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Original Research Article

Prevalence of thyroid dysfunction in pregnancy and its impact on maternal and fetal outcome: a prospective study in a tertiary care hospital in Maharashtra, India

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ABSTRACT

Background: Thyroid dysfunction is the commonest endocrinological disorder in pregnancy. A broad spectrum of adverse outcomes in pregnant women and the fetus have been reported which can be prevented by early diagnosis and treatment of thyroid dysfunction. Thyroid dysfunction in pregnancy has not yet been extensively studied in India. Hence, this study was conducted for assessment of the prevalence of thyroid dysfunction in pregnancy and effect on the mother and her fetus.
Methods: This study is a prospective study conducted in the department of obstetrics and gynecology, MIMER Medical College and Hospital, Talegaon Dabhade, Maharashtra. A 3 years study. Antenatal women attending the outpatient and inpatient department of the hospital. The total sample population comprised of 698 pregnant women with uncomplicated singleton intra-uterine pregnancy. All participants were screened by estimation for serum TSH in first trimester. Immediately after delivery the cord blood sample was collected and cord blood TSH levels were estimated. Babies, whose cord blood TSH levels were elevated, were called for follow-up on day 5 of neonatal life and TSH, free T3 and free T4 levels were estimated. Among these babies, those diagnosed with congenital hypothyroidism were started on appropriate treatment.
Results: The prevalence of thyroid dysfunction in pregnancy in present study was 17.90% whereas 82.1% patients were euthyroid (control group). Among the 17.9% patients with thyroid dysfunction, 14.6% had subclinical hypothyroidism, 1.9% had overt hypothyroidism and 1.4% had hyperthyroidism.
Conclusions: With this study, we can come to the conclusion that there is high prevalence of thyroid dysfunction in pregnancy. Thus, an early diagnosis and prevention of the aftermaths of thyroid dysfunction in pregnancy is of utmost importance.

Keywords: Hyperthyroidism, Hypothyroidism, Thyroid dysfunction

INTRODUCTION

Hypothyroidism

Subclinical hypothyroidism (SCH) is defined an elevated serum TSH level with normal serum thyroxine level and Overt/Clinical hypothyroidism is defined as high serum TSH with low serum thyroxine levels. Hypothyroidism is characterized by fatigue, constipation, cold intolerance, muscle cramps and excessive weight gain. A pathologically enlarged thyroid gland depends on the etiology of hypothyroidism and is more likely in women in areas of iodine deficiency or those with hashimoto thyroiditis. Additional features include oedema, dry skin, hair loss and prolonged relaxation phase of deep tendon reflexes. The most common cause of hypothyroidism in

pregnancy is hashimoto thyroiditis which is characterized by glandular destruction from autoimmune antibodies, particularly anti-thyroid peroxidase antibodies. Clinical identification is difficult as many of the signs and symptoms are common to pregnancy itself.

Hypothyroidism in pregnancy is associated with complications of spontaneous/threatened abortion, pre-eclampsia, preterm delivery, low birth weight, intra-uterine growth retardation and high perinatal mortality. Neonatal hyperbillirubinemia and hypo-/hyper-thyroidism are reported too.[3] These children may also develop attention deficit disorder and hyperactivity syndrome.[4]

Hyperthyroidism

Subclinical hyperthyroidism is defined as low serum TSH level with normal serum thyroxine level and overt hyperthyroidism is defined as low serum TSH level with elevated serum thyroxine level.

Hyperthyroidism is characterized by tachycardia that exceeds of what is seen in normal pregnancy, failure to gain weight despite of adequate food intake, exophthalmos, thyromegaly, anxiety, palpitations, heat intolerance, warm and wet skin, hand tremors and systolic murmur. The most common cause of hyperthyroidism in pregnancy is Grave's disease, an organ specific autoimmune process, associated with thyroid stimulating TSH receptor antibodies.

Subclinical hyperthyroidism is not associated with adverse outcomes. But if left untreated, it may progress to overt hyperthyroidism and result in complications like pre-eclampsia, preterm labour, low birth weight, fetal and perinatal loss.[6]

Thyroid storm and heart failure

Both these conditions are acute and life-threatening in pregnancy. Thyroid storm is a hyper-metabolic state and is rare in pregnancy. On the other hand, pulmonary hypertension and heart failure from cardiomyopathy caused by the profound myocardial effects of thyroxin is common in pregnant women. In these women, cardiomyopathy is characterised by high output state which may lead to dilated cardiomyopathy. The pregnant women with uncontrolled thyrotoxicosis have minimal cardiac reserve and the cardiac decompensation is usually precipitated by pre-eclampsia, anemia, sepsis. Frequently thyroxine-induced cardiomyopathy and pulmonary hypertension are reversible.

METHODS

This prospective study was conducted in the department of obstetrics and gynecology, MIMER medical college and Bhausaheb Sardesai Talegaon Rural Hospital. All antenatal women with uncomplicated intra-uterine pregnancies attending the OPD and IPD in study hospital were included in the study. On enrolment of the patients, a detailed history was taken and complete examination was done. Selected patients for study were tested for serum TSH. If it was deranged, then free T3 and free T4 levels was estimated. Patients were treated accordingly and followed up till delivery.

Reference ranges of thyroid hormone levels are (ACOG guidelines 2015)

Normal TSH levels

- First trimester: 0.1-2.5 microIU/ml
- Second trimester: 0.2-3.0 microIU/ml
- Third trimester: 0.3-3.0 microIU/ml

Normal T3 [T3]: 60-200 ng/dl

Normal T4 [T4]: 4.5-12 microgm/dl

A 3-year study with all healthy antenatal women with singleton pregnancies and no medical disorder were included in this study. Women with multiple pregnancies, known thyroid abnormalities, known metabolic disorders like diabetes, hypertension and abnormal pregnancies like vesicular mole were excluded from the study. The fetal outcome were noted in terms of preterm delivery, intrauterine growth restriction, intrauterine demise, birth weight, Apgar score at one and five minutes, neonatal intensive care unit admission. Immediately after delivery the cord blood sample was collected and cord blood TSH levels were estimated.

Statistical analysis

Data were statistically described in terms of mean (±SD), frequencies (number of cases) and percentages when appropriate. Comparison of quantitative variables between the study groups was done using ANOVA test for normally distributed data or Kruskal Wallis test for non-normally distributed or ordinal data with post-hoc Tukey's test. For comparing categorical data, Chi square test was performed. The same test was used instead when the expected frequency is less than 5. A probability value (p value) of less than 0.05 was concluded as statistically significant. Each of the statistical calculation were done using computer programs Microsoft excel 2013 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 21. In the present study, 698 antenatal women were evaluated and prevalence of thyroid dysfunction along with various other parameters were assessed.

RESULTS

The prevalence of thyroid dysfunction in pregnancy in present study was 17.90% whereas 82.1% patients were euthyroid (control group). Among the 17.9% patients

with thyroid dysfunction, 14.6% had subclinical hypothyroidism, 1.9% had overt hypothyroidism and 1.4% had hyperthyroidism.

Table 1: Prevalence of different types of thyroid dysfunction.

Diagnosis	N	%
Euthyroid (control group)	573	82.1%
Subclinical hypothyroidism (SCH)	102	14.6%
Overt hypothyroidism (OH)	13	1.9%
Hyperthyroidism	10	1.4%
Total	698	100.0%

Table 2: Distribution of cases according to age.

Variables	Group	N	Mean (age)	SD
Age	Euthyroid (control group)	573	23.97	3.55
	SCH	102	24.63	3.83
	OH	13	28.50	4.54
	Hyperthyroidism	10	24.38	4.14

In present study, 82.1% patients were euthyroid (control group). The prevalence of thyroid dysfunction in pregnancy was 17.90%. Of these, subclinical hypothyroidism was 14.6%, overt hypothyroidism was 1.9% and hyperthyroidism was 1.4% (Table 1).

The mean age of patients included in the study 250.37 years and was comparable in all groups (Table 2).

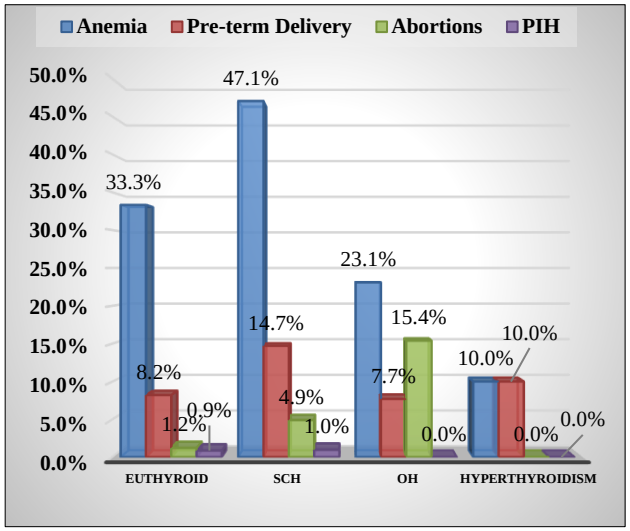

Figure 1: Maternal complications in different types of thyroid dysfunction.

It has been observed that anaemia itself is very common in different countries. In the present study, the prevalence of anaemia was about 33.3% in euthyroid (control group) patients. Anaemia was observed in 23.1% of overt hypothyroidism and 10% of hyperthyroidism (Figure 1).

The occurrence of anaemia and abortions was significantly high in patients with thyroid dysfunction compared to euthyroid patients (p-value <0.05) (Figure 1).

In the present study, abortions were observed to be higher in subclinical (4.9%) and overt hypothyroidism (15.4%) which was significant (p-value <0.01). However, abortions were not observed in hyperthyroidism (Figure 1).

Pre-term delivery was highest among subclinical hypothyroidism (14.7%) and markedly raised compared to euthyroid women (8.2%), but was not observed to be clinically significant (p-value=0.21).

Table 3: Distribution of cases according to birth weight.

Variables	Group	N	Mean	SD
Birth weight (kg)	Euthyroid (control group)	573	2.72	0.43
	SCH	102	2.70	0.43
	OH	13	2.85	0.53
	Hyperthyroidism	10	2.47	0.27
	Total	698	2.71	0.43

In present study, there is significant co-relation between low birth weight and hyperthyroidism (mean birth weight=2.47 kg). But, no correlation was observed between low birth weight and hypothyroidism (Table 3).

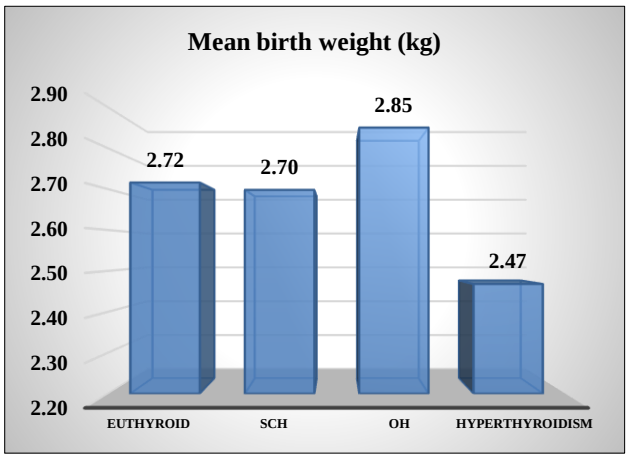

Figure 2: Mean birth weight in different types of thyroid dysfunctions.

The mean birth weight of all babies of patients included in this study was 2.68±0.005 kg. Of these, the mean birth weight in euthyroid women was 2.72 kg, subclinical hypothyroidism was 2.7 kg, overt hypothyroidism was 2.85 kg and hyperthyroidism was 2.47 kg (Figure 2).

In the present study, prevalence of low birth weight (LBW) was significantly high in women with thyroid

dysfunction compared to euthyroid women [p-value <0.01]. LBW is observed in 16.7% of subclinical hypothyroidism, 23.1% of overt hypothyroidism and 30% of hyperthyroidism. Intra-uterine growth restriction (IUGR) was observed significantly high in thyroid dysfunction than in euthyroid women (p-value <0.05). It is found in 2% of subclinical hypothyroidism, 7.7% of overt hypothyroidism and 10% of hyperthyroidism (Table 4).

Table 4: Distribution of cases according to fetal complications.

	Euthyroid (control group) (N=572)	SCH (N=102)	OH (N=13)	Hyperthyroidism (N=10)	Total (N=698)	p value
LBW	47	17	3	3	70	<0.01
%	8.2%	16.7%	23.1%	30.0%	10.1%	
IUGR	4	2	1	1	8	<0.05
%	0.7%	2.0%	7.7%	10.0%	1.2%	
MSL	15	4	1	1	21	0.35
%	2.6%	3.9%	7.7%	10.0%	3.0%	
NICU	33	12	2	2	49	<0.05
%	5.8%	11.8%	15.4%	20.0%	7.1%	

NICU admissions were also significantly high in thyroid dysfunction than in neonates of euthyroid women. It was 11.8% in subclinical hypothyroidism, 15.4% in overt hypothyroidism and 20% in hyperthyroidism (Table 4). MSL was seen in 7.7% of overt hypothyroidism and 10% of hyperthyroidism, but was not statistically significant (Table 4).

IUGR, low birth weight (LBW) and NICU admission were observed more in women with thyroid dysfunction than euthyroid women. Also, IUGR, low birth weight (LBW) and NICU admission were highest in neonates of hyperthyroid women (Table 4).

Cord blood TSH

The TSH levels in cord blood were raised in babies of women with thyroid dysfunction compared to euthyroid (control group) women. This increase is found to be statistically significant (p-value <0.05). It was observed to be significantly increased in babies of mothers with overt hypothyroidism compared to subclinical hypothyroidism. Thus, indicating that early diagnosis and treatment will prevent progression to overt hypothyroidism and development of congenital hypothyroidism.

These 40 neonates with elevated cord blood TSH levels were resampled on day five during hospital stay. 8 of the 40 neonates had elevated TSH and low fT4 on retesting on day 5 of life. Of these 8 neonates, 2 belonged to euthyroid women, 3 neonates were of women with subclinical hypothyroidism and 3 of overt hypothyroidism.

Even in euthyroid women, 5.2% babies had raised cord blood TSH levels, that is, TSH >20 mIU/L (Figure 3) This rise suggests that the raised cord blood TSH may be attributed to stress during labour or women who were euthyroid during the first screening test may have developed hypothyroidism as they reached the third trimester. So, this study can conclude that screening should be repeated in third trimester to detect these euthyroid women developing hypothyroidism in late pregnancy.

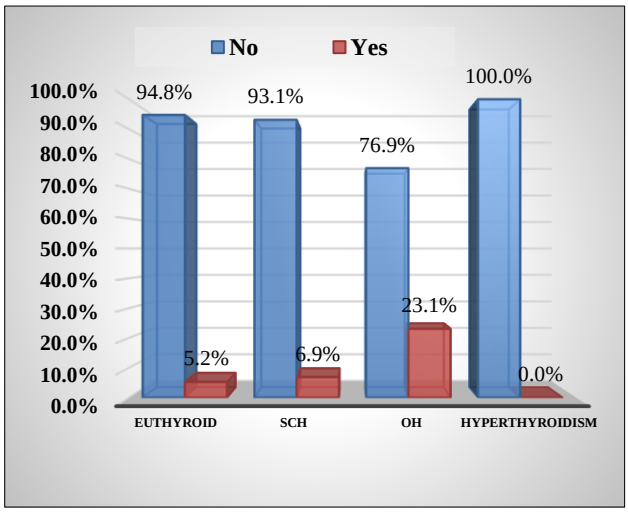

Figure 3: Distribution of cases according to raised cord blood TSH.

The cord blood TSH levels were observed to be significantly raised in babies of women with hypothyroidism. This was observed to be more marked among overt hypothyroidism (23.1%) than subclinical hypothyroidism (6.9%) (Figure 4). Thus, we conclude that the timely treatment given to women with subclinical hypothyroidism prevented the babies from getting affected. Congenital hypothyroidism is known to be the

preventable cause of mental retardation. Thus, by early diagnosis and treatment of babies diagnosed with congenital hypothyroidism, a deleterious consequence like mental retardation can be prevented.

Thus, out of 102 women with subclinical hypothyroidism, 3 babies developed congenital hypothyroidism. Out of 13 women with overt hypothyroidism, 3 babies developed congenital hypothyroidism.

Hence, Study conclude that even though we detect thyroid dysfunction in pregnancy, neonatal screening is equally important to prevent congenital hypothyroidism.

DISCUSSION

In western countries, many studies have shown a lower prevalence of thyroid disorders in pregnancy which is approximately 2.5%.[6-9] There are a number of reasons for increased prevalence of hypothyroidism in pregnancy in Asia. For example, diet deficient in iodine, presence of goitrogens in diet, deficiency of micronutrients like selenium and iron.[10-12] There are few Indian studies regarding the prevalence of thyroid disorders in pregnancy. Sahu et al, have done thyroid function in second trimester and reported prevalence of thyroid disorders, especially overt and subclinical hypothyroidism to be 6.47%.[13] Dhanwal et al conducted a study in1000 pregnant women in Delhi (2013) reporting a prevalence of 14.3% of hypothyroidism, with a cut off of 4.5m IU/L as upper limit of normal.[14]

A study in Telangana by Nabi VRM et al, reported a prevalence of 26% with a cut off of 3.0 mIU/L as per ATA guidelines.[15]

In a study conducted by Krishnamma B et al, the prevalence of thyroid dysfunction was 18.7 with that of hypothyroidism being 13.4% and of hyperthyroidism 1.3%.[16]

Nambiar V et al, studied the Asian-Indian pregnant women and found the prevalence of hypothyroidism to be 4.8%.[17] Dhanwal D et al conducted a multicentric study in 11 cities all over India in 2599 pregnant women and found the prevalence of hypothyroidism to be 13.13% which is comparable to this study.[18]

Table 5: Comparison of prevalence of different thyroid dysfunction with various studies.

Different studies	Year	No. of patients	Hypothyroidism (%)	Hyperthyroidism (%)
Taghavi et al	2009	1000	9.2%	2.4%
Nambiar et al	2011	2500	4.8%	-
Wang, et al	2011	2899	17.9%	4.3%
Nangia et al	2013	400	1-2%	1%
Ajmani et al	2014	400	12%	1.25%
Rajput et al	2015	461	27.8%	3.7%
Krishnamma B et al	2017	380	17.4%	1.3%

Table 6: Comparison of complications observed in sub-clinical hypothyroidism in various studies.

	Anaemia (%)	Abortion (%)	PE (%)	PTD (%)	IUGR (%)	LBW (%)	NICU (%)
Present study	47.1%	4.9 %	1%	14.7%	2%	16.7%	11.8
Sahu et al	0%	0%	9.8%	10.3%	2.4%	0%	0%
Thanuja et al[26]	0%	50%	0%	0%	0%	50%	0%
Manju et al	12%	7.7%	13.6%	0%	0%	0%	0%
Saraladevi et al	0%	4.68%	9.3%	7.81%	6.25%	4.68%	0%
Pokhanna et al	13.3%	2%	9%	30%	10%	9%	0%
Taghavi et al	0%	0%	2.7%	2.7%	0%	0%	0%
Ajmani et al	0%	2.39%	22.3%	5.8%	4.9%	12.11%	0%

Cases of subclinical hypothyroidism were 102 out of 698 (14.78%). PE: pre-eclampsia, PTD: preterm delivery, IUGR: Intra-uterine growth restriction, LBW: Low birth weight, NICU: Neonatal intensive care unit.

In one study by Nangia S et al, in two hospitals together in Delhi, a prevalence of thyroid disorders was 1-2% amongst 400 pregnant women.[19] Prevalence of hyperthyroidism, both overt and Subclinical in various studies has been reported to be around 1%.[20]

In the study conducted by Wang W et al, the prevalence of thyroid disorders was 10.2%.[21] Also a study conducted by Taghavi et al, reported a prevalence of 14.6%.[22] The study conducted by Ajmani et al, evaluated 400 pregnant women which concluded a prevalence of 13.25%.[23]

In the study conducted by Thanuja et al, the prevalence of thyroid disorder was comparatively low, about 5%.[24]

A cross sectional study conducted by Rajput et al, studied 461 pregnant women with uncomplicated intrauterine singleton pregnancies in the first trimester of gestation without any history of thyroid disease or intake of any thyroid medication, the prevalence of thyroid disorder was more (26.5%).[25]

On comparison with various studies conducted previously, prevalence of hypothyroidism in pregnancy ranged from 1-2% to 27.8% and that of hyperthyroidism ranged from 1% to 4.3% (Table 6).

Also, in every study, it was observed that the prevalence of hypothyroidism was greater than that of hyperthyroidism (Table 6).

Table 7: Comparison of complications observed in overt hypothyroidism in various studies.

Studies	Anaemia (%)	Abortion (%)	PE (%)	Abruption (%)	PTD (%)	IUGR (%)	LBW (%)
Present study	23.1%	15.4%	0%	0%	7.6%	7.7%	23.1%
Sahu et al	0%	0%	20.7%	0%	4.7%	13.8%	0%
Thanuja et al	0%	66.7%	0%	33.4%	0%	0%	1%
Manju et al	5.4%	9.7%	19.4%	6.5%	0%	0%	0%
Saraladevi et al	0%	7.14%	14.28%	3.57%	10.71%	10.71%	10.71%
Abalovich	0%	0%	0%	19%	0%	0%	6v
Ajmani et al	0%	16.6%	16.6%	16.6%	33.3%	25%	50%

Cases of overt hypothyroidism were 13 out of 698 (1.86%).

Table 8: Comparison of complications observed in hyperthyroidism in various studies.

Studies	Anaemia (%)	Abortion (%)	PE (%)	AP (%)	PTD (%)	IUGR (%)	LBW (%)
Present study	10%	0%	0%	0%	10%	10%	30%
Sahu et al	0%	0%	9.8%	0%	10.3%	2.4%	0%
Thanuja et al	0%	37.5%	50%	0%	12.5%	12.5%	0%
Saraladevi et al	0%	12.5%	11.11%	0%	5.55%	11.11%	0%
Pokhanna et Al	16.66%	16.66%	0%	0%	0%	0%	0%
Robert negro et al	0%	14.3%	0%	0%	6.7%	0%	0%
Tuija mannisto	0%	0%	3.5%	1%	0%	0%	0%
Miller et al	0%	0%	4.7%	0%	0%	0%	2.3%
Kriplani et al	0%	0%	22%	0%	25%	0%	0%

Cases of hyperthyroidism were 10 out of 698 (1.4%).

In present study of 698 patients, 102 (14.78%) had subclinical hypothyroidism. Of these, anaemia was observed in 47.1% patients and was statistically significant (p-value <0.05) (Table 7).

In the present study, abortions were observed in 4.9% women with subclinical hypothyroidism and was statistically significant (p-value <0.01).

In the present study, preterm deliveries was seen in 14.7%, and was comparable with the observation of Sahu et al of 10.3%.

In the present study, IUGR was observed in 2% which was comparable with the study by Sahu et al of 2.4%.

Cases of overt hypothyroidism were 13 out of 698 (1.86%).

In present study, the occurrence of overt hypothyroidism was seen in 13 patients (1.86%). Of these, the maternal complications included anaemia 23.1%, abortions (15.4%), preterm delivery (7.6%) and fetal complications were IUGR (7.7%), LBW (23.1%). The prevalence of abortion (15.4%) was comparable with the study of Ajmani et al of 16.6%. In the study by Thanuja et al, the occurrence of overt hypothyroidism was 3 (1%). Of these, the maternal complications included 2 abortions (66.7%) and 1 case of abruptio placenta (33.4%).

Cases of hyperthyroidism were 10 out of 698 (1.4%).

In the present study, the prevalence of preterm delivery in hyperthyroidism was 10% which was statistically significant (Table 8).

In the present study, the prevalence of IUGR was 10% which was significant (p-value <0.05).

Thyroid dysfunction in the neonate is known to hamper not only the mental development but also the somatic growth.

Congenital hypothyroidism is known to result in mental retardation.[27]

In the early days of infancy, the baby may appear normal with no obvious pathological indicators. But symptoms or signs, when present, may appear in the form of prolonged neonatal jaundice, constipation, lethargy and poor muscle tone, poor feeding, a large tongue, coarse facies, wide fontanelle, distended abdomen and umbilical hernia.[28]

In some studies, the risk of cerebral white matter damage is found to be doubled in neonates with hypothyroidism in the form of echolucencies in infants with low T4.[29]

It has been observed that infants with T4 levels below threshold develop respiratory distress and need to be supplemented with oxygen for more days, more days on the ventilator and longer hospitalization.[30]

Cord blood can be used for screening of congenital hypothyroidism in situations of early discharge before 3 days.[31]

Cord blood samples for TSH values have compared well with heel prick filter paper samples taken after day 5 of life. In rural population the major drawback is women getting their neonates for follow-up in order to screen for thyroid disorder. Thus, cord blood TSH screening provides us with a feasible option to screen babies for development of hypothyroidism at the earliest.

CONCLUSION

As a result of this study, we conclude that there is high prevalence of thyroid dysfunction in pregnancy. Majority among these being subclinical hypothyroidism. As maternal thyroid dysfunction has significant impact on maternal and fetal outcomes, early identification of thyroid dysfunction and timely initiation of treatment is required. Thus, universal screening of pregnant women in first trimester with Sr. TSH should be insisted on, especially in a country like India due to the high prevalence of undiagnosed thyroid dysfunction. Study recommend screening with cord blood TSH of neonates.

Avoiding maternal thyroid disease is of major importance because of the potential damage to fetal neural development, congenital hypothyroidism and eventually development of mental retardation. Early diagnosis and prompt treatment can prevent the adverse maternal and fetal outcomes along with preventing the development of congenital hypothyroidism. Universal screening of pregnant women for thyroid dysfunction is not yet recommended by many guidelines. However, studies have been conducted to prove the adverse obstetric outcomes of thyroid dysfunction in pregnancy if left untreated.

Thus, routine screening of thyroid dysfunction should be recommended to prevent adverse fetal and maternal outcome.

Thus, an early detection of thyroid dysfunctions and treatment of mother during gestation improves the maternal as well as fetal outcome.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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