ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 17, Issue 2, 2024

Online - 2455-3891
Print - 0974-2441

Research Article

EVALUATION OF ADVERSE EFFECTS OF HYPOTHYROIDISM DURING ANTENATAL PERIOD WITH MATERNAL AND FETAL OUTCOMES IN SUBJECTS WITH SUBCLINICAL AND OVERT HYPOTHYROIDISM

DALJEET KAUR, BEANT SINGH, PARNEET KAUR, SHELLY KHILLAN*

Department of Obstetrics and Gynaecology, Government Medical College and Rajindra Hospital, Patiala, Punjab, India.
***Corresponding author: Shelly Khillan; E-mail: rosetaylorindia@gmail.com**

Received: 19 November 2023, Revised and Accepted: 15 January 2024

ABSTRACT

Objectives: Maternal thyroid hormone excess or deficiency can influence the outcome of the mother and fetus at all stages of pregnancy as well as interfere with ovulation and infertility. In females who suffer from thyroid diseases before pregnancy or during pregnancy, these hormonal changes are magnified leading to adverse maternal and fetal outcomes. This study is done to evaluate the adverse effects of hypothyroidism during the antenatal period, maternal and fetal outcomes in patients with subclinical and overt hypothyroidism (OH).

Methods: The present prospective case–control study was conducted in the Department of Obstetrics and Gynaecology, Government Medical College and Rajindra Hospital Patiala, Punjab, from August 2018 to July 2019. The study was conducted among 150 antenatal patients, who had singleton pregnancy irrespective of age and parity. A complete thyroid profile was done to segregate them into euthyroid, subclinical hypothyroidism, and OH. Patients were divided into two groups, In group I, there were 75 antenatal patients who were euthyroid, and in group II, there were 75 antenatal patients with subclinical or OH diagnosed in pregnancy or already on treatment. The adverse maternal and fetal complications were noted in two groups. Data were compared using t-test for parametric data and Chi-square test for non-parametric data. Data presented as mean and standard deviation with $p \leq 0.05$ was considered statistically significant.

Results: In the current study, 4 (5.33%) patients in group II, 0 patient in group I had abortions giving p=0.011. 7 (9.3%) patients of group II, 0 patient in group I had intra uterine death giving a p=0.001. In group I, 1 (1.33%) patient, 8 (10.6%) patients in group II developed pregnancy-induced hypertension giving p=0.025. In group I, 6 (8%) patients, 25 (33.3%) in group II had preterm delivery giving p=0.018. In group I, 7 (9.33%) patients underwent induction of labor, and in group II, 19 (25.3%) patients were induced giving p=0.009. In group I, 2 (2.67%) patients, 10 (13.3%) patients in group II had undergone C-section giving p=0.006. In group I, 2 (2.67%) patients had fetal growth restriction babies as compared to 10 (13.3%) in group II giving p=0.006. In group I, 1 (1.33%) baby had an APGAR score <9 at 5 min and 15 (20%) in group II patients giving p=0.001. Neonatal intensive care unit admissions were 7 (9.33%) in group I as compared to 19 (25.33%) in group II giving p=0.018.

Conclusion: In the present study, it was observed that the prevalence of thyroid disorder in pregnant women is considerably high with subclinical hypothyroidism being most common followed by OH. A simple screening test of thyroid profile, if used to timely diagnose hypothyroidism a large number of maternal and fetal complications can be prevented.

Keywords: Fetal complications, Maternal complications, Maternal hypothyroidism, Thyroid hormones.

 DOI: http://dx.doi.org/10.22159/ajpcr.2024v17i2.48651. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Thyroid hormones are the two hormones secreted by the thyroid gland and are primarily responsible for the regulation of metabolism. They are tyrosine-based hormone triiodothyronine (T3) and thyroxine (T4) and are partially composed of iodine. T4 is converted to the active T3 (3–4 times more potent than T4) within cells by deiodinases (5'-iodinase) [1]. Three glycoprotein thyroid stimulators have been identified in the placenta, namely human chorionic gonadotropin (HCG), human chorionic thyrotropin (HCT), and human molar thyrotropin. HCT is present from early pregnancy but unlike HCG its concentration rises progressively throughout pregnancy. Maternal HCG shares structural similarity with thyroid-stimulating hormone (TSH) which directly stimulates the production of T3, T4 while decreasing TSH levels during the first trimester [2]. As HCG is thyrotrophic its high levels, especially in 1st trimester result in low TSH values and thus cutoffs become less. In women with low thyroid reserves, the stress of pregnancy manifests as overt disease. In an iodide-sufficient area, thyroid adaptations are well tolerated, as stored inner thyroid iodide is adequate; however, in iodide-deficient areas, these physiological adaptations lead to significant changes in pregnancy [3].

Pregnancy is an important life event in females that has a significant but reversible effect on the thyroid gland and its function. To meet the maternal and fetal needs during pregnancy, the thyroid gland has to increase thyroid hormone production by 40–100%. To accommodate this, the gland undergoes moderate glandular hyperplasia and increased vascularity causing increase in mean volume from 12 mL in first trimester to up to 15 mL at the time of delivery [4]. Maternal thyroid hormone excess or deficiency can influence the outcome of the mother and fetus at all stages of pregnancy as well as interfere with ovulation and infertility. In females who suffer from thyroid diseases before pregnancy, these hormonal changes are magnified leading to adverse maternal and fetal outcomes [5]. Pregnancy can mask some signs of hypothyroidism such as fatigue, anxiety, constipation, and weight gain making the clinical diagnosis difficult. A careful clinical history may identify the patients at increased risk. If any of the risk factors are present in history further workup should be done. Untreated hypothyroidism in pregnancy is associated with adverse maternal and fetal effects. Maternal hypothyroidism leads to abortions, fetal growth restriction (FGR), intrauterine fetal demise intrauterine death (IUD), low birth weight babies [6]. This study is thus planned to evaluate the adverse effects of hypothyroidism during the antenatal period and

Table 1: Thyroid levels in two groups

Variable with reference value	Group 1 Mean±SD		Group 2 Mean±SD	
T3 (ng/mL) (0.75–2.77)	2.42±0.46		1.02±0.57	
T4 (nmol/L) (100–250)	166±10.03		91.58±5.77	
TSH (mIu/L) (0.2–3)	2.30±0.46		8.39±0.82	
Type of hypothyroidism	**Group 1**		**Group 2**	
	Number of subjects	**%age**	**Number of subjects**	**%age**
Subclinical hypothyroidism	-	-	62	82.67
Overt hypothyroidism	-	-	13	17.33
Total			75	100

study maternal and fetal outcomes in subjects with subclinical and overt hypothyroidism (OH).

METHODS

The present prospective case–control study was conducted in the Department of Obstetrics and Gynaecology at Government Medical College and Rajindra Hospital, Patiala, from August 2018 to July 2019. The ethical committee approval was obtained from the Ethical Committee of Government Medical College and Rajindra Hospital, Patiala (No. Tgr. 9 (310) 2022/11065).

Inclusion criteria

A total of 150 antenatal patients with single-ton pregnancy irrespective of age and parity were included in the study.

Exclusion criteria

The patients with chronic hypertension, diabetes mellitus, multiple pregnancies, gestational trophoblastic diseases, and patients not willing to participate in the study were excluded from the study.

After selection 150 antenatal patients were enrolled for this study. When enrolled patients were divided into two groups:

- Group I: **(**75 patients) Euthyroid antenatal patients
- Group II: (75 patients) Overt or subclinical hypothyroid antenatal patients (diagnosed with hypothyroidism in pregnancy or were already on treatment).

Study procedure

A complete thyroid profile was done to segregate them into euthyroid, sub-clinical hypothyroidism, and OH. Hypothyroidism was categorized as OH when TSH levels were elevated and total T_4 was low. TSH ≥10 mIU/L was taken as OH irrespective of T_4 levels [7]. Subclinical hypothyroidism (SCH) was defined as elevated TSH levels ≤10 mIU/L but with normal total T_3 and T_4 levels [8]. The normal reference value for T_3 was 0.75–2.77 ng/mL, T_4 was 100–250 nmol/L and TSH was 0.2–3 mIU/L [9]. Subjects were followed till delivery with monitoring of TSH levels every 4th week. Titration of levothyroxine dose was done as required. All the patients were observed for the development of any maternal complications during the antenatal period. They were followed till delivery for maternal and fetal outcome. The adverse maternal complications in the form of abortions, pregnancy-induced hypertension (PIH), preterm premature rupture of membrane (PPROM), FGR, IUD, rate of induction of labor and incidence of C-section were studied in two groups. In fetal complication mean birth weight of babies, congenital abnormalities, neonatal intensive care unit (NICU) admissions and Appearance, Pulse, Grimace, Activity and Respiration (APGAR) scoring at 5 min were noted in two groups.

Statistical analysis

Data were compared using *t*-test for parametric data and Chi-square test for non-parametric data. Data presented as mean and standard deviation with $p<0.05$ was considered statistically significant.

Table 2: Demographic profile of patients

Parameters	Group 1	Group 2	p-value
Mean age (in years)	23.86±2.79	22.32±2.62	0.1
Parity			
Primi	45 (60)	51 (68)	0.658
Second	17 (22.7)	14 (18.7)	0.538
Multi	13 (17.3)	10 (13.3)	0.626
Total	75	75	

RESULTS

In the current study, mean T_3 levels in group I was 2.42±0.46 ng/mL and 1.02±0.57 ng/mL in group II. Mean T_4 levels in group I was 166±10.03 nmol/L and in group II it was 91.58±5.77 nmol/L. Mean TSH levels in group I were 2.30±0.46 mIU/L and 8.39±0.82 mIU/L in group II. 62 (82.67%) patients had SCH and 13 (17.33%) patients had OH (Table 1).

The mean age of patients in Group I was 23.86±2.79 years, and in group II was 22.32±2.62 years. The groups were comparable in terms of mean age. In group I 45 (60%) patients were primigravida, 17 (22.7%) were second gravida and 13 (17.3%) were multigravida. In group II, 51 (68%) were primigravida, 14 (18.7%) were second gravida, and 10 (13.3%) were multigravida (Table 2).

In group II, 4 (5.33%) patients had abortions as compared to 0 patients in group I giving p=0.011. Gestational diabetes mellitus (GDM) was found in 1 (1.33%) patient in group I as compared to 2 (2.6%) in group II giving p=0.151 which was not significant. 7 (9.3%) patients of group II had IUD as compared to none in group I giving a p=0.001. In group I, 1 (1.33%) patient developed PIH as compared to 8 (10.6%) patients in group II giving p=0.025. In group I, 6 (8%) patients had preterm delivery as compared to 25 (33.3%) in group II giving p=0.018. In group I, 1 (1.33%) patient had PPROM as compared to 5 (6.6%) in group II giving p=0.01. In group I, 2 (2.67%) patients had FGR babies as compared to 10 (13.3%) in group II giving p=0.006. In group I, 7 (9.33%) patients underwent induction of labor, in group II, 19 (25.3%) patients were induced giving p=0.009. In group I, 2 (2.67%) patients had undergone C-section as compared to 10 (13.3%) patients in group II giving p=0.006 (Table 3).

The mean birth weight in group I was 2464.81±478.19 g as compared to 2162.71±733.5 g in group II giving p=0.003. In group I 1 (1.33%) baby had APGAR score <9 at 5 min and 15 (20%) in group II patients giving p=0.001. In group I no patients had congenital abnormalities in fetus as compared to 2 (2.67%) patients in group II giving p=0.868 which was non-significant. NICU admissions were 7 (9.33%) in group I as compared to 19 (25.33%) in group II giving p=0.018 (Table 4).

DISCUSSION

In the present study, the prevalence of SCH was 82.67% and OH was 17.33% which was in accordance with the study done by Ajmani

Table 3: Maternal complications (75 patients in each group)

Maternal complications	Group I (No. of subjects) n=75	(%age)	Group II (No. of subjects) n=75	(%age)	p-value	Significance
Abortions	0	0	4	5.33	0.011	Significant
GDM	1	1.33	2	2.6	0.151	Non-significant
IUD	0	0	7	9.3	0.001	Significant
PIH	1	1.33	8	10.6	0.025	Significant
Preterm	6	8	25	33.3	0.018	Significant
PPROM	1	1.33	5	6.6	0.01	Significant
FGR	2	2.6	10	13.3	0.006	Significant
Induced Labor	7	9.33	19	25.3	0.009	Significant
C-section	2	2.67	10	13.3	0.006	Significant

GDM: Gestational diabetes mellitus, IUD: Intrauterine death, PIH: Pregnancy-induced hypertension, PPROM: Preterm premature rupture of membranes, FGR: Fetal growth restriction

Table 4: Perinatal complications (75 patients in each group)

Fetal complications	Group I (No. of subjects) n=75	(%age)	Group II (No. of subjects) n=75	(%age)	p-value	Significance
Birth weight (Mean±SD) in grams	2464.81±478.19		2162.7±733.5		0.003	Significant
APGAR score<9 at 5 minutes	1	1.33	15	20	0.001	Significant
Congenital Abnormalities	0	0	2	2.67	0.868	Non-significant
NICU Admission	7	9.33	19	25.33	0.018	Significant

NICU: Neonatal intensive care unit, APGAR: Appearance, Pulse, Grimace, Activity and Respiration

et al. [3] which also showed prevalence of SCH is more than OH. In Group II 5.33% of patients underwent abortions as compared to none in Group I. This was in accordance to study done by Pokhanna *et al*. [10] which showed that there was increased incidence of abortions in hypothyroid patients. In the current study, there was not much difference in terms of the incidence of GDM in Group I and Group II patients. This was comparable to study done by Abiramavalli and Vanitha [4] which also showed that there is no association of hypothyroidism with GDM. In the present study, the incidence of IUD was 9.3% in Group II patients as compared to 0% in Group I patients. It was Comparable to a study done by Patel *et al*. [5] which stated that IUD are more common in hypothyroid patients. In the current study, the incidence of PIH was 10.6% in Group II as compared to 1.33% in Group I, it was in accordance with a study done by Sreelatha *et al*. [11] which showed that there is an increased incidence of PIH in hypothyroid patients. In Group I, 8% of patients underwent preterm delivery as compared to 33.3% in Group II which was in accordance to work done by Bajaj *et al*. [12]. In the present study, the incidence of PPROM was 6.6% in Group II as compared to 1.33% in Group I, this was in accordance with a study done by Mahadik *et al*. [9] which also showed PPROM was more common in patients with hypothyroidism. Incidence of FGR was 13.3% in Group II and 2.67% in Group I which was comparable to study done by Sibia *et al*. [13] which also showed FGR babies are more common in patients of hypothyroidism. In Group I, 9.33% of patients underwent inductions of labor as compared to 25.33% of patients in Group II. It was in accordance to study done by Singh *et al*. [14] which showed the incidence of induction of labor is more common in hypothyroid patients. Incidence of C-section was 13.3% in Group II and 2.67% in Group I which was in accordance with study done by Alexander *et al*. [2] which showed hypothyroid patients needed C-sections more commonly. In the present study, the mean birth weight in group II was 2162±733.5 g and in Group I 2464.81±478.19 g which was comparable to study done by Tingi *et al*. [1], which showed mean birth weight is less in the hypothyroid patients. In the current study, the incidence of APGAR Score <9 at 5 min was 1.33% in Group I and 20% in Group II, it was comparable with study done by Ramachandran *et al*. [15] which showed that neonates of hypothyroid patients had lower APGAR score at 5 min more commonly. In the present study, in Group I, 9.33% of babies were admitted to NICU as compared to 25.33% in Group II which was in accordance to study done by Praveena *et al*. [16] which showed an increased incidence of admissions to NICU of neonate of hypothyroid patients. The incidence of congenital abnormalities in two Groups was statistically non-significant in this study which was in accordance to study done by Pokhanna *et al*. [10] which also showed no relation of congenital malformations of fetus with hypothyroidism.

Limitation(s)

Due to the small sample size, the results could not be generalized.

CONCLUSION

In the present study, it was observed that the prevalence of thyroid disorder in pregnant women is considerably high with subclinical hypothyroidism being most common followed by OH. Pregnancy with hypothyroidism is significantly associated with maternal and fetal complications. A simple screening test of thyroid profile, if used to timely diagnose hypothyroidism a large number of maternal and fetal complications can be prevented.

ETHICAL COMMITTEE APPROVAL TAKEN

Yes.

CONFLICTS OF INTERESTS

None.

FINANCIAL INTEREST

None.

REFERENCES

1. Tingi E, Syed A, Kyriacou A, Mastorakos G, Kyriacou A. Benign thyroid disease in pregnancy: A state of the art review. J Clin Transl Endocrinol 2016;6:37-49.
2. Alexander EK, Pearce EN, Brent GA, Brown RS, Chen H, Dosiou C. 2017 Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum. Thyroid 2017;27:315-89.
3. Ajmani SN, Aggarwal D, Bhatia P, Sharma M, Sarabhai V, Paul M. Prevalence of overt and subclinical thyroid dysfunction among pregnant women and its effect on maternal and fetal outcome. J Obstet Gynaecol India 2014;64:105-10. doi: 10.1007/s13224-013-0487-y, PMID 24757337
4. Abiramavalli K, Vanitha D. Foeto maternal outcomes of hypothyroidism in pregnancy: A prospective study. IntJ Clin Obstet Gynaecol 2019;3:205-8.

5. Patel RD, Deliwala KJ, Shah PT, Singh RK. Fetomaternal outcome of thyroid disorder in pregnancy. Int J Reproduct Contracept Obstetr Gynecol 2016;5:4466-69.
6. Kalra B, Choudhary M, Thakral M, Kalra S. Prevalence of hypothyroidism in term pregnancies in North India. Indian J Endocrinol Metab 2018;22:13-5. doi: 10.4103/ijem.IJEM_189_17, PMID 29535930
7. Nazarpour S, Ramezani Tehrani F, Simbar M, Azizi F. Thyroid dysfunction and pregnancy outcomes. Iran J Reprod Med. 2015;13:387-96. PMID 26494985
8. Jefferys A, Vanderpump M, Yasmin E. Thyroid dysfunction and reproductive health. Obstetr Gynaecologis 2015;17:39-45. doi: 10.1111/tog.12161
9. Mahadik K, Choudhary P, Roy PK. Study of thyroid function in pregnancy, its feto-maternal outcome; a prospective observational study. BMC Pregnancy Childbirth 2020;20:769. doi: 10.1186/s12884-020-03448-z, PMID 33302910
10. Pokhanna J, Gupta U, Alwani M, Tiwari SP. Prevalence of thyroid dysfunction and impact on maternal and fetal outcome in Central Indian pregnant women. Int J Reprod Contracept Obstet Gynecol 2017;6:4666-70. doi: 10.18203/2320-1770.ijrcog20174461
11. Sreelatha S, Nadagoudar S, Asha D. The study of maternal and fetal outcome in pregnant women with thyroid disorders. Int J Reprod Contracept Obstet Gynecol 2017;6:3507-14. doi: 10.18203/2320-1770.ijrcog20173473
12. Bajaj S, Chawla T, Gupta P, Chaurasia A, Mehrotra R. Thyroid dysfunction in pregnancy-a tertiary care centre experience. Sri Lanka J Diabetes Endocrinol Metab 2018;6:7297.
13. Sibia P, Chaudhary A, Sibia R, Singh I, Jain M. Study of thyroid disorders in pregnancy. IOSR J Dent Med Sci 2019;18:39-48.
14. Singh G, Kaul I, Singh A, Meinia K. Maternal and fetal outcome in subclinical hypothyroidism in Jammu region, North India. Int J Reprod Contracept Obstetr Gynecol 2017;5:2362-66.
15. Ramachandran R, Mohan L, Jose S. Prevalence of thyroid disorders in antenatal women and its impact on maternal and foetal outcome. Indian J Forensic Community Med 2020;7:29-32.
16. Praveena R, Pramod R, Prasuna K, Krishna V. Prevalence of thyroid disorder in pregnancy and pregnancy outcome. Int Arch Integr Med 2018;5:113-8.