.7 %) as compared to the euthyroid women. No significant increase was seen in subclinical hypothyroid group in any of the neonatal outcomes.

The mean birth weight in the group 1 was 2.76 ± 0.8,in group 2 was 2.52 ± 0.7, in group 3 was 2.32 ± 0.7, ingroup 4 was 2.9 ± 0.3, and in group 5 was 3.0 ± 0.2.

DISCUSSION:

This cross-sectional survey was conducted within higher socio-economic poulation in Ahmedabad city of Gujarat State during January 2013 to December 2014.Prevalence of hypothyroidism was high in our studywith 7.43 % of overt and 5.71 % of subclinical hypothyroidpatients, thus necessitating the need for universal screening for thyroid dysfunction.

In our study, it was noted that overt hypothyroid andovert hyperthyroid women had higher maternal age ascompared to women in the other groups. It was seen thatincreased maternal age was associated with higher incidenceof thyroid dysfunction. The increase in prevalence ofhypothyroidism in the older age group is due to currenttrend of older women becoming pregnant.

In our study anemia was the most common maternal complicationin hypothyroid patients followed by PPH, preeclampsia and GDM.LBW was the most common fetal outcome in hypothyroid patients followed by preterm, spontaneous abortion and IUGR. Hyperbilirubinemia was the most common neonatal outcome in hypothyroid patients followed by ARDS.

Fetal loss was 9 times greater in the pregnant womenwith hypothyroidism compared with those from theeuthyroid group. Allan et al[22]showed that TSH levelsgreater than 6 mU/liter were significantly associated with ahigher frequency of stillbirth. Benhadi et al[23] found thathigh maternal TSH levels were associated with anincreased risk of pregnancy loss. Because TSH is inverselyrelated to hCG levels, women with low hCG levels are at agreater risk of child loss.TP-3

Fetal distress was 3times greater in the pregnant womenwith hypothyroidism compared with those from theeuthyroid group. Goel et al [24] also reported a higher
incidence of fetal distress in pregnancies complicated bymaternal hypothyroidism. Fetal distress may impair infant developmental ofthe nervous system.

Sahu et al[25] analyzed thyroidfunction during the second trimester in high-risk pregnantwomen and reported that prevalence of thyroid disorders,especially overt and subclinical hypothyroidism, was6.47 %.

This study concludes that there is a high prevalence ofhypothyroidism (14.3 %), the majority being subclinical inpregnant women, and universal screening of thyroid dysfunctionmay be desirable in our country.

Vaidya et al[26], who concluded that targeted thyroidfunction testing of only high-risk pregnant womenwould miss nearly one third of women with overt/subclinical hypothyroidism during early pregnancy.[26]

In study of Rodrigo Moreno-Reyes et al, the prevalence of thyroid disorders was high, affecting one in six pregnant women (16.7%) in Belgium.[27]

CONCLUSION:

(1) The mean birth weight in the group 1 was 2.76 ± 0.8, in group 2 was 2.52 ± 0.7, in group 3 was 2.32 ± 0.7, in group 4 was 2.9 ± 0.3, and in group 5 was 3.0 ± 0.2.
(2) In our study prevalence of hypothyroidism was 7.43 % and 5.71 % of overt and subclinical hypothyroid patients respectively.
(3) Increased maternal age was associated with higher incidence of thyroid dysfunction.
(4) Chances of fetal distress as well as fetal loss were much greater in the pregnant women with hypothyroidism compared with those from the euthyroid group.
(5) To screen pregnant women for serum TSH concentrations in the first trimester of pregnancy was cost saving compared with no screening.
(6) Uncorrected thyroid dysfunction in pregnancy has adverse effects on fetal and maternal well-being.

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