EFFECT OF THYROID DYSFUNCTION IN ANTENATAL MOTHERS

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ABSTRACT

BACKGROUND

The aim of the study is to study the effect of thyroid dysfunction in antenatal mothers in Alappuzha one of the coastal areas in South Kerala over a period from January 2012 to January 2015.

MATERIALS AND METHODS

It is a descriptive study of the effect of thyroid dysfunction among pregnant ladies attending OBG Department in Government Medical College, Alappuzha, a rural medical college at coastal areas of Kerala over a period of 3 years.

RESULTS

The incidence is found to be maximum in the coastal area, i.e. 84.9%, but p-valve 0.625 is not statistically significant. Thyroid disorder is mostly seen in primigravida (57.8%) and between the age of 20 and 25 yrs. (43.2%) and the most commonly seen disorder among is subclinical hypothyroidism (73.7%) (p valve <.005, which is statistically significant). There is significant increase in maternal complications like preeclampsia, (RR-8.54, p-value 0.014) recurrent abortion (RR-91.13, p-value 0.000), prolonged period of infertility (RR-55.16, p-value 0.000), anaemia (RR-11.37, p-value 0.003) is seen in subclinical hypothyroidism. The foetal complications seen are oligamnios (7.8%), MSAF (9.2%), foetal distress (12.1%), PROM (5.1%) and FGR (10.9%). The neonates were admitted in NICU in view of NEC (1.5%), NNJ (24.1%), MAS (6.9%), TTNB (9.5%) and HIE (2.9%).

CONCLUSION

The present study is intended to study the maternal and foetal effects of thyroid dysfunction. After the study, we concluded that there are many adverse maternal, foetal and neonatal effects in pregnancies complicated with thyroid dysfunction. In coastal area, the disease has got a high prevalence and hence there is a need for proper screening and early diagnosis. Proper treatment options are given to the patient.

KEYWORDS

Thyroid Disorders, Maternal Effect, Foetal Complications, NICU Admission.

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BACKGROUND

Endocrine disorders are increasingly encountered in pregnancy. Thyroid disorders are one among them.[1] The prevalence of thyroid disorder varies worldwide. Thyroid disorder in pregnancy are on a rise in India with prevalence of subclinical hypothyroidism being around 7% and overt being around 5%.[1] Hyperthyroidism in pregnancy is less prevalent with <0.05%. In developed countries like USA, the prevalence is less around 4% and mostly in subclinical range. Overt disease is less commonly found.[2]

To optimise pregnancy outcome, it is essential to understand the physiology underlying these conditions. Changes in pregnancy; the demand for thyroid hormones is increased during pregnancy.[1] The thyroid function test changes because of two main hormones hCG (human chorionic gonadotropin) and oestrogen. In pregnancy, TSH is suppressed, thyroid binding globulin is increased. Total T3 and T4 increased and free T3 and T4 remain unchanged. Renal clearance of iodine increased.[1]

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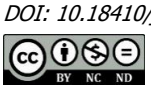

Normal Physiology

The hypothalamic pituitary axis- Thyrotropin-Releasing Hormone (TRH) produced in a tonic fashion in the paraventricular nucleus of the hypothalamus. TRH stimulate the pituitary to secrete TSH. TSH has an α and β subunit; β subunit confers specificity.[3] TSH secretion regulated by negative feedback from circulating thyroid hormone, dopamine and somatostatin. TSH then stimulates the thyroid gland to produce as well as secrete thyroxine (T4) and triiodothyronine (T3). The rate-limiting step is iodide trapping mediated by TSH. Non-pregnant state, 80 mg/dL to 100 mg/dL of iodine taken up, 20% of the intake is cleared by the thyroid gland and the rest renally.[1]

Physiologic adaptation during pregnancy[4]- Increase in thyroid-binding globulin secondary to an oestrogenic stimulation of TBG synthesis and reduced hepatic clearance of TBG; two to threefold levels of bound proteins, total

thyroxine and total triiodothyronine are increased and Resin Triiodothyronine Uptake (RT3U) is decreased. This begins early in the first trimester, plateaus during mid-gestation and persists until shortly after delivery. Human Chorionic Gonadotropin (HCG) has intrinsic thyrotrophic activity begins shortly after conception, peaks around gestational week 10, declines to a nadir by about week 20. It directly activate the TSH receptor partial inhibition of the pituitary gland (by cross-reactivity of the α subunit), transient decrease in TSH between weeks 8 and 14 mirrors the peak in hCG concentrations.[5] In 20% of normal women, TSH levels decrease to less than the lower limit of normal. A decrease in basal TSH of 0.1 mU/L was observed for every 10,000 IU/L increment in hCG. Also, transplacental passage of T4 and iodide and placental metabolism of iodothyronines stimulate the maternal thyroid and depleting the maternal circulation of thyroid hormone and its precursors. In cases of patients with overt hypothyroid, 25% to 47% average dosage of thyroxine increases during pregnancy, increased serum Thyroid Stimulating Hormone (TSH) and thyroglobulin concentrations, relative hypothyroxinemia and occasional goiter formation esp. from area with borderline iodine sufficiency associated with increase in thyroid gland size in 15%.[6]

Foetal thyroid- 7-9 weeks formation of thyroid gland.

10 weeks- TSH and thyroxine dateable, 17 weeks- Maturation of the gland, >18 weeks- Response to TSH stimulation.[7,8,9,10]

The major thyroid disorder in pregnancy are, 1) Hypothyroidism; 2) Hyperthyroidism; 3) Overt hypothyroidism; 4) Overt hyperthyroidism; 5) Thyroid nodule and thyroid cancer; 6) Postpartum thyroiditis.

The thyroid dysfunction in pregnancy is associated with increased risk of stillbirth, preterm delivery, intrauterine growth restriction, preeclampsia, heart failure, spontaneous abortion, foetal thyroid hyperfunction or hypofunction caused by TSHRAbs, foetal goiter from excessive antithyroid drug treatment.[4]

MATERIALS AND METHODS

This is a descriptive study in which effects of thyroid disease in pregnancy is studied who presented to the OBG Department of Government Medical College, Alappuzha. The patient population of Alappuzha Medical College is mainly from the costal areas as Alappuzha is on a landmass between the broad Arabian Sea and a network of rivers flowing into it, which is righty said the Venice of east. The questionnaires asked for the presence of thyroid disease and also abnormal lab valves of thyroid function at any antenatal checkup throughout pregnancy.

The audit group comprised of 952 pregnancies, of which, 75.1% has subclinical disease and 24.5% has overt hypo and hyperthyroidism.

American thyroid association guidelines[1] are taken as reference in which;

First trimester TSH	-0.1-2.5
Second trimester	-0.2-3
Third trimester	-0.3-3

Any values below are hyperthyroidism and/or hypothyroidism. When free T3 and T4 are normal, the disease is subclinical. The study was conducted between January 2012 to January 2015.

Inclusion Criteria

Pregnant ladies with thyroid disorder diagnosed at any time before or during pregnancy.

Exclusion Criteria

Mothers with any medical or surgical illness in the past or diagnosed in present pregnancy.

Statistical Analysis

Data entered in MS Excel and was analysed using computer software, Statistical Package for Social Sciences (SPSS) version 16. Data are expressed in its frequency and percentage. Chi-square test was used as the non-parametric test to elucidate the association and comparison between different parameters. The quantitative variables were compared by independent Student's t-test. For all statistical evaluations, a two-tailed probability of value <0.05 was considered significant. Descriptive statistics was used to describe data. Qualitative variables was summarised using percentage. Quantitative variables was summarised using mean with standard deviation. Sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Values (NPV) for variables were calculated using standard formulae.

RESULTS

Total about 952 pregnant ladies are analysed. 43.2% were between 20 and 25 yrs. of age and 34% between 26 and 30 yrs. and the disorder is significantly high in subclinical hypothyroidism.

Age	Subclinical Hypothyroidism		Overt Hypothyroidism		Others		χ^2	p
	Count	Percent	Count	Percent	Count	Percent		
<20 yrs.	34	73.9	8	17.4	4	8.7	81.32**	0.000
20-25 yrs.	345	83.9	46	11.2	20	4.9		
26-30 yrs.	232	71.6	69	21.3	23	7.1		
31-35 yrs.	85	58.6	50	34.5	10	6.9		
>35 yrs.	6	23.1	17	65.4	3	11.5		

Table 1. Comparison of Age Based on Thyroid Dysfunction

Though, no statistical significance obtained, most of the patients (84.9%), we analysed were belonging to coastal area. Primi were 57.8% and grand multi were few about 4%. Subclinical hypothyroidism were the one, which was detected to be highest 73.7% followed by overt hypothyroidism 20%. Both, overt and subclinical hypothyroidism came around 5%. Only, 0.4% detected to have thyroid nodule.

Most of the patients are diagnosed in the first trimester by routine screening with TSH 83.6%. 16.0% of the patients had disease before pregnancy. Multigravidas with previous history of any thyroid disorder 77.3% of the previous pregnancy went uneventful. 10.7% got aborted. History of neonatal death was present in 2.3% and 4.8% underwent lower segment caesarean section for MSAF or foetal distress.

There is significant increase in maternal complications like preeclampsia, (RR-8.54, p-value 0.014) recurrent abortion (RR-91.13, p-value 0.000), prolonged period of infertility (RR-55.16, p-value 0.000), anaemia (RR-11.37, p-value 0.003) is seen in subclinical hypothyroidism.

The foetal complications seen are oligamnios (7.8%), MSAF (9.2%), foetal distress (12.1%), PROM (5.1%) and FGR (10.9%). The neonates were admitted in NICU in view of NEC (1.5%), NNJ (24.1%), MAS (6.9%), TTNB (9.5%) and HIE (2.9%).

Maternal Effect	Subclinical Hypothyroidism		Overt Hypothyroidism		Others		χ^2	p
	Count	Percent	Count	Percent	Count	Percent		
Spontaneous abortion	68	77.3	18	20.5	2	2.3	2.67	0.263
Preeclampsia	102	71.3	38	26.6	3	2.1	8.54*	0.014
Anaemia	83	84.7	7	7.1	8	8.2	11.37**	0.003
Recurrent pregnancy loss	30	37.0	49	60.5	2	2.5	91.13**	0.000
Prolonged period of infertility	17	34.7	30	61.2	2	4.1	55.16**	0.000

Table 2. Comparison of Maternal Effect Based on Thyroid Dysfunction

Most of the babies were delivered at term (88.4%) and 68.9% delivered vaginally and 31.1% by lower segment caesarean section. 64.8% of the babies had normal birth weight and about 30% had weight below 2.5%. Though, confounding factors are not evaluated about 50% babies had NICU admission. 24.1% admissions are for the evaluation of neonatal jaundice.

NICU Admission and Neonatal Outcome	Count	Percent
Nil/NA	514	54.0
Hypotonia	9	0.9
Sepsis	13	1.4
NEC	14	1.5
NND	10	1.1
NNJ	229	24.1
MAS	66	6.9
Hypoglycaemia	11	1.2
TTNB	90	9.5
HIE	28	2.9

Table 3. Percentage Distribution of the Sample According to NICU Admission and Neonatal Outcome

DISCUSSION

The study is mainly intended to know the maternal foetal and neonatal complications in thyroid disorders complicating pregnancy and the importance of routine screening for thyroid disorders. Total about 952 pregnant ladies are analysed. 43.2% were between 20 and 25 yrs. of age and 34% between 26 and 30 yrs. The age distribution is significantly high in subclinical hypothyroidism. Klein et al[11] studied the frequency of subclinical and overt hypothyroidism in pregnant women who found a serum TSH level greater than 6 mIU/L in 2.5% (49 of 2,000) of women at 15-18 weeks gestation. Overt hypothyroidism (i.e. an elevated serum TSH plus a T4 2.5 SD below the mean or lower) was present in 0.3% of women. Our study gives the same result as the literature as the subclinical hypothyroidism is more common among pregnant females.

There is significant increase in maternal complications like preeclampsia, (RR-8.54, p-value 0.014), recurrent abortion (RR-91.13, p value 0.000), prolonged period of infertility (RR-55.16, p value 0.000) and anaemia (RR-11.37, p value 0.003) is seen in subclinical hypothyroidism. The foetal complications seen are oligamnios (7.8%), MSAF (9.2%), foetal distress (12.1%), PROM (5.1%) and FGR (10.9%). The neonates were admitted in NICU in view of NEC (1.5%), NNJ (24.1%), MAS (6.9%), TTNB (9.5%) and HIE (2.9%).

In a study done by Cassey BM et al,[2] pregnancies in women with subclinical hypothyroidism were 3 times more likely to be complicated by placental abruption (relative risk 3.0, 95% confidence interval 1.1-8.2). Preterm birth, defined as delivery at or before 34 weeks of gestation was almost 2-fold higher in women with subclinical hypothyroidism (relative risk 1.8, 95% confidence interval 1.1-2.9).

All the literatures give a significantly increased maternal, foetal and neonatal complications for thyroid disorders complicating pregnancy where the largest prevalence is for subclinical hypothyroidism.

CONCLUSION

Thyroid disorder is mostly seen in primigravida (57.8%) and between the age of 20 and 25 yrs. and the most commonly seen disorder among is subclinical hypothyroidism. There is significant increase in maternal complications like preeclampsia, recurrent abortion, prolonged period of

infertility and anaemia is seen in subclinical hypothyroidism. The foetal complications seen are oligamnios, MSAF, foetal distress, PROM and FGR. NICU admission for the babies in this group is high. After the study, we concluded that there are many adverse maternal, foetal and neonatal effects in pregnancies complicated with thyroid dysfunction. In costal area, the disease has got a high prevalence and hence there is a need for proper screening and early diagnosis. Proper treatment options are given to the patient.

ABBREVIATIONS

MSAF Meconium-stained amniotic fluid.
ATA American thyroid association.
FGR Foetal growth restriction.
PROM Premature rupture of membranes.
PPROM Preterm premature rupture of membranes.
MAS Meconium aspiration syndrome.
NNJ Neonatal jaundice.
NEC Necrotising enterocolitis.
HIE Hypoxic-ischaemic encephalopathy.

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