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Original Research Article

A Study to Evaluate Maternal and Fetal Outcomes of Hypothyroidism Complicating Pregnancy

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Abstract

Background: Pregnancy plays as a stress test to assess the function of maternal thyroid system. Thyroid dysfunction occurs very commonly in the pregnant women. Hypothyroidism occurs in more than 10% of all the pregnant women. Hypothyroidism may result in anaemia, low birth weight and mental retardation in the newborns. The present study analyzed the maternal and fetal outcomes of Thyroid dysfunction in pregnant women.

Aim of the Study: To investigate the maternal and fetal outcomes in women who presented with Thyroid dysfunction during their pregnancy. To compare the same outcome variables with the pregnant women with normal thyroid function, attending Viswabharathi Medical College Hospital and General hospital, Kurnool.

Materials and methods: This was a Prospective and comparative clinical study which included 50 pregnant women with hypothyroid status and 50 pregnant women with normal thyroid function results. The maternal and fetal outcomes of these pregnant women of two groups were studied and analyzed. Thyroid Function tests values of women were compared with American Pregnancy and Thyroid Association; the cut off values used were: The usual value for participants in the control arm was 0.1 to 2.5 uI U/L in the 1st trimester and 0.2 to 3 uI U/L in the second trimester. Those with TSH concentrations of more than 2.5 uI U/L in the 1st trimester and more than 3 uI U/L, in the second trimester were enrolled in the trial andtheir fT4 and anti-TPO levels were estimated. Results: The prevalence of normal deliveries and Abortions were statistically significant (p-value <0.05) and the other variables were not significant. 29/50 (58%) of the pregnant women with hypothyroidism and 18/50 (36%) of the pregnant women without hypothyroidism had Anemia and the difference was found to be statistically significant (p value <0.05).

Conclusion: It is mandatory to estimate the targeted TSH screening for pregnant women especially those at high risk for thyroid deficiency before or during early pregnancy. It was necessary to estimate TPO antibodies in all the pregnant women who have higher levels of TSH values. The risk of pregnancy loss to mothers and preventing low birth weights in the newborns could be avoided effectively. The risk of pregnancy was more in patients with positive TPO antibodies.

Keywords: Hypothyroidism, mental retardation, pregnant women, abortions, antibodies, newborns

Introduction

Pregnancy though a normal physiological event, plays as a stress factor resulting in hormonal imbalance in the human body. It could cause clinical or sub clinical hypothyroidism in pregnant women with limited reserve. The normal reference ranges of TSH or free thyroxine (fT4) obtained from non-pregnant women change in pregnant women due to the pregnancy. The fT4 and fT3 levels changes in pregnancy to a higher level by up to 50%. This in turn causes an increase in a woman's daily iodide requirement, at the same time thyroid-stimulating hormone (TSH) levels decrease, especially in the first trimester [1]. The Human Chorionic Gonadotrophin (HCG) levels in 1st trimester of pregnancy increases which results in low TSH values and thus cut offs also become less. It was observed that women with low thyroid reserves, due to pregnancy stress convert to overt disease [2]. If the iodide supplements are sufficient, thyroid adaptations are well tolerated, because of sufficient inner thyroid iodide. However, in situations of iodide deficiency, these physiological adaptations would lead to significant changes in pregnancy [3]. Prevalence of Hypothyroidism (2 to 3%) is high especially in India but its rate of detection, its effects on pregnancy and the newborns has not kept pace with the magnitude of the problem. Hypothyroidism could be easily treated when timely detection and treatment of the dysfunction was implemented once diagnosed. This could minimize the burden of adverse fetal and maternal outcomes in pregnancy [4,5]. The prevalence of sub-clinical thyroid dysfunction in the general population was as high as 10% in India [5]. The fetus undergoes many periodical changes and develops its own hypothalamic pituitary axis. The placenta plays an important role in the iodide and T4 transport to the fetus and its metabolism. The thyroid gland increases in its size by 10% in geographical areas where iodine is rich and by 20 to 40% in geographical areas where iodine is deficient [6]. Similarly the production of T3 and demand of daily intake of Iodine increases by 50% [7]. Nearly 02 to 03% pregnancies per 1000 were found to be complicated by overt hypothyroidism. But 05% of the pregnant women with subclinical hypothyroidism develop maternal complications if untreated [8]. Miscarriage, preeclampsia, anemia, placental abruption, preterm delivery, gestational hypertension, increased rate of caesarean section and postpartum hemorrhage were the common effects on 40% of the pregnant women with overt hypothyroidism [9]. Not only during but also during delivery the stress on the fetal-pituitary-thyroid axis was observed in many studies [10]. The fetal outcomes were pre-term birth, low birth weight (LBW), neonatal respiratory distress syndrome, peri-natal morbidity and mortality, increased NICU admission and neuropsychological and cognitive impairment were observed in 30% of the pregnant women with overt hypothyroidism [11]. Children with congenital hypothyroidism have severe cognitive, neurological and development abnormalities as thyroid hones ar necessary for the growth and development of the brain of the fetus and the newborn [12]. Such children have a lower IQ when compared to the children with normal thyroid hormones in their mothers during pregnancy [13]. In the present study pregnant women with hypothyroidism were studied to investigate their maternal and fetal outcomes of their pregnancy. The same variables were

analyzed in the pregnant women with normal thyroid function.

Materials and Methods

A Comparative prospective clinical study was conducted including 50 hypothyroid pregnant women and 50 normal pregnant women to investigate their maternal and fetal outcomes. An institutional ethics committee clearance was obtained before commencing the study and a ethics committee approved consent form and proforma was used for the study.

Inclusion criteria: Pregnant women with singleton pregnancy were included. Pregnant women with primigravida and multigravida of all ages were included. Women in the 1st and 2nd trimesters were included. Pregnant women who were already diagnosed and being treated as hypothyroidism were included.

Exclusion criteria: Pregnant women with history of multiple pregnancies were excluded. Pregnant women with obstetric or medical complications other than hypothyroidism were excluded. Pregnant women refusing to participate in the study were excluded.

Methods of collection: All the subjects who came to the Obstetrics and Gynecology OPD or admitted to the Viswabharathi Medical College and General Hospital, Kurnool, between December 1, 2019 and November 30, 2020 with singleton pregnancies were administered TSH test. The usual value for participants in the control arm was 0.1 to 2.5 uI U/L in the 1st trimester and 0.2 to 3 uI U/L in the second trimester. Those with TSH concentrations of greater than 2.5 uI U/L in the 1st trimester and more than 3 uI U/L in the second trimester were tested for their fT4 and anti-TPO levels. All the patients diagnosed with hypothyroid state were treated with 50 to 100 mg L-thyroxine based on their gestational age, body weight, and TSH levels as prescribed by an endocrinologist. Patients diagnosed with hypothyroidism during their 1st trimester were reviewed every four weeks for further dose adjustments and follow-up. Hypothyroidisms in Patients with second trimester were also reviewed bi-monthly. Pregnancy-induced anaemia, hypertension, gestational diabetes mellitus, preterm labour, placental abruption, and fetal problems such as RDS and NICU care for the infants, premature stillbirths, and fetal hypothyroidism were all monitored in all of these individuals and analyzed. Statistical Analysis: All the data was analyzed using standard statistical methods using number, percentage and association and correlation was calculated using student T test with p value taken as significant at 0.05.

Results

A comparative clinical study with 50 pregnant women with hypothyroidism and 50 normal pregnant women were included in the study and their maternal and fetal outcomes were investigated and analyzed. In the present study 26/50 (52%) of the women and 38/50 (76%) of the normal pregnant women had full term un eventful delivery. Abortion was noted in 08/50 (16%) in hypothyroid women and 02/50 (04%) normal pregnant women. Fetal distress was observed in 07 (14%) in hypothyroid and 04/50 (08%) normal pregnant women. PROM was noted in 03/50 (06%) and 02/50 (04%) normal pregnant women. MSL was noted in 03/50 (06%) and 02/50 (04%) 0f normal pregnant women. Among the difference in the incidence of these variables, only incidence of normal delivery and Abortion were statistically significant (p value <0.05) and the other variables were not significant (Table 1).

Table 1: Distribution of study subjects by reason for termination of pregnancy (n-50 in both groups)

Indications of pregnancy	Cases (n = 50)		Controls (n = 50)		P value
	Number	Percentage	Number	Percentage	
Uneventful/Term	26	52%	38	76%	**0.004**
Fetal distress	07	14%	04	08%	0.337
Abortion	08	16%	02	04%	**0.029**
Still birth + IUD	02	04%	01	02%	0.557
Abruption	01	02%	01	02%	1
PROM	03	06%	02	04%	0.645
MSL	03	06%	02	04%	0.645
Total	50	100%	50	100%	--

In the present study 29/50 (58%) of the pregnant women with hypothyroidism and 18/50 (36%) of the pregnant women without hypothyroidism had Anemia and the difference was found to be statistically significant (p value <0.05), **(Fig 1).**

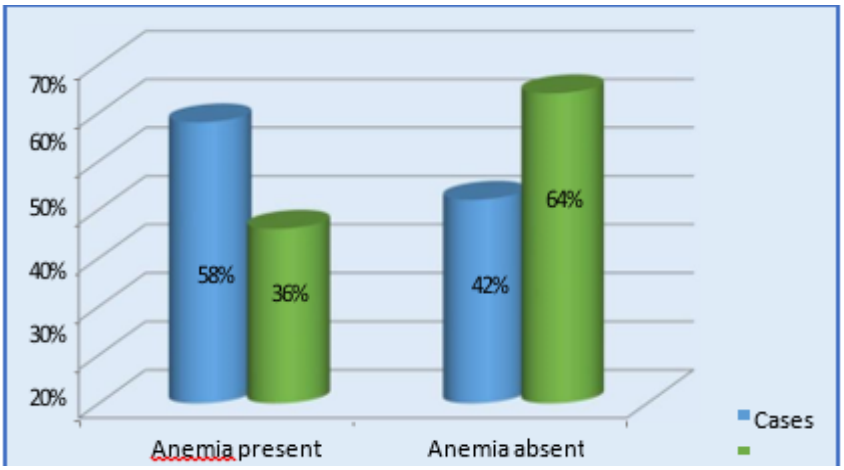

Figure 1: Comparison of Incidence of Anaemia between hypothyroid and normal pregnant women (n-50 in both groups), p value 0.01

In the present study 14/50 (28%) of the pregnant women with hypothyroidism and 08/50 (16%) of the controls had incidence of PIH and the difference of incidence wasfound to be statistically significant **(Table 2).**

Table 2: Comparison of Incidence of PIH in hypothyroid pregnant women and normal pregnant women (n-50 in both groups)

PIH	Women with hypothyroid state		Normal thyroid state	
	Number	Percentage	Number	Percentage
Yes	14	28%	08	16%
No	36	72%	42	84%
Total	50	100%	50	100%

In the present study 10/42 (23.80%) of the hypothyroid pregnant women and 07/48 (14.58%) of the normal pregnant women had Pre-term labour. The difference of incidence was found to be

statistically not significant. (p value >0.05)

Table 3: Comparison of Incidence of Pre-term labour hypothyroid pregnant women and normal pregnant women (n-42 in hypothyroid women and n-48 in normal pregnant women)

Pre-term labour	Cases (n = 42)		Controls (n = 48)	
	Number	Percentage	Number	Percentage
Yes	10	23.80	07	14.58
No	32	76.19	41	84.41
Total	42	100%	48	100%

In the present study Birth weight of the newborn children was less than 1.5kg in 14.28% of the hypothyroid pregnant women and 06.3% of the normal pregnant women, 1.5 -2kg in 07.2% of the hypothyroid pregnant women and 02.08% of the normal pregnant women, 02 – 2.5 kg in 14.3% of the hypothyroid pregnant women and 12.5% in the normal pregnant women, 2.5 – 3 kg in 54.7% of the hypothyroid pregnant women and 70.8% of the normal pregnant women and >3.5kg in 09.5% of the hypothyroid pregnant women and 08.3% of the normal pregnant women **(Table 4).**

Table 4: Comparison of Birth Weight of the baby between Cases and Controls

Birth Weight of the baby	Cases (n = 42)		Controls (n = 48)	
	Number	Percentage	Number	Percentage
<1.5 kg	06	14.28%	03	06.25%
1.5 – 2.0 kg	03	07.14%	01	02.08%
2.0 – 2.5 kg	06	14.28%	06	12.50%
2.5 – 3.0 kg	23	54.76%	34	70.83%
>3.5 kg	04	09.52%	04	8.33%
Total	42	100%	48	100%

In the present study the APGAR score at 1 minute was less than 08/10 in 11.9% of newborns of hypothyroid pregnant women and 04.2% of the 11.9% of normal pregnant women with the difference found to be statistically not significant (p value more than 0.05), **(Table 5).**

Table 5: Comparison of APGAR score of newborns at 1 minute between hypothyroid pregnant women and normal women (n-42 and n-48 respectively)

APGAR at 1 minute	Cases (n = 42)		Controls (n = 48)	
	Number	Percentage	Number	Percentage
≥8/10	37	88.1%	46	95.8%
<8/10	05	11.9%	02	4.2%
Total	42	100%	48	100%
Chi – square = 1.87, df = 1, p = 0.330				

In the present study the APGAR score at 05 minutes was less than 8/10 in 7.1% of the pregnant women with thyroid deficiency and 02.1% of the normal pregnant women. This was found to be not significant statistically (p at more than 0.05) controls the difference was found to be statistically not significant **(Table 6).**

Table 6: Comparison of APGAR score of newborns at 05 minutes between hypothyroid pregnant women and normal women (n-42 and n-48 respectively)

APGAR at 5 minutes	Cases (n = 42)		Controls (n = 48)	
	Number	Percentage	Number	Percentage
More or equal to 8/10	39	92.85	47	97.91
Less than 8/10	03	07.14	01	02.8
Total	42	100%	48	100%
Chi – square = 1.35, df = 1, p = 0.245				

In the present study 23.8% of the newborns of pregnant women with hypothyroidism and 20.8% of the normal pregnant women had NICU admissions for the newborns. The difference between the two groups was found to be statistically not significant. (p value >0.05), **(Table 7).**

In the present study in 50% newborns of pregnant women with hypothyroidism with the raised Anti TPO levels had NICU admissions, 62.5% of the newborns were born out of LSCS and 30% had low birth weights less than 1.5Kgs **(Table 7).**

Table 7: Comparison of Incidence of maternal complications LSCS, NICU admissions and Baby weightby Anti TPO levels in hypothyroid and normal pregnant women (n-16 and n- 3

	Anti TPO				P value
	Raised (n = 16)		Not raised (n = 34)		
	Number	Percentage	Number	Percentage	
Maternal Complications					
Yes	12	75%	20	58.8%	0.266
No	04	25%	14	41.2%	
NICU admissions					
Present	08	50%	04	11.7%	0.003
Absent	08	50%	30	88.3%	
LSCS					
Yes	10	62.5%	08	23.5%	0.007
No	06	37.5%	26	76.5%	
Birth weight					
<1.5 kg	03	30%	03	9.4%	
1.5 – 2.0 kg	01	10%	02	6.2%	0.107
2.0 – 2.5 kg	03	30%	03	9.4%	
2.5 – 3.0 kg	02	20%	21	65.6%	
>3.5 kg	01	10%	03	9.4%	
Total (n = 42)	10	100%	32	100%	

Discussion

Thyroid functional disorders are very common in the women of child bearing age. It is also a hormonal disorder next common to Diabetes Mellitus in the general population as well as child bearing age of women [14]. The prevalence of thyroid dysfunctions during pregnancy varies from region to region in India. [15] The outcomes are divided as maternal and fetal outcomes and they also vary from region to region in India

[15]. The studies related to the prevalence and outcomes of thyroid deficiency in pregnant women are less in the medical literature especially from the southern India [15]. The geographic prevalence of the thyroid deficiency was based on the amount of iodine in common salt and consumption of salt. The present study was an attempt to find the above issue in this part of Andhra Pradesh and its maternal and fetal outcomes. Observing the prevalence of thyroid deficiencies in the first trimester of pregnancies in this study, it was noted that the first trimester values were more significant and important than in the 2nd and 3rd trimester. There exists a debate on the upper limit of TSH values for defining 1st trimester reference value [16]. For the most assays, the upper limit of TSH was 0.1 to 2.5 uI U/L in the 1st trimester.; for 2nd trimester: 0.2–3.0mIU/L and for 3rd trimester: 0.3 -3mIU/L [17]. Very few studies have reduced the upper limit of TSH in 1st trimester from a non-pregnant value are published from India and Korea after 2011 [18]. In India, the prevalence of hypothyroidism was found to be higher than in the Western countries. Iodine deficiency could be a contributing cause for such prevalence. The percentage of households consuming iodized salt in India, as per the Iodine Network Global score card 2010, is 51% [19]. Hashimoto's thyroiditis was observed to be one of the causes of hypothyroidism in iodine-sufficient areas, such as North America and Western Europe. In this study the prevalence of subclinical, overt and manifest hypothyroidism were 4.6 %, 2.10% and 1.41% percentages respectively. In an Indian study of 2016 the prevalence reported were 3.47%, 2.05% and 0.50% respectively for subclinical hypothyroidism, overt and manifest hypothyroidism patients [20]. Thyroid peroxidase (TPO) enzyme was said to be responsible for the oxidation and organization of iodine, and for the formation of fT4 and fT3 hormones [21]. Thyroglobulin (TG) was considered as a precursor glycoprotein which acts as a substrate for the synthesis and storage of thyroid hormones [22]. Autoimmune thyroid diseases always present with antibodies to TPO and Thyroglobulin resulting in miscarriages which are likely to develop due to generalized activation of the immune system and transplacental transfer of antibodies, causing fetal rejection [23,24]. In the present study there was significant association between thyroid dysfunction and maternal outcomes such as preterm deliveries, abortions. (Table 1) In the present study 29/50 (58%) of the pregnant women with hypothyroidism and 18/50 (36%) of the pregnant women without hypothyroidism had Anemia and the difference was found to be statistically significant (p value <0.05), (Fig 1). Iron deficiency was found to result in impaired heme-dependent enzyme thyroid peroxidase which in turn causes limited synthesis T3 and T4 levels. Bit Iron repletion always reverses the state of hypothyroidism [25]. In a study by Baghel *et al* [26] the prevalence of anemia in women with hypothyroidism was as high as 60% due to iron deficiency. In the north India anemia and pregnancy were very commonly associated [26]. In the present study 14/50 (28%) of the pregnant women with hypothyroidism and 08/50 (16%) of the controls had incidence of PIH and the difference of incidence was found to be statistically significant (Table 2). These results were comparable to similar studies in which PIH observed in 13.6% women with SCH and 14.7 in overt hypothyroidism [27]. Low birth weight was found in the newborns of hypothyroid mothers due to its association with preeclampsia. Similarly fall in fetal thyroxine may cause delay in pituitary-thyroid axis development resulting in reduced fetal pituitary growth hormone secretion, vascular responsiveness and

maturation, and cardiovascular homeostasis in utero [28]. In the present study Birth weight of the newborn children was less than 1.5kg in 14.28% of the hypothyroid pregnant women and 06.3% of the normal pregnant women, 1.5 -2kg in 07.2% of the hypothyroid pregnant women and 02.08% of the normal pregnant women, 02 – 2.5 kg in 14.3% of the hypothyroid pregnant women and 12.5% in the normal pregnant women, 2.5 – 3 kg in 54.7% of the hypothyroid pregnant women and 70.8% of the normal pregnant women and >3.5kg in 09.5% of the hypothyroid pregnant women and 08.3% of the normal pregnant women (Table 4). In a study by Mahadik, K., Choudhary, P. & Roy *et al* [29] NICU admission in thyroid dysfunction was reported in 42.1%, which is similar to the rates observed in this study where in 23.8% of the newborns of pregnant women with hypothyroidism and 20.8% of the normal pregnant women had NICU admissions for the newborns. The difference between the two groups was found to be statistically not significant. (p value >0.05), (Table 7). In the present study in 50% newborns of pregnant women with hypothyroidism with the raised Anti TPO levels had NICU admissions, 62.5% of the newborns were born out of LSCS and 30% had low birth weights less than 1.5Kgs (Table 7). In the present study the APGAR score at 05 minutes was less than 8/10 in 7.1% of the pregnant women with thyroid deficiency and 02.1% of the normal pregnant women. This was found to be not significant statistically (p at more than 0.05) controls the difference was found to be statistically not significant (Table 6). In a study by Mahadik, K., Choudhary, P. & Roy *et al* the Low Apgar scores were reported in 21.1% of babies born to women with hypothyroidism. IN a similar study the APGAR scores were low in 20% of the delivered newborns born to hypothyroid mothers [14]. In view of the results observed in this study the authors felt that estimation and diagnosis of thyroid hormones in the first trimester itself gave a very high clinical relevance in diagnosing hypothyroid state and treating accordingly.

Conclusions

It is mandatory to estimate the targeted TSH screening for pregnant women especially those at high risk for thyroid deficiency before or during early pregnancy. It was necessary to estimate TPO antibodies in all the pregnant women who have higher levels of TSH values. The risk of pregnancy loss to mothers and preventing low birth weights in the newborns could be avoided effectively. The risk of pregnancy was more in patients with positive TPO antibodies.

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