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FETOMATERNAL OUTCOME IN MATERNAL HYPOTHYROIDISM COMPLICATING PREGNANCIES AT RIMS: A PROSPECTIVE STUDY.

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ABSTRACT

Objective: To analyze the fetomaternal outcome in maternal hypothyroidism complicating pregnancies at RIMS, Imphal. **Study Design:** We conducted a Prospective Study in the Department of Obstetrics and Gynaecology, RIMS, Imphal, Manipur. The study included 300 pregnant women attending antenatal clinic of Obstetrics and Gynecology, RIMS, Imphal between October 2013 to March 2015.The variables were age, parity, period of gestation, obstetrical history, haemoglobin of mother, Apgar score, birth weight etc. Data were analyzed by Chi-square test using SPSS Programme. **Results:** Among 300 selected women overt hypothyroid patients were 14 (4.7%) and subclinical hypothyroid patients were 286(95.3%). Threatened abortion, as a complication occurred in 10 patients (3.3%). In the 2nd trimester follow up 268 patients (92.3%) were compliant and in the third trimester 236 patients (78.7%) were compliant. 16(5.5%) Patients had pre eclampsia (overt hypothyroids were 2 and subclinical hypothyroids were 14). Preterm labour was found in 12 cases. Maternal complications like PPH were found in 48.1% of the patients, who were not compliant. Low birth weight is reported in 22.2% of respondents who were non compliant and only in 14.4% of who were compliant, P value (<0.05) is significant. In non compliant group, 74.1% of the neonates developed RDS compared to only 6.7% of the neonates in the compliant group. . NICU admissions contributed to 63% in the non compliant group compared to 0.8% in the other group. Neonatal thyroid screening was abnormal in 7.4% of non compliant group and nil in the other group. **Conclusion:** Our study proves significant association between uncontrolled hypothyroidism and adverse fetomaternal outcome The pregnancy outcome observed in our subjects (compliant) was better. There was very low incidence of still birth, preterm deliveries, deaths etc. This might have been due to the thyroid hormones of mother which were maintained within the reference range.

KEYWORDS: haemoglobin, fetomaternal, hypothyroids.

INTRODUCTION

Both hypothyroidism and hyperthyroidism complicate antenatal period, resulting in maternal and fetal jeopardy. TSH is a very sensitive indicator of thyroid hormone action at the tissue level; slight changes in T4 are reflected in a many-fold greater response in TSH.[1]

In response to the metabolic demands of pregnancy, there is an increase in the basal metabolic rate (which is mainly due to fetal metabolism), iodine uptake and the size of the thyroid gland caused by hyperplasia and increased vascularity. However, despite this increase in thyroid activity, a pregnant woman is euthyroid with levels of TSH, free T4 and free T3 remaining within the normal range; during pregnancy, iodide clearance by the kidney increases. In many parts of the world, iodine is not sufficiently available in the environment and pregnancy increases the risk of iodine deficiency.

Throughout the pregnancy, maternal thyroxine is transferred to the fetus. Maternal thyroxine is important for fetal brain development, especially prior to the development fetal thyroid gland function. Maternal thyroid autoimmunity predisposes to aneuploidy in the child and plays a major role in the birth of children with Down syndrome in younger women. Any thyroid hormone necessary for fetal growth before second trimester must come from the maternal side. The requirement for thyroid hormone replacement therapy is increased during pregnancy, suggesting an increased demand on the thyroid gland. Dose of thyroxine has to be increased during pregnancy.[2, 3]

Overt hypothyroidism (TSH – Elevated, T4- Low) occurs in 1 in 1000 to 1in 1600 Deliveries, subclinical hypothyroidism (TSH – Elevated, T4- Normal) accounts for 2.0 – 3.0% of pregnancies (Goitrous form is more frequent).[4,5]

Although several studies conducted in different parts of the world regarding the same issue. Furthermore, the study was conducted in RIMS, Imphal which expressed an exact picture of all the Blackholes as well as miserable consequences of the disease problem in Manipur.

It was well known that not only overt, but subclinical thyroid dysfunction also had adverse effects on maternal and fetal outcome. There were few data from India about the prevalence of thyroid dysfunction in pregnancy. With this background, this study was conducted to find out impact of thyroid hypo function on pregnancy and its effect on obstetrical and neonatal outcome in Manipur.

AIMS AND OBJECTIVES

1. To find out the incidence of overt and subclinical hypothyroidism in pregnancy.
2. To analyze the fetomaternal outcome in maternal hypothyroidism complicating pregnancies at RIMS, Imphal.

MATERIALS AND METHODS

STUDY DESIGN

A Prospective Study.

STUDY SET- UP

The study was carried out in the Department of Obstetrics and Gynaecology, Regional institute of medical sciences, Imphal, Manipur.

DURATION

The study was conducted with data collection for a period of one and half calendar years with effect from October 2013 to March 2015.

STUDY POPULATION

Study population included all cases of pregnant women attending the outpatient Department of Obstetrics and Gynaecology, RIMS, hospital diagnosed to have thyroid hypo function, admitted for the hypothyroid related complications during pregnancy & delivered in RIMS during the tenure of study.

PATIENT SELECTION

Patient selection will be according to ATA guidelines high risk screening recommendation.

Women with previous H/o thyroid dysfunction (goiter, thyroid antibodies) and thyroid surgery

Women with family H/o thyroid disease

Women with type 1 diabetes, other autoimmune disorders like adrenal insufficiency, atrophic gastritis, pernicious anemia, systemic sclerosis, SLE, sjogrens syndrome, hyperparathyroidism, vitiligo etc

Women with H/o either miscarriage or preterm delivery

Women with infertility as a part of work up

Women with prior therapeutic head or neck irradiation

Women with age > 30 yrs

Women with morbid obesity

METHODS OF COLLECTION OF DATA

Inclusion Criteria

- Pregnant women attending antenatal clinics (with thyroid hypo function)
- Cases willing to undergo required investigations and participate in the study
- Singletone pregnancy
- Primigravida/ Multigravida

Exclusion Criteria

- hyperthyroid pregnant women
- multiple gestation
- drug Induced
- molar pregnancies
- patients with hyper emesis Gravidarum
- known chronic disorders- hypertension & DM
- previous bad obstetric history with known cause
- planned to deliver in other hospital

METHODS

Ethical approval was taken from Institutional Ethics Committee, RIMS, Imphal, Manipur, before starting the study. Informed consent was taken from all subjects willing to participate before enrolling them in the study.

PROCEDURE

- Detailed clinical history including parity, obstetrical history was taken as per proforma attached.
- General examination, systemic examination with reference to CVS, RS, CNS & thyroid and obstetrical examination.
- All the routine investigations including complete hemogram, urine routine examination, liver and kidney function test, ABO grouping and Rh typing, blood sugar and thyroid profile estimation carried out.
- Patients sent for TSH levels testing.
- If TSH was deranged (high,>2.5µU/L in 1st trimester &>3.0µU/L in 2nd and 3rd trimester) then FT4 and FT3 levels were checked.
- When TSH was increased and FT4 was decreased then it was overt hypothyroidism. It was diagnosed subclinical when FT4-normal. thyroxine 1.6 µg / kg / day was given in both types.
- Every 8 weeks TSH level was estimated and the dose of the drug adjusted.
- At the end, the obstetric outcome and perinatal outcome of the pregnancy was noted.
- The pattern of labour recorded for all the subjects, regarding duration of labour, mode of delivery etc.
- Third stage complications like retained placenta, post partum hemorrhage, inversion of uterus, rupture uterus etc. were noted.
- Examination of the neonate for its Apgar score, birth weight, date and time of birth, maturity, congenital anomalies, sex were noted.
- Examination of the placenta and the umbilical cord for any abnormalities. Also estimation of neonatal thyroid profile on 3rd day postpartum was done.

STUDY VARIABLES

The variables used as determinants for the maternal outcome were age, parity, period of gestation, obstetrical history, hemoglobin level etc. and variables for fetal outcome were Apgar score, birth weight, maturity, congenital anomalies etc.

DATA COLLECTION: Data of the patient were recorded in pre-designed proforma.

STATISTICAL ANALYSIS

The observation of the study was recorded in a suitable data base programme. Chi-square test for statistical analysis was done using SPSS programme.

ETHICAL APPROVAL

The protocol of the thesis was submitted to the Institutional Ethics Committee, RIMS, Imphal for further processing and approval.

RESULTS AND OBSERVATION

The study included 300 pregnant women attending antenatal clinic of Obstetrics and Gynaecology RIMS, Imphal between October 2013 to March 2015.

Table 1: Distribution of respondents based on age

No	AGE IN YEARS	NUMBER	PERCENTAGE
1	≤20	38	12.7
2	21-29	108	36
3	≥30	154	51.3
	TOTAL	300	100.0

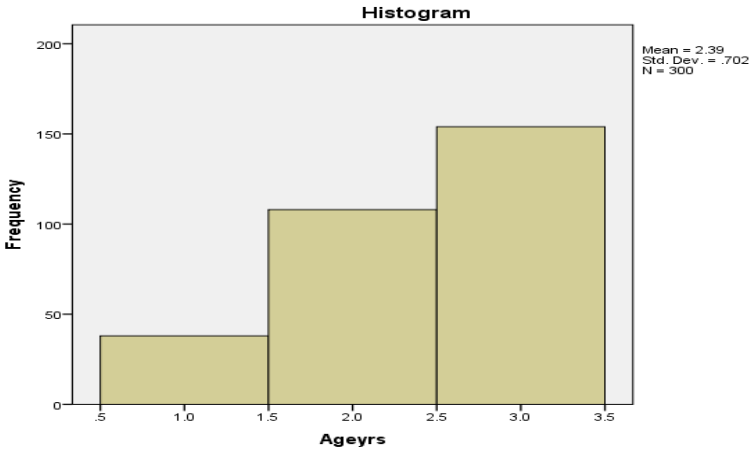

Table 2: Distribution of respondents by religion

No	RELIGION	NUMBER	PERCENTAGE
1	Hindu	244	81.3
2	Christian	22	7.3
3	Muslim	34	11.7
	TOTAL	300	100.0

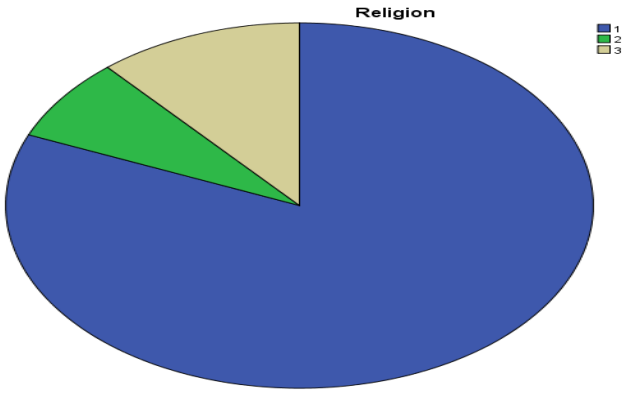

FIGURE 2: Distribution of respondents by religion

Nearly 2/3th of the pregnant women were Hindu (81.3%) followed by Muslim (11.7%) and Christian (7.3%).

Table 3: Distribution of respondents by occupation

No	OCCUPATION	NUMBER	PERCENTAGE
1	Housewife	238	79.3
2	Shopkeeper	40	13.3
3	Govt Employee	22	7.3
	TOTAL	300	100.0

Table 4: Distribution of respondents by address

ADDRESS	NUMBER	PERCENTAGE
Rural	206	68.7
Urban	94	31.3
TOTAL	300	100.0

Table 5: Distribution of respondents by educational qualification

No	EDUCATIONAL QUALIFICATION	NUMBER	PERCENTAGE
1	Illiterate	52	17.3
2	< X standard	84	28
3	X to XII standard	142	47.3
4	Graduate and above	22	7.3
	TOTAL	300	100.0

Table 6: Distribution of respondents by parity

No	PARITY	NUMBER	PERCENTAGE
1	Primigravida	104	34.7
2	Multigravida(Gravida-2)	86	28.7
3	Multigravida(Gravida-3)	50	16.6
4	Multigravida(Gravida ≥4)	60	20.0
	TOTAL	300	100.0

Primigravida constituted majority (34.7%) of the cases followed by Multigravida (Gravida-2 and Gravida-4)

Table 8: Distribution of respondents based on other menstrual history

No	MENSTRUAL HISTORY	NUMBER	PERCENTAGE
1	Regular	122	40.7
2	Regular, Scanty	62	20.6
3	Irregular	116	38.7
	TOTAL	300	100.0

Table 9: Haemoglobin Profile

Hemoglobin **Hypothyroidism**	**≤ 7g/dl**	**8- 10g/dl**	**≥10g/dl**
Overt	0	14	0
Subclinical	6	224	56
Total	6(0.02%)	238(79.3%)	56(18.6%)

Table 10: Thyroid profile inference

No	Hypothyroidism	Frequency	Percentage
1.	Overt	14	4.7
2.	Subclinical	286	95.3
Total		300	100

Table 11: Percentage distribution of Hypothyroidism and Miscarriage Miscarriage

No	Hypothyroidism	present	Absent
1	Overt	10	4
2	Subclinical	0	286
Total		10(3.3%)	290(96.6%)

Table 12: Percentage distribution of Hypothyroidism and Threatened abortion

Threatened abortion

No	Hypothyroidism	Present	Absent
1	Overt	4	10
2	Subclinical	6	280
Total	300	10(3.3%)	290(96.6%)

MID TRIMESTER COMPLICATIONS

Table 13: Percentage distribution of hypothyroidism and Preeclampsia Pre eclampsia

No	Hypothyroidism	Present	Absent
1	Overt	2	2
2	Subclinical	14	272
Total	290	16(5.5%)	274(94.4%)

Table 14: Percentage distribution of hypothyroidism and Gestational diabetes Gestational diabetes

No	Hypothyroidism	present	Absent
1	Overt	0	4
2	Subclinical	8	278
Total	290	8(2.7%)	282(97.2%)

Table 15: Percentage distribution of intrauterine growth Restriction with Hypothyroidism Intrauterine growth restriction

No	Hypothyroidism	Present	Absent
1	Overt	2	2
2	subclinical	0	286
Total	290	2(0.7%)	288(99.3%)

THIRD TRIMESTER COMPLICATIONS AND SUBSEQUENT OUTCOME

Table 16: Percentage distribution of intrauterine death with Hypothyroidism Intrauterine death

No	Hypothyroidism	present	Absent
1	Overt	0	4
2	Subclinical	4	282
Total	290	4(1.3%)	286(98.6%)

Table 17: Percentage distribution of Abruptio placenta & preterm labour with respect to Hypothyroidism

		Overt	Subclinical	Total
Abruptio placenta	1. present	0	4	4(1.3%)
	2. absent	4	282	286(98.6%)
Preterm labour	1. Early (28-34 weeks)	0	6	6(2.06%)
	2. Late (34-36weeks 6 days)	0	6	6(2.06%)
	3. Term	4	274	278(95.8%)

No case of placenta praevia was reported.

Preterm labour was found in 12 cases, Early preterm labour (<34 weeks) in 6 cases and Late preterm labour (34-36 weeks) in 6 cases.

Patients admitted with preterm labour were managed conservatively till term.

There was no recorded case of preterm delivery in our study.

Table 18: Distribution of Mode of Delivery and associated Complications

Variables	Respondents		Chi square test
	Non Compliant	compliant	
NORMAL DELIVERY			
1.NVD	10(18.5%)	40(16.9%)	0.000
2.NVD+Episiotomy	16(29.6%)	154(65.2%)	
3.Instrumental Delivery	2(3.7%)	12(5.0%)	
CAESAREAN DELIVERY			
1.Present	26(48.1%)	30(12.7%)	0.003

Table 19: Distribution of Respondents with respect to Neonatal Complications

Variables	Respondents		Chi square test
	Non compliant	Compliant	
BIRTH WEIGHT			
1. ≤ 2.5 kg	12(22.2%)	34(14.4%)	56.42 0.002
2. 2.6 – 3.5 kg	36(66.6%)	200(84.7%)	
3. 3.6 – 4.5 kg	6(11.1%)	2(0.9%)	
NEONATAL RDS			
1. Present	40(74.1%)	16(6.7%)	53.4 0.001
2. Absent	14(25.9%)	220(93.2%)	
CONGENITAL DEFORMITY			
1. Present	2(3.7%)	0	46.1 0.000
2. Absent	52(96.3%)	236	
STILL BIRTH			
1. Present	2(3.7%)	2(0.8%)	40.5 0.001
2. Absent	52(96.3%)	234(99.2%)	
NICU ADMISSION			
1. Present	34(63%)	2(0.8%)	78.9 0.002
2.Absent	20(37%)	234(99.1%)	
NEONATAL THYROID SCREENING			
1.Abnormal	4(7.4%)	0	54.1 0.000
2.Normal	50(92.6%)	236	

DISCUSSION

Our study consisted of 300 antenatal patients, Majority of the patients in the age group of > 30 yrs (51.3%) with mean age of 34 yrs. According to religion Hindu were majority of population (81.3%) which reflects the major group of people in Manipur, followed by Muslim (11.7%). In terms of occupation, housewives dominated the study with (79.3%) followed by shopkeeper (13.3%) and Government employee (7.3%) most of them were school teachers. By terms of locality rural population were majority (68.7%) and urban area (31.3%). According to parity, Primigravida dominated the study population (34.7%) followed by Multigravida (Gravida-2 = 28.7%, Gravida-3 =16.6% and gravida-4=20%).

Hemoglobin profile of our patients in the study group, 79.3% of the respondents had mild degree of Anemia, among them 5.9% had overt hypothyroidism and 94.1% had subclinical hypothyroidism severe anemia in only 6 respondents.

Thyroid profile inference in the first trimester of our study population, According to the thyroid profile inference in the first trimester, overt hypothyroid patients were 14 (4.7%) and subclinical hypothyroid patients were 286 (95.3%).

Overt or inadequately treated hypothyroidism is a risk factor of miscarriage and possibly preterm birth and fetal death, as a reflection of which in our study 10 patients (3.3%) had spontaneous miscarriage due to overt hypothyroidism.[11,12,16]

In our study, Threatened abortion, as a complication occurred in 10 patients (3.3%) SCH (6/10) and overt (4/10). In the 2nd trimester follow up, among 290 patients 22 (7.7%) were non compliant, all of them from rural locality and 268 patients (92.3%) were compliant.

Mid trimester complications like IUGR (Asymmetrical) was present in 2 patients, 2 out of 20 patients who were non compliant (drug dosage not properly adjusted) developed IUGR. Our results were supported by studies of Titoria M et al and Sahu M et al[7,13] in which cases of hypothyroid patients untreated had similar findings. Both the cases had pre eclampsia as additional complication.

Gestational diabetes was recorded in 8 patients (2.7%) all had subclinical hypothyroidism, out of 22 non compliant patients 8 developed Gestational Diabetes, Karakosta P[6] in his study has substantiated the combination of high TSH and positive thyroid antibodies in early pregnancy was associated with a 4-fold increased risk for gestational diabetes in the mother during pregnancy.

Among these 8 patients, 4 cases underwent LSCS, 4 had postpartum hemorrhage, 2 neonates had RDS and there were 2 NICU admissions. There was no maternal or neonatal mortality reported. Pre eclampsia was reported in 16 patients (5.5%), overt (2/16) & SCH (14/16) out of 22 patients who were non compliant, significant association was evaluated through chi square test (p-0.001). Our findings were emphasized by studies Sahu M and Titoria Met al.[7,13]

In the second trimester, TSH level estimated, if TSH was deranged then free T4 level was done. Patients were managed accordingly and followed till delivery, their obstetrical and perinatal outcome were noted. Overt Hypothyroids were prone to have pregnancy induced hypertension (P= 0.04). Intrauterine growth restriction (P= 0.01) and Intrauterine demise (P= 0.0004) as

compared to control. CS rate for fetal distress was significantly higher among subclinical hypothyroid women (P=0.04).

In the third trimester follow up, among 290 patients, 54patients (21.3%) were noncompliant, 48patients (88.8%) from rural area, 6 patients (11.1%) from urban area and 236 patients (78.7%) were compliant. Intrauterine death was documented in 4 patients (1.3%) of the total respondents, all were SCH, out of 54 patients who were non compliant, 4 patients had IUD (2 cases @ 33 weeks and 2 cases @ 35 weeks), Findings of our study were consistently substantiated by studies of Sahu M and Titoria M et al[7,13] with uncontrolled hypothyroidism leading to Intrauterine death. Preterm labour, one of the common obstetrical complications was reported in 12 patients, all were SCH (4.1%) Among the non compliant respondents (10/54) had preterm labour, In the compliant group (2/54) had preterm labour. Several literatures including Karakosta P et al, Casey BM et al, Abalovich M et al and Cao XY et al[6,9,10,12] supported our findings with preterm labour as the common complication with untreated hypothyroidism and patients who had proper follow up incidence of preterm labour has been reduced. In our study, patients got admitted with preterm labour and were managed conservatively till term. No case of preterm delivery has been reported.

Abruptio placenta was reported in 4 patients (1.3%), all were SCH, 2 cases @ 31 weeks and 2 cases @ 33weeks, all the 4 cases were non compliant during 2nd & 3rd trimester with no proper adjustment of thyroxine replacement, Our findings were also similar to literature by Ghanavati MA et al andCasey BM et al[8,9] in showing significant association between untreated Hypothyroidism and Abruption.

Delivery by Caesarean section was conducted in 48.1% of the patients (non compliant group) compared to 12.7% of the patients (compliant group) Major indication for LSCS was fetal distress. same findings were supported by studies Sahu M and Titoria M et al[7,13], Overt Hypothyroids were prone to have pregnancy induced hypertension (P= 0.04). Intrauterine growth restriction (P= 0.01) and Intrauterine demise (P= 0.0004) as compared to control. CS rate for fetal distress was significantly higher among subclinical hypothyroid women (P=0.04). Significant adverse effects on maternal and fetal outcome were seen emphasizing the importance of routine antenatal thyroid screening. Postpartum hemorrhage as 3rd stage complication occurred in 48.1% of the patients, (non compliant) whereas only in 18.6% of the patients in the compliant group.

Neonatal complications like Low birth weight accounted for 22.2% of the babies in the non compliant group, our findings were consistent with the findings of study by Shields BM et al and Cao XY et al.[14,15] both clinical and subclinical hypothyroidism have significant adverse effects on pregnancy and fetal development, more frequently seen in symptomatic women. The obstetric complications of hypothyroidism contribute to the overall increase in frequency of adverse neonatal outcomes, which include preterm birth, low birth weight, increased perinatal morbidity and mortality. Perinatal morbidity in the form of Neonatal RDS, NICU Admission were increased in the non compliant group (RDS- 74.1%, NICU admission – 63%) significant association has been found with Chi square test and P value was significant(0.001). Our findings of perinatal and neonatal morbidity were correlating with the studies by Sahu M and Cao XY et al.[13,16] Congenital deformity and stillbirth were present in 2 cases respectively.

The association between thyroid hormone and measurement of obstetrical and perinatal outcome is consistent with the previous studies cited in the review of literature.

Although the optimal TSH value for pregnant women with hypothyroidism has not been rigorously established, it has been suggested that the goal of therapy should be to maintain TSH levels between 0.5 and 2.5 mIU/L. Free thyroxine should be brought into the upper normal range. As pregnancy is a time of complex hormonal changes affecting T4 availability to the mother and fetus, therefore it is necessary to establish trimester- specific-reference intervals of TSH and FT4 as use of non-pregnant reference intervals maybe misleading during this time. This can lead to misdiagnosis of many at-risk women. Hence in our study we followed the trimester specific ranges for all the selected patients in order to get an optimum result.

The pregnancy outcome observed in our subjects was better. There was very low incidence of still birth, preterm deliveries, deaths etc. This might have been due to the thyroid hormones of mother which were maintained within the reference ranges. They were serially followed throughout pregnancy and those found to be thyroid-insufficient were placed on levothyroxine dosage as soon as diagnosed. It was observed that the absolute percentage increase in dose during pregnancy in newly diagnosed hypothyroid subjects were 30-50%.

CONCLUSION

Incidence of Hypothyroidism was found to be 0.3% for overt hypothyroidism and 3% for subclinical hypothyroidism during the tenure of study in obstetrics and gynecology Department, Regional institute of medical sciences, Imphal. Compliant Respondents had few complications when compared to non compliant patients. Thyroid profile evaluation showed 4.7% patients of overt hypothyroidism and 95.3% patients of subclinical hypothyroidism. Our study proves significant association between uncontrolled hypothyroidism and adverse fetomaternal outcome. The pregnancy outcome observed in our subjects (compliant) was better. There was very low incidence of still birth, preterm deliveries,

deaths etc. This might have been due to the thyroid hormones of mother which were maintained within the reference ranges. They were serially followed throughout pregnancy and those found to be thyroid-insufficient were placed on levothyroxine dosage as soon as diagnosed.

Recommendations

All the women who already have known thyroid dysfunction should immediately go for thyroid function tests as soon as the pregnancy is confirmed.

Careful monitoring of the medicine should be done during the course of pregnancy.

All women should be screened for thyroid dysfunction as soon as pregnancy is confirmed.

The trimester- specific reference intervals for thyroid hormones established for pregnant Indian population after serially following the pregnant women should be used to identify at- risk women.

A routine screening for thyroid dysfunction in women during childbearing years does not exist and should be established not only by gynecologists, but also by general practitioners.

Iodine supplementation of 250 µg per day and TSH adjustment in hypothyroid women to values <2.5 mIU/l are strongly recommended to improve pregnancy outcomes.

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