



## Hypothyroidism Among Diabetic Pregnancy and its Effect on Maternal and Fetal Outcome

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### Abstract

**Background:** Diabetic Pregnant women with hypothyroidism are associated with adverse obstetric outcome with various maternal and fetal complications. The aim of this study was to evaluate hypothyroidism in diabetic pregnancy and its effect on maternal and fetal outcome. **Material & Methods:** This cross-sectional study was conducted in department of Obstetrics and Gynaecology, Women & Children Hospital, NHN, Uttara, Dhaka, Bangladesh, during the period from 13th February 2020 to 9th December 2021. Total 120 pregnant women with diabetes were included in this study. All patients were divided into two groups which include- Group A: 60 pregnant women with diabetes and Group B: 60 pregnant women with diabetes and hypothyroidism. **Results:** Mean age was 29.3 years (SD±4.9 years) in group A and 29.9 years (SD±6.1 years) in group B. Mean TSH was 2.2 µIU/ml (SD±1.7 µIU/ml) and in group A and 4.4 µIU/ml (SD±3.0 µIU/ml) in group B. Mean TSH was higher in group B than group A with statistically significantly difference ( $p < 0.0001$ ). Most of the pregnant women had lower uterine cesarean section in both group A (51.7%) and in group B (68.3%) with statistically significant difference ( $p = 0.0409$ ) between the groups. The commonest maternal complication was fetal distress in both group A (13.3%) and in group B (16.7%). Most of the neonates had normal weight in both group A (83.3%) and group B (78.3%). Majority of the neonates had normal Apgar score in one minute in both group A (50%) and group B (58.3%). The Apgar score in 5 minutes was also normal in most of the neonates of both group A (71.7%) and group B (78.3%). The neonatal mortality rate in group B was 1.7%. The commonest fetal complication was low birth weight in both group A (16.7%) and in group B (21.7%). There was no statistically significant ( $>0.05$ ) difference among both groups in neonate's outcome. **Conclusion:** Fetal distress and preeclampsia are most common complication in diabetic pregnant women with hypothyroidism. For neonates, low birth weight, hypothyroidism and respiratory distress are commonly seen. There is higher death rate of neonates in diabetic pregnant women with hypothyroidism. Majority of the pregnant women needed lower uterine cesarean section for the complications.

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## INTRODUCTION

Along with diabetes mellitus, thyroid disorders are a typical occurrence in pregnant women and those in the reproductive age range.<sup>[1]</sup> The primary causes of hypothyroidism continue to be Hashimoto's illness and endemic iodine shortage.<sup>[2]</sup> The thyroid glands and its functions' effects during pregnancy are significant. In iodine-rich nations, the thyroid gland may grow by 10% during pregnancy, whereas in iodine-deficient places, it may grow by 20–40%.<sup>[3]</sup> Due to increased renal loss brought on by increased renal blood flow, higher glomerular filtration rate, and increased renal clearance as a result of decreased tubular reabsorption of iodine, both thyroid hormone production and the demand for iodine both rise by around 50% during. The fetus receives maternal thyroxin throughout the pregnancy.<sup>[4,5,6,7]</sup> Maternal thyroxin is important for normal fetal brain development, neural implication, migration and structural organization, thus, future intellectual development especially before the development of fetal thyroid gland.<sup>[3]</sup> This insult is likely to occur in the first trimester and, therefore, periconceptional optimization of thyroxin therapy is important.<sup>[8]</sup> Maternal thyroxin contribution remains important sources before 12 weeks of gestation after which fetal thyroid synthesized hormone.<sup>[9]</sup> Diabetic patients attending hospital-based clinics, especially those with Type 1 diabetes mellitus, have a higher prevalence of thyroid disease than the general population.<sup>[10,11]</sup> The prevalence of DM during pregnancy is about 7%, most of them are gestational, of note there is a constant increase of the prevalence of DM due to the gradual increase in pregnant women's BMI (Body Mass Index) and the epidemic of obesity during

recent decades.<sup>[12]</sup> Gestational diabetes mellitus (GDM) and especially pregestational DM, are known as risk factors for pregnancy complications, effecting both the mother and the fetus and include among the rest gestational hypertension, cesarean sections, macrosomic fetuses and shoulder dystocia.<sup>[13,14]</sup> These patients also have increased neonatal morbidity including fetal demise, neonatal hypoglycemia, jaundice, polycythemia and hypocalcemia.<sup>[12,13,14]</sup> Pregnancy is a stress test for the thyroid and the physiological changes may result in hypothyroidism in the later stages in women with limited thyroidal reserve with underlying autoimmune disease or iodine deficiency who were euthyroid prior to conception.<sup>[3]</sup> Serum thyroid stimulating hormone (TSH) level in early pregnancy decline because of weak TSH reception stimulation from massive quantities of human chorionic gonadotropin (hcG) secreted by placental trophoblast during the first trimester. The TSH level is the lowest and FT4 level is the highest when hcG levels peak.<sup>[2]</sup> The pregnancy-related changes in thyroid physiology make diagnosis of thyroid disorder difficult, because it can simulate signs and symptoms of physiological changes of pregnancy.<sup>[2]</sup> Symptoms of heat intolerance, sluggishness, fatigue, and examination findings of tachycardia, edema, hair changes, and weight gain are common to pregnancy and thyroid disease much in same way.<sup>[2]</sup> Untreated SCH is probably linked to several unfavorable pregnancy outcomes. It may develop to overt thyroid failure, and the pace of progression is influenced by TSH levels, a woman's age, a condition like diabetes, the existence of TPO antibodies, and their concentration.<sup>[2]</sup> The fetus depends on the mother's thyroid hormone levels, especially in

the first trimester because iodothyronines cannot be produced before ten weeks of pregnancy. Due to a lack of iodothyronines, the neurodevelopment of the fetus may be affected at this time.<sup>[15]</sup> Untreated overt hypothyroidism during pregnancy has been linked to postpartum hemorrhage, gestational hypertension, abruptio placenta, anemia, and gestational diabetes.<sup>[16,17]</sup> Negative birth outcomes are more likely in people with overt hypothyroidism. Spontaneous miscarriage, low birth weight, early birth, fetal distress, perinatal mortality, and stillbirth are frequently seen birth outcomes.<sup>[18,19,20]</sup> The neurocognitive growth of the fetus is adversely affected by overt hypothyroidism. Similar negative consequences may also be caused by subclinical hypothyroidism; however, the data is inconclusive.<sup>[21]</sup> Additionally, a number of studies have revealed that children born to mothers with untreated hypothyroidism are considerably more likely to experience cognitive developmental abnormalities, which can cause lower IQs and other learning difficulties.<sup>[22,23]</sup> Feely & Isles,<sup>[24]</sup> reported that among diabetic patients, 2.7% had also overt hypothyroidism, while the prevalence of subclinical hypothyroidism reached up to 30% in these patients. Other studies reported a prevalence of 10.8–13.4% of thyroid diseases (mostly hypothyroid disorders) in diabetic patients, and the highest rates were recorded among type I diabetes patients and in females.<sup>[10,25]</sup> There are very few studies about hypothyroidism among diabetic pregnant women and its effect on maternal and fetal outcome. Thus, this study was conducted to evaluate hypothyroidism among diabetic pregnant women and its effect on maternal and fetal outcome.

## Objective

To evaluate hypothyroidism in diabetic pregnancy and its effect on maternal and fetal outcome.

## MATERIAL AND METHODS

This cross-sectional study was conducted in department of Obstetrics and Gynaecology, Women & Children Hospital, NHN, Uttara, Dhaka, Bangladesh, during the period from 13th February 2020 to 9th December 2021. Total 120 pregnant women with diabetes were included in this study where 60 of them had hypothyroidism. All patients were divided into two groups which include-

Group A: 60 pregnant women with diabetes and

Group B: 60 pregnant women with diabetes and hypothyroidism.

Consent of the patients and guardians were taken before collecting data. After collection of data, all data were checked and cleaned. After cleaning, the data were entered into computer and statistical analysis of the results being obtained by using windows-based computer software devised with Statistical Packages for Social Sciences version 22. After compilation, data were presented in the form of tables, figures and charts, as necessary. Numerical variables were expressed as mean and standard deviation, whereas categorical variables were count with percentage. Quantitative data among groups were analyzed by ANOVA test followed by exploration of significant difference between all possible paired group means by Bonferroni test. P value of less than 0.05 was considered statistically significant.

### Inclusion Criteria

- All individuals diagnosed with hypothyroidism and diabetes in indoor patient
- Child bearing age groups

### Exclusion Criteria

- Individuals with negative result in diagnosis of hypothyroidism
- Individuals with negative result in diagnosis of diabetes
- Patients transferred to another hospital

## RESULTS

The current study was conducted among 120 diabetic pregnant women where 60 of them had hypothyroidism. Group A indicates pregnant women with diabetes and Group B indicates pregnant women with diabetes and hypothyroidism. [Table 1] demonstrates the baseline information of the pregnant women. Mean age was 29.3 years (SD±4.9 years) in group A and 29.9 years (SD±6.1 years) in group B. The mean age difference was not statistically significant (>0.05). Most of the pregnant women were overweight in both group A (60%) and group B (58.3%). There is no statistically significant (>0.05) difference in BMI among the groups. Majority pregnant women were in multigravida group in both group A (75%) and group B (71.7%) and there was no statistically significant (>0.05) difference among the groups. Mean gestational age in group A was 36.7 weeks (SD±1.7 weeks) and in group B 36.9 weeks (SD±1.5 weeks) with no statistically significant (>0.05) difference. In group A, 3.3% had hypertension, 3.3% had bronchial asthma, and 01.7% had breech as comorbidity. In group B, 1.7% had hypertension as comorbidity. There

was no statistically significant (>0.05) difference among the groups. [Table 2] shows the clinical characteristics of the pregnant women. Mean TSH was 2.2  $\mu$ IU/ml (SD±1.7  $\mu$ IU/ml) and in group A and 4.4  $\mu$ IU/ml (SD±3.0  $\mu$ IU/ml) in group B. Mean TSH was higher in group B than group A with statistically significantly difference ( $p < 0.0001$ ). Mean Hb% was 11.1 gm/dl (SD±1.3 gm/dl) in group A and 11.3 gm/dl (SD±1.1 gm/dl) in group B. There was no statistically significant (>0.05) difference among the groups. Mean fasting blood sugar (FBS) was 5.8 mmol/L (SD±1.7 mmol/L) in group A and 7.0 mmol/L (SD±1.9 mmol/L) in group B. Mean FBS was higher in group B compared to group A with statistically significantly difference ( $p = 0.0004$ ). [Table 3] shows the maternal outcome of the study people. Most of the pregnant women had lower uterine cesarean section in both group A (51.7%) and in group B (68.3%). There was statistically significant difference ( $p = 0.0409$ ) between the groups. In group A, the commonest (13.3%) maternal complication was fetal distress. In group B, the commonest (16.7%) maternal complication was also fetal distress. There was no statistically significant (>0.05) difference in complications among the groups. [Table 4] demonstrates the neonates' outcome. Majority of the neonates were male in both group A (51.7%) and group B (65%). Most of the neonates had normal weight in both group A (83.3%) and group B (78.3%). Majority of the neonates had normal Apgar score in one minute in both group A (50%) and group B (58.3%). The Apgar score in 5 minutes was also normal in most of the neonates of both group A (71.7%) and group B (78.3%). The neonatal mortality rate in group A was zero and in group B was 1.7%. In group A, the commonest fetal complications were low

birth weight (16.7%), hypothyroidism (15%), respiratory distress (13.3%), preterm delivery (11.7%) etc. In group B, the commonest fetal complications were low birth weight (21.7%),

hypothyroidism (16.7%), respiratory distress (16.7%), preterm delivery (13.3%) etc. All the neonates' outcome had no statistically significant (>0.05) difference among the groups.

**Table 1:** Baseline information of the pregnant women. (n=120)

Characteristics		Group A		Group B		P-value
		n	%	n	%	
Age (Years)	≤20	3	5.0	4	6.7	0.5537 <sup>NS</sup>
	21-30	32	53.3	35	58.3	
	>30	25	41.7	21	35.0	
	Mean±SD	29.3±4.9		29.9±6.1		
BMI (Kg/m <sup>2</sup> )	Underweight (<18.5)	0	0.0	1	1.7	0.6026 <sup>NS</sup>
	Normal (18.5–24.9)	9	15.0	10	16.7	
	Overweight (25–29.9)	36	60.0	35	58.3	
	Obese (≥30)	15	25.0	14	23.3	
Parity	Primi	15	25.0	17	28.3	0.6839 <sup>NS</sup>
	Multigravida	45	75.0	43	71.7	
Gestational age (Weeks)	Mean±SD	36.7±1.7		36.9±1.5		0.4957 <sup>NS</sup>
Comorbidities	Hypertension	2	3.3	1	1.7	0.3488 <sup>NS</sup>
	Bronchial asthma	2	3.3	0	0.0	
	Breech	1	1.7	0	0.0	

Group A = Pregnant women with diabetes

Group B = Pregnant women with diabetes and hypothyroidism

P= Value reached from unpaired t-test

S= Significant (p<0.05), NS = Not Significant (p>0.05)

**Table 2:** Clinical characteristics of the pregnant women. (n=120)

Characteristics	Group A (Mean±SD)	Group B (Mean±SD)	P-value
TSH(μIU/ml)	2.2±1.7	4.4±3.0	< 0.0001 <sup>S</sup>
Hb%(gm/dl)	11.1±1.3	11.3±1.1	0.4011 <sup>NS</sup>
FBS (mmol/L)	5.8±1.7	7.0±1.9	0.0004 <sup>S</sup>

Group A = Pregnant women with diabetes

Group B = Pregnant women with diabetes and hypothyroidism

P= Value reached from unpaired t-test

S= Significant (p<0.05), NS = Not Significant (p>0.05)

**Table 3:** Maternal outcome. (n=120)

Maternal outcome		Group A		Group B		P-value
		n	%	n	%	
Mode of delivery	Vaginal delivery.	31	48.3	18	30.0	0.0409 <sup>S</sup>
	LUCS	29	51.7	42	68.3	



Complication	Fetal distress	8	13.3	10	16.7	0.7480 <sup>NS</sup>
	Preeclampsia	6	10.0	5	8.3	
	Oligohydramnios	5	8.3	4	6.7	
	PROM	4	6.7	5	8.3	
	Cephalopelvic Disproportion	4	6.7	3	5.0	
	LP	3	5.0	2	3.3	
	IUGR	1	1.7	2	3.3	
	Anemia	1	1.7	1	1.7	
	UTI	1	1.7	1	1.7	

Group A = Pregnant women with diabetes

Group B = Pregnant women with diabetes and hypothyroidism

P= Value reached from unpaired t-test

S= Significant (p<0.05), NS = Not Significant (p>0.05)

**Table 4:** Neonates' outcome. (n=120)

Neonates' outcome		Group A		Group B		P-value
		n	%	n	%	
Sex	Male	31	51.7	39	65.0	0.1411 <sup>NS</sup>
	Female	29	48.3	21	35.0	
Weight	Normal weight	50	83.3	47	78.3	0.4887 <sup>NS</sup>
	Underweight	10	16.7	13	21.7	
Apgar score (1 minute)	0-3	11	18.3	16	26.7	0.2284 <sup>NS</sup>
	4-6	19	31.7	9	15.0	
	≥7	30	50.0	35	58.3	
Apgar score (5 minutes)	0-3	5	8.3	9	15.0	0.2311 <sup>NS</sup>
	4-6	12	20.0	4	6.7	
	≥7	43	71.7	47	78.3	
Death		0	0.0	1	1.7	0.1577 <sup>NS</sup>
Fetal complications	Low birth weight	10	16.7	13	21.7	0.7416 <sup>NS</sup>
	Hypothyroidism	9	15.0	10	16.7	
	Respiratory distress	8	13.3	10	16.7	
	Preterm	7	11.7	8	13.3	
	TTN	7	11.7	6	10.0	
	Hyper bilirubin	6	10.0	7	11.7	

Group A = Pregnant women with diabetes

Group B = Pregnant women with diabetes and hypothyroidism

P= Value reached from unpaired t-test

S= Significant (p<0.05), NS = Not Significant (p>0.05)

## DISCUSSION

Total 120 pregnant women with diabetes were included in this study. All patients were

divided into two groups which include- Group A: 60 pregnant women with diabetes and Group B: 60 pregnant women with diabetes and

hypothyroidism. Mean age was 29.3 years (SD±4.9 years) in group A and 29.9 years (SD±6.1 years) in group B. The mean age difference was not statistically significant ( $>0.05$ ). In the study of Biradar KD,<sup>[26]</sup> mean age was 23.6 years (SD±2.5 years). Most of the pregnant women were overweight in both group A (60%) and group B (58.3%). There is no statistically significant ( $>0.05$ ) difference in BMI among the groups. In the study of Kiran Z et al,<sup>[27]</sup> majority of the pregnant women were overweight which is similar to our study. This indicates that, overweight women have more risk of hypothyroidism. Majority pregnant women were in multigravida group in both group A (75%) and group B (71.7%) and there was no statistically significant ( $>0.05$ ) difference among the groups. Mean gestational age in group A was 36.7 weeks (SD±1.7 weeks) and in group B 36.9 weeks (SD±1.5 weeks) with no statistically significant ( $>0.05$ ) difference. In group A, 3.3% had hypertension, 3.3% had bronchial asthma, and 01.7% had breech as comorbidity. In group B, 1.7% had hypertension as comorbidity. There was no statistically significant ( $>0.05$ ) difference among the groups. Mean TSH was 2.2  $\mu$ IU/ml (SD±1.7  $\mu$ IU/ml) and in group A and 4.4  $\mu$ IU/ml (SD±3.0  $\mu$ IU/ml) in group B. Mean TSH was higher in group B than group A with statistically significantly difference ( $p < 0.0001$ ). Mean Hb% was 11.1 gm/dl (SD±1.3 gm/dl) in group A and 11.3 gm/dl (SD±1.1 gm/dl) in group B. There was no statistically significant ( $>0.05$ ) difference among the groups. Mean fasting blood sugar (FBS) was 5.8 mmol/L (SD±1.7 mmol/L) in group A and 7.0 mmol/L (SD±1.9 mmol/L) in group B. Mean FBS was higher in group B compared to group A with statistically significantly difference ( $p = 0.0004$ ). In the study

of Hirsch D et al.<sup>[28]</sup>, maximum serum TSH level ranged from 20.11 to 150.0 mIU/l (median 32.95 mIU/l); in 73 pregnancies (70.9%). The median level ranged from 0.36 to 75.17 mIU/l (median 7.44 mIU/l). The last antenatal serum TSH level ranged from 0.03 to 132.05 mIU/l (median 3.2 mIU/l). Most of the pregnant women had lower uterine cesarean section in both group A (51.7%) and in group B (68.3%). There was statistically significant difference ( $p = 0.0409$ ) between the groups. In the study of Tirosh D et al,<sup>[29]</sup> cesarean section was done in 44.4% diabetic pregnant women with hypothyroidism compared to 27% in diabetic pregnant women. In our study, in group A, the commonest maternal complications were fetal distress (13.3%) and preeclampsia (10%). In group B, the commonest maternal complications were also fetal distress (16.7%) and preeclampsia (8.3%). There was no statistically significant ( $>0.05$ ) difference in complications among the groups. Colatrella et al,<sup>[30]</sup> reported that the prevalence of chronic hypertension was up to 18%, preeclampsia up to 15% (50% when nephropathy is pre-existing), and gestational hypertension up to 28% in pregnant women with different types of DM. Patients with hypothyroidism show impaired blood flow in response to tissue ischemia or to the administration of endothelial dependent vasodilators, suggesting endothelial dysfunction in these patients.<sup>[31,32]</sup> Thus, the presence of hypothyroidism might enhance the risk for hypertension and preeclampsia. Majority of the neonates were male in both group A (51.7%) and group B (65%). Most of the neonates had normal weight in both group A (83.3%) and group B (78.3%). Majority of the neonates had normal Apgar score in one minute in both group A (50%) and group B (58.3%). The

Apgar score in 5 minutes was also normal in most of the neonates of both group A (71.7%) and group B (78.3%). The neonatal mortality rate in group A was zero and in group B was 1.7%. In group A, the commonest fetal complications were low birth weight (16.7%), hypothyroidism (15%), respiratory distress (13.3%), preterm delivery (11.7%) etc. In group B, the commonest fetal complications were low birth weight (21.7%), hypothyroidism (16.7%), respiratory distress (16.7%), preterm delivery (13.3%) etc. All the neonates' outcome had no statistically significant ( $>0.05$ ) difference among the groups. In the study of Tirosh D et al,<sup>[29]</sup> women with the combined endocrinopathy had a higher rate of preterm delivery between 32–34 weeks (2.3% vs. 0.8%;  $p=0.024$ ), late preterm birth (8.8% vs. 5%;  $p < 0.024$ ), and a higher rate of newborns with a birth weight below 2500g (11.1% vs. 8.2%;  $p=0.165$ ). In the study of Buckshee K et al,<sup>[33]</sup> among 26 pregnant women, neonatal death was 3.9%. In fetal complication, 20% had low birth weight, 15.8% had hypothyroidism, 15.8% had fetal distress, 13.3% had preterm birth, 12.5% had TTN, and 10% hyper bilirubin. In the study of George M et al,<sup>[34]</sup> fetal complication included low birth weight 4%, Prematurity 10%, NICU admission 4%, Hyperbilirubinemia 8%, and no neonates had hypothyroidism.

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## Limitations of the study

In our study, there was small sample size and absence of control for comparison. Study population was selected from one center in Dhaka city, so may not represent wider population. The study was conducted at a short period of time. The sampling was retrospective and there was no random allocation, so there is risk of selection bias.

## CONCLUSIONS

Fetal distress and preeclampsia are most common complication in diabetic pregnant women with hypothyroidism. For neonates, low birth weight, hypothyroidism and respiratory distress are commonly seen. There is higher death rate of neonates in diabetic pregnant women with hypothyroidism. Majority of the pregnant women needed lower uterine cesarean section for the complications. To maintain an optimal thyroid hormone concentration during pregnancy and prevent maternal and fetal complications, close monitoring is necessary, and rigorous fetal monitoring is necessary to have a positive perinatal result. Further study with larger sample size is necessary to have better understanding.

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