Original Article

Association of Neonatal Outcome with Maternal Thyroid Dysfunction

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Abstract

Objective: To explore the association of neonatal and maternal outcome with maternal thyroid dysfunction during pregnancy.
Methodology: This case control study was conducted in the department of Obstetrics & Gynecology CMH Kharian Medical College and Dr. Jawairiah Gynae care and IVF center, from February 2022 to December 2023. The study sample consisted of all pregnant women between the ages of 18 and 40, regardless of gestational age, who were carrying singletons. A detailed history was taken, and then an obstetric and general physical examination were conducted. 5–10 ml of the venous blood were first drawn while fasting and their TSH levels were measured for the biochemical parameters. Their free T3 and T4 levels were examined if their serum TSH levels were elevated. Following diagnosis, the patient received appropriate thyroxine treatment for hypothyroidism. Every patient in the research sample had their labour induced at 37 weeks or later. The outcomes for mothers and fetuses were also mentioned.
Results: The mean age of females was noted 26.45 ± 4.62 years in cases group and 27.81 ± 4.93 years in control group. The rate of caesarean section deliveries (66.22% vs 37.85%) was significantly (P-value < 0.05) higher among females having thyroid dysfunction. Overall maternal complications had significant (P-value < 0.05) relationship with thyroid dysfunction status. The rate of low birth weight (51.35% vs. 32.43%) was significantly higher among neonates of women having thyroid dysfunction. The overall neonatal complications rate was also observed to be significantly (P-value < 0.05) higher among neonates belonged to females having thyroid dysfunction (41.89% vs. 20.27%) as compared to females without thyroid dysfunction.
Conclusions: The increased incidence of caesarean sections, preeclampsia, anaemia, low birth weight, low APGAR score, respiratory distress, neonatal jaundice, and sepsis were found to be significantly correlated with maternal thyroid disorders.
Key words: Neonatal Outcome, Thyroid Disorder, Pregnancy

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Introduction

Thyroid dysfunction is the second most common endocrinological condition during pregnancy, after diabetes. Thyroid function evaluation is important during pregnancy due to its established impact on the outcomes for the foetus and the mother. Thyroid physiology begins to change as soon as pregnancy is confirmed and continues to do so during the gestation, however it is reversible after delivery.[1] The causes include elevated levels of thyroxine-binding globulin (TBG), elevated renal iodine loss, modified peripheral thyroid hormone metabolism, and altered placental iodine transfer. These modifications aid in preparing the thyroid gland of the mother to lessen the elevated physiological demands.[2]

Pregnant women's immune systems alter and they release large amounts of hormones, that alter the thyroid glands synthesis and metabolism and ultimately result in thyroid dysfunction, which is harmful to the health of both the mother and the unborn child. In human growth, differentiation, development, and maintenance of metabolic equilibrium, thyroid hormone is crucial.[3]

In addition to having an impact on the foetal venous system's growth and maturation, thyroid hormones are

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primarily responsible for the occurrence, proliferation, and migration of neural tissues. Thyroid hormone abnormalities resulting from either excessive or insufficient secretion can impact gonadal and sex hormone functions as well as cause disruptions in the human endocrine system. A thyroid hormone deficit causes neuronal tissue to immature, which has a major impact on brain function.[4,5]

Due to the vague symptoms and hypermetabolic state that characterise a typical pregnancy, thyroid dysfunction (TD) in pregnancy may go undiagnosed. The effects of thyroid malfunction on the outcome of pregnancy vary. Thyroid autoimmune illness raises the risk of miscarriage. A severe hypothyroidism in the mother can leave her offspring with an irreparable neurological impairment. Foetal thyroid dysfunction and pregnancy loss are two outcomes of Graves' disease (GD).[6] Experimental results as well as historical accounts of cretinism in offspring of mothers with severe hypothyroidism due to iodine deprivation[7] demonstrate the importance of maternal thyroid hormones and the detrimental effects of hypothyroidism when left untreated. Additionally, the seminal study by Haddow et al. established a risk of unfavourable child outcomes linked to untreated hypothyroidism in mothers, a finding that has been supported by several publications.[8,9]

The scientific community now focuses on isolated variations in free thyroxine (fT4), thyroid autoimmunity in general, and subclinical maternal thyroid function disorders, even if further investigation is required for universal screening for overt hypothyroidism in pregnant women. Large-scale randomised controlled trials (RCTs) haven't, however, revealed any therapy impact.[10]

A substantial risk of unfavourable maternal and foetal outcomes has been linked to hyperthyroidism, according to previous study findings on based on populations and case-control studies. Studies have shown that groups with untreated hyperthyroidism had a greater incidence of unfavourable pregnancy problems than groups with treatment. In our nation, there is a dearth of research on the effects of hyper- or hypothyroidism on pregnancy outcomes. The goal of the current study was to look at the outcomes for mothers and foetuses in our study population who had thyroid illness.

Methodology

This case control study was carried in the department of Obstetrics & Gynaecology CMH Kharian Medical College and Dr. Jawairiah Gynae Care and IVF centre, from February 2022 to December 2023.

The WHO sample size calculator was used to determine the sample size, with a significance level of 5% and an 80% test power. Proportion of neonates without complications among mothers with thyroid dysfunction 35.8% and in controls 52%,[1]. The sample size turned out to be 148 in total consisting of 74 cases of hypothyroidism and 74 controls. From every patient, informed consent was obtained. Patients' privacy and confidentiality were preserved by withholding their identities on study-related proformas.

The study sample consisted of all pregnant women between the ages of 18 and 40, regardless of gestational age, who were carrying singletons. Exclusions from the study included women who had undergone multiple caesarean sections in the past, had multiple pregnancies, had pre-existing medical conditions or disorders induced by pregnancy, such as hypertensive disorders in pregnancy, chronic hypertension, established diabetes, gestational diabetes, anaemia with haemoglobin <10g/dl, or chronic renal disease.

A detailed history was taken, and then an obstetric and general physical examination were conducted. 5–10 ml of the venous blood were first drawn while fasting and their TSH levels were measured for the biochemical parameters. Their free T3 and T4 levels were examined if their serum TSH levels were elevated. The 2011 American Thyroid Association Guidelines were followed in evaluating the reference ranges of the test results, including a

- First trimester reference range of TSH (0.1–2.5 mIU/L)
- In the second trimester (0.2–3.0 m IU/L), and
- In the third trimester (0.3–3.0 m IU/L)

Following diagnosis, the patient received appropriate thyroxine treatment for hypothyroidism. Every patient in the study sample had their labour induced at 37 weeks or later, and either had a successful vaginal delivery or had a caesarean section. Similar to this, foetal outcome was identified based on the presence of meconium-stained liquid during active labour or non-reactive traces of CTG in patients undergoing labour induction. Low birth weight and a poor APGAR score of less than seven at five minutes are indicators that the newborn has to be admitted to neonatal intensive care due to foetal distress. All of this data was entered onto a proforma that was created especially for that purpose.

The statistical package for social sciences (SPSS v 25) was used to enter and analyse the data. Regarding quantitative data, the mean and standard deviation were calculated. For the qualitative variables, percentages and frequencies were reported. For the quantitative data, the independent sample t-test was employed, and for the qualitative data, the Chi-square test. A P-value of less than 0.05 was considered significant.

Results

In this study a total of 148 females were enrolled comprising of 74 cases of hypothyroidism during pregnancy and 74 controls without having hypothyroidism. The mean age of females in cases group was 26.45 ± 4.62 years and 27.81 ± 4.93 years of females in control group. Most (36.49%) of the females in cases group had education level of intermediate followed by (25.68%) females who were graduate. In controls group majority (32.43%) females had education of intermediate followed by (22.97%) females having education level of matric. The study sample did not have any significant difference on the basis of parity and time to include in the study as elaborated in details in table I.

Table I: Distribution of demographic Characteristics of the cases and controls.

Characteristics	Hypothyroid Cases		Controls		P-value
	N	%	N	%	
Age of participants					
Mean ± SD	26.45 ± 4.62		27.81 ± 4.93		0.085
Education of the participants					
Illiterate	6	8.11%	5	6.76%	0.829
Matric	13	17.57%	17	22.97%	
Intermediate	27	36.49%	24	32.43%	
Graduate	19	25.68%	16	21.62%	
Postgraduate	9	12.16%	12	16.22%	
Parity					
Primigravida	31	41.89%	28	37.84%	0.614
Multigravida	43	58.11%	46	62.16%	
Time to include in the study					
1st Trimester	16	21.62%	21	28.38%	0.314
2nd Trimester	9	12.16%	13	17.57%	
3rd Trimester	49	66.22%	40	54.05%	
Total	**74**	**100.00**	**74**	**100.00**	

The comparison of maternal outcome showed that there was no significant (P-value > 0.05) difference between cases and controls on the basis of mean gestational age (34.71 ± 2.34 vs 35.21 ± 2.84 weeks) and incidence of preterm delivery (29.73% vs. 41.89%). Mode of delivery showed a significant (P-value < 0.05) association with thyroid dysfunction and it was observed that the rate of caesarean section deliveries (66.22% vs 37.85%) was significantly (P-value < 0.05) higher among females having thyroid dysfunction as compared to normal controls. From the results it was also noted that the maternal complications also have significant (P-value < 0.05) relationship with thyroid dysfunction status of the females during pregnancy. It was observed that overall complications rate (63.51%) among females having thyroid dysfunction was significantly higher as compared to (39.19%) females without thyroid dysfunction. The most common complications among case were preeclampsia (17.57% vs. 8.11%), anemia (12.16% vs. 5.41%) and IUGR (10.81% vs. 6.76%) as compared to female without thyroid dysfunction as elaborated in table II.

Table II: Comparison of Maternal pregnancy outcome between females with and without thyroid dysfunction.

Characteristics	Hypothyroid Cases		Controls		P-value
	N	%	N	%	
Gestational age					
Mean ± SD	34.71 ± 2.34		35.21 ± 2.84		0.244
Preterm delivery status					
Preterm	22	29.73%	31	41.89%	0.123
Term	52	70.27%	43	58.11%	
Mode of delivery					
Elective LSCS	13	17.57%	7	9.46%	0.005
Emergency LSCS	36	48.65%	21	28.38%	
Vaginal Delivery	23	31.08%	39	52.70%	
Instrumental delivery	2	2.70%	7	9.46%	
Maternal Complications					
No complication	27	36.49%	45	60.81%	0.000
Preeclampsia	13	17.57%	6	8.11%	
Anemia	9	12.16%	4	5.41%	
IUGR	8	10.81%	5	6.76%	
Abortion	5	6.76%	2	2.70%	
Meconium stained liquor	4	5.41%	2	2.70%	
Other	8	10.81%	10	13.51%	
Total	**74**	**100.00%**	**74**	**100.00%**	

The comparison of fetal outcome showed that there was no significant (P-value > 0.05) relationship of fetal live and still birth between cases and controls. Birth weight of the neonates showed a significant (P-value < 0.05) association with hypothyroid dysfunction status of the mothers during pregnancy and it was observed that the rate of low birth weight (51.35% vs. 32.43%) was significantly higher among neonates of women having thyroid dysfunction. The rate of good APGAR score (≥ 7) was also significantly (P-value < 0.05) higher among (90.54%) neonates of the females in normal control group as compared to (78.38%) neonates of mothers having thyroid dysfunction. The overall neonatal complications rate was also observed to be significantly

(P-value < 0.05) higher among neonates belonged to females having thyroid dysfunction (41.89% vs. 20.27%) as compared to females without thyroid dysfunction. The most common neonatal complications in cases vs. control groups were respiratory distress (14.86% vs. 8.11%), neonatal jaundice (13.561% vs. 6.76%) and Sepsis (10.81% vs. 1.35%) as elaborated in detail in table III.

Table III: Comparison of fetal outcome of females with and without thyroid dysfunction.

Characteristics	Hypothyroid Cases		Controls		P-value
	N	%	N	%	
Fetal birth					
Live	67	90.54%	72	97.30%	0.085
Still birth	7	9.46%	2	2.70%	
Birth Weight					
Low birth weight	38	51.35%	24	32.43%	0.014
Normal	32	43.24%	49	66.22%	
Macrosomia	4	5.41%	1	1.35%	
APGAR Score at 5 minutes					
< 7	16	21.62%	7	9.46%	0.041
≥ 7	58	78.38%	67	90.54%	
Neonatal complications					
Nil	43	58.11%	59	79.73%	0.023
Respiratory distress	11	14.86%	6	8.11%	
Neonatal jaundice	10	13.51%	5	6.76%	
Sepsis	8	10.81%	1	1.35%	
Meconium aspiration	2	2.70%	3	4.05%	
Total	**74**	**100.00%**	**74**	**100.00%**	

Discussion

Maintaining appropriate thyroid functioning and managing the higher physiological demands of pregnancy depend heavily on a healthy thyroid gland. Changes in the levels of thyroid hormone in the mother subsequently impact the feto-maternal outcomes. The development of the foetal brain depends on thyroid hormones, and thyroid disorders have a negative impact on the cognitive development of the offspring.[11, 12] Premature birth, gestational hypertension, foetal death, and other grave consequences are caused by thyroid problems. Thyroid function screening is therefore required in the early stages of pregnancy. There is evidence linking thyroid disorders to higher chances of problems for both mothers and foetuses.[13]

The research has demonstrated that thyroid dysfunction patients' ability to conceive was impacted. Presumptive patients had higher rates of preterm labour, preeclampsia, premature rupture of membranes, abruptio, missed abortion, IUGR IUD, perinatal morbidity, and mortality than did those with normal thyroid function. The worst pregnancy outcomes were experienced by patients with thyroid insufficiency who did not get treatment.[14]

The results of this present study revealed that mode of delivery had a significant association with thyroid dysfunction and the rate of normal vaginal deliveries decreased significantly among females having thyroid dysfunction as compared to normal controls. It was observed that overall complications rate (63.51%) among females having thyroid dysfunction was significantly higher as compared to (39.19%) females without thyroid dysfunction. The most common complications among case were preeclampsia (17.57% vs. 8.11%), anemia (12.16% vs. 5.41%) and IUGR (10.81% vs. 6.76%) as compared to female without thyroid dysfunction.

The literature confirms all of these findings. For example, a large-scale study found a link between hypothyroidism and a higher risk of pregnancy problems such as preeclampsia, gestational diabetes, preterm birth, induction of labor, and caesarean section.[15] Preterm birth rates were shown to be higher in cases of both overt hypothyroidism and hyperthyroidism, according to a meta-analysis.[16]

The results of this present study showed that there was no significant relationship of preterm delivery with thyroid dysfunction status of the females. Preterm birth is both a negative result and an independent risk factor for neonatal outcomes, according to a study by Kankanamalage MO, despite the fact that several studies have established a high correlation between these two parameters. Recent decades have yielded persuasive data suggesting a significant link between preterm birth and hypothyroidism during pregnancy.[17]

The comparison of fetal outcome in this present study showed that birth weight of the neonates had a significant (P-value < 0.05) association with hypothyroid dysfunction status of the mothers and it was observed that the rate of low birth weight (51.35% vs. 32.43%) was significantly higher among neonates of women having thyroid dysfunction. The rate of good APGAR score (≥ 7) was also significantly (P-value < 0.05) higher among (90.54%) neonates of the females in normal control group as compared to (78.38%) neonates of mothers having thyroid dysfunction. The overall neonatal complications rate was also observed to be significantly (P-value < 0.05) higher among neonates belonged to females having thyroid dysfunction (41.89% vs. 20.27%)

as compared to females without thyroid dysfunction. All of these results are consistent with other research, such as a study by Mahadik K et al.[18] that found that LBW was more prevalent among hypothyroid women (31.6%). Because LBW is linked to preeclampsia, it is related with hypothyroidism. Decreased foetal thyroxine can interfere with foetal pituitary growth hormone secretion, vascular maturation and responsiveness, foetal thyroid axis development, and foetal cardiovascular homeostasis. These are the reasons why children born to mothers whose hypothyroidism is not properly managed have lower birth weights. Neonates born to mothers with thyroid abnormalities also had increased rates of other problems such as birth asphyxia, meconium aspiration syndrome, jaundice, preterm birth, and respiratory distress syndrome.[19, 20] The results presented are consistent with the findings of the current study.

All females who are pregnant should get routine TSH testing. Thyroxine medication and early screening are recommended since thyroid dysfunction has a negative impact on both maternal and foetal outcomes. It has been discovered that unbooked patients experience complications at a higher rate than booked individuals. Early thyroid function testing in the first trimester can allow for earlier therapy and possibly even prevent difficulties for both the mother and the foetus. The best course of action may involve prenatal counselling and thyroid function testing. [21]

Conclusion

The findings demonstrated a significant association between the high rate of caesarean sections, anaemia, preeclampsia, low birth weight, low APGAR score, respiratory distress, neonatal jaundice, sepsis and maternal thyroid disorders. Maternal thyroid problems greatly impact the results for both the mother and the foetus. To diagnose and treat thyroid diseases early on, routine examinations should include serum TSH testing. This will assist in lowering the morbidity and mortality rates among mothers and newborns. To prevent obstetric difficulties, women with thyroid abnormalities should be constantly monitored during their pregnancies. Additionally, their newborn children should be closely monitored for thyroid dysfunction in the early postnatal months.

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