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Original Research Article

Study on the occurrence of gestational diabetes mellitus in first trimester hypothyroid and euthyroid pregnant women

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ABSTRACT

Background: Hypothyroidism and gestational diabetes mellitus are two common endocrine complications in pregnancy. Individually, contributing to adverse outcomes. With the increase in the prevalence of subclinical hypothyroidism, the risk of the occurrence of gestational diabetes mellitus among pregnant women has increased. Thus, the purpose of this study is to determine the association between hypothyroidism and the subsequent onset of gestational diabetes. Introducing universal thyroid screening in the early stages of pregnancy, along with timely intervention, may help reduce the impact of both conditions on expectant mothers, thereby promoting healthier pregnancies and overall maternal well-being. This study aimed to determine the proportion of pregnant women with gestational diabetes mellitus among first-trimester (0- 12 weeks) hypothyroid and euthyroid pregnant women.
Methods: This is a Prospective study conducted in the Department of OBG, ESIC-PGIMSR Bangalore between April 2023 to October 2024. Pregnant women who registered at the Antenatal OPD during their first visit, including both euthyroid and hypothyroid individuals, were followed up, and the prevalence of gestational diabetes mellitus among them, with maternal and fetal outcomes, has been evaluated.
Results: In our study, the prevalence of GDM in patients with hypothyroidism is found to be 80%, with adverse maternal and fetal outcomes. Thus, the association of GDM with hypothyroidism has an increased risk of preterm delivery (22.5%), severe preeclampsia (10%), gestational hypertension (7.5%), anaemia (30%), placental abruption (5%), and an increased number of caesarean sections (72.5%), with an increased neonatal morbidity.
Conclusions: Early universal screening and timely intervention for hypothyroidism in the first trimester can reduce the subsequent occurrence of gestational diabetes mellitus in later trimesters of pregnancy, with a reduction in the adverse maternal and fetal outcomes.

Keywords: Anemia, Caesarean section, Gestational diabetes mellitus, Hypothyroidism, Neonatal outcome, Pre-eclampsia, Preterm delivery

INTRODUCTION

The most common endocrine disorders in pregnancy are hypothyroidism and gestational diabetes mellitus (GDM), both of which can result in adverse outcomes for both the mother and the fetus. Globally, subclinical hypothyroidism affects 2-5% of pregnant women, but in India, this figure rises to 11.07% (95% CI: 8.79-13.84), while the prevalence of GDM, according to DIPSI criteria, is 13.21% as noted by Divakar et al in 2017.[1] In their study involving 251 participants, 29 were diagnosed with GDM (12%), and among those, 24 were found to be hypothyroid [OR= 12.11; 95% CI: 4.42-33.15]. They concluded that hypothyroidism is highly prevalent among pregnant women with GDM.[2] The likelihood of developing GDM among hypothyroid pregnant women stands at 27.6%, compared to only 3.5% in women with normal thyroid function.[3]

About 10-15% of pregnant women have thyroid dysfunction during the first half of pregnancy, which may be hypothyroidism or hyperthyroidism.[4] The main factor contributing to GDM is an increase in insulin resistance. This resistance intensifies during the second and early third trimesters, but returns to normal late in the third trimester. The first half of pregnancy features "facilitated insulin action," while the second half involves "diabetogenic stress" caused by high levels of counter-regulatory hormones (like progesterone and estriol), decreased hepatic glucose uptake, and reduced postprandial insulin secretion. A healthy pancreas can usually counteract this insulin resistance to keep glucose stable. However, in GDM, the body fails to manage this stress, leading to hyperglycemia that necessitates medical treatment. Due to the association with insulin resistance, hypothyroidism negatively impacts glucose regulation. Consequently, pregnant women with hypothyroidism exhibit heightened insulin resistance, which raises their risk of developing gestational diabetes.[5] In pregnant women with hypothyroidism, the risk of GDM is elevated because the condition causes reduced peripheral glucose uptake and a diminished rate of glucose oxidation and glycogen synthesis, leading to insulin resistance.[2] Hallmarks of hypothyroidism that affect glucose metabolism include: decreased glucose absorption from the gastrointestinal tract, prolonged glucose retention in peripheral tissues, and gluconeogenesis coupled with decreased hepatic glucose production and clearance.[6]

In combination, they have shown increased risk of complications such as first-trimester miscarriage, pre-eclampsia, polyhydramnios, placental abruption, preterm birth, caesarean delivery, and postpartum haemorrhage in mothers. In the fetus, conditions like intrauterine growth restriction, prematurity, intrauterine demise, and stillbirth have been documented.[7,8] Hence, an early screening with an appropriate strategy could reduce the burden of both conditions on pregnant women, contributing to healthier motherhood.

This study aimed to determine the proportion of pregnant women with gestational diabetes mellitus among first-trimester (0-12 weeks) hypothyroid and euthyroid pregnant women.

METHODS

Source of data

Total 100 gravid women registered in antenatal OPD, Department of Obstetrics and Gynaecology, ESIMC and PGIMSR, Rajajinagar, Bengaluru.

Methods of collection of data

A prospective cohort study with 100 gravid women registered in the antenatal outpatient, Department of Obstetrics and Gynaecology, ESIMC and PGIMSR Hospital, Bengaluru, for a study period of 1 year and 6 months.

Inclusion criteria

Inclusion criteria involved that participants be pregnant women above 18 years of age with a singleton pregnancy who provided informed written consent. Participants were classified as hypothyroid if their TSH was >2.5 microIU/l, as per the American Thyroid Association guidelines.[9] GDM was diagnosed as per DIPSI (Diabetes in Pregnancy Study Group of India) criteria, if blood sugar levels were more than or equal to 140 mg/dl.[10]

Exclusion criteria

Exclusion criteria comprised women with pre-gestational diabetes mellitus, pre-existing thyroid disease, autoimmune diseases, renal diseases, or Systemic Lupus Erythematosus (SLE).

Methodology

Pregnant women meeting the inclusion criteria are recruited during their first antenatal clinic visit after obtaining informed consent. Then, collected a detailed patient history (general, obstetric, past, family, diet and personal) and performed comprehensive physical, systemic, and obstetric examinations. Gestational age is confirmed using the last menstrual date (Naegele's rule) and an early trimester dating scan.

Screening for hypothyroidism

A fasting sample of 5ml venous blood is drawn, and Serum TSH, FT3, and FT4 levels are estimated using Chemiluminescence Immunoassay on a Beckman Coulter Access 2 Analyser. According to American Thyroid Association guidelines, normal serum TSH during pregnancy ranges between 0.2-2.5 mIU/ml.[9] Based on American Thyroid Association guidelines 2017 and FOGSI 2021, the trimester-specific recommended TSH reference is as follows: 1st trimester-2.5 mIU/l, 2nd trimester-3 mIU/l, and 3rd trimester-3 mIU/l.

Based on their initial TSH results, participants are divided into two main groups: Group A: Subclinical hypothyroid, Group B: Euthyroid (normal thyroid function).

TSH values >2.5 mIU/ml are considered as Hypothyroidism. All are advised for routine antenatal care, and those diagnosed with hypothyroidism are treated with levothyroxine 2-2.4 microgram/kg/day.

Screening for GDM

All pregnant women who met the study criteria and had normal first-trimester glucose levels regardless of their thyroid status (hypothyroid or euthyroid) were screened for GDM between 24 and 28 weeks of gestation. The

screening used an Oral Glucose Tolerance Test (OGTT), where the women ingested 75 grams of glucose (dissolved in 300 ml of water), irrespective of last meal or fasting status. According to the Diabetes in Pregnancy Society of India (DIPSI) criteria, GDM was diagnosed if the blood sugar level was more than or equal to 140 mg/dl.[10] Women diagnosed with GDM were immediately advised to begin intensive management, which included frequent prenatal visits, Medical Nutritional Therapy (MNT), self-monitoring of blood glucose, and potentially pharmacological therapy.[11] They also received counselling on the risks of fetal and neonatal complications and the need for regular fetal surveillance.

Based on the combined thyroid and GDM status, the participants are further divided into the following four subgroups:

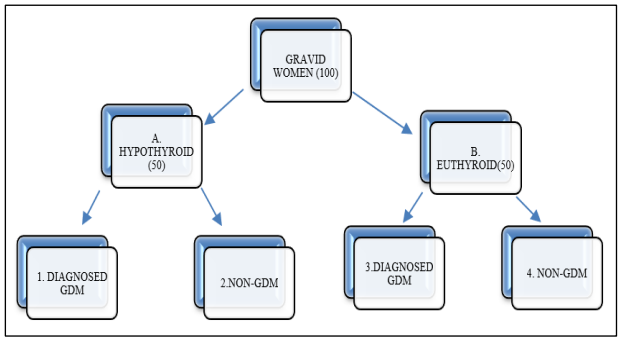

Figure 1: Schematic representation of the study.

The data are documented and analysed statistically for the rate of occurrence of GDM in both euthyroid and hypothyroid patients. Data collection will be done using a pre-structured proforma.

Outcome measures

The exposure variables included hypothyroid pregnant women and euthyroid pregnant women. The outcome variables focused on the occurrence of gestational diabetes mellitus. Specific outcome measures included the number of hypothyroid mothers with an increased occurrence of GDM, and comparing the occurrence of GDM with that of euthyroid pregnant controls.

Sample size

A study was conducted by Divakar et al in 2017 in India. The occurrence of GDM among hypothyroid pregnant women was 27.6% and euthyroid was 3.5%. At a 5% level of significance and 80% power with a ratio of 1:1, and a risk ratio of 8. The estimated sample size is 43 per group. The sample size is calculated using Open Epi version 3. Considering the loss of follow-up, the sample size per group is 50. Therefore, the total sample size of 100.

Statistical analysis

Data analysis was performed using SPSS 26 and Microsoft Excel, employing the Chi-square test, t-test, and Mann-Whitney U test for significance. A p-value of <0.05 was considered statistically significant

RESULTS

Maternal age beyond 25 years significantly compounds GDM risk in hypothyroid pregnancies, necessitating targeted surveillance. Regarding parity, primigravida status is higher in non-GDM euthyroid women but shows similar distribution rates across hypothyroid groups.

Table 1: Age and parity distribution of the pregnant women among the study groups.

Subjects (n=100)	Groups								P value#
	Euthyroid (n=50)				Hypothyroid (n=50)				
	Non-GDM (n=40)		GDM (n=10)		Non-GDM (n=10)		GDM (n=40)		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Age (years)	26.70	4.05	28.50	3.60	23.90	3.57	27.90	4.50	0.036
Parity									
Primigravida	24	60.0%	4	40.0%	6	60.0%	23	57.5%	0.713
Multigravida	16	40.0%	6	60.0%	4	40.0%	17	42.5%	

#Chi-square test.

First trimester TSH levels varied widely (mean 3.28 ± 1.39 mIU/l), frequently exceeding the ATA cutoff, while FT3 (3.09±0.41 µg/dl) and FT4 (0.99±0.10 µg/dl) remained stable. This identifies TSH as the most sensitive screening marker, confirming that a significant portion of the cohort was biochemically hypothyroid.

OGTT values raised from 100.82±15.25 mg/dl to 127.14±28.35 mg/dl in the second trimester (max 199 mg/dl), reflecting an increased glycemic burden. This trend highlights the necessity of GDM screening at 24-28 weeks, particularly for women with early hypothyroidism.

GDM developed in 80% (n=40) of hypothyroid women compared to only 20% (n=10) of euthyroid women ($p<0.001$), demonstrating a robust correlation between first-trimester hypothyroidism and subsequent glucose intolerance.

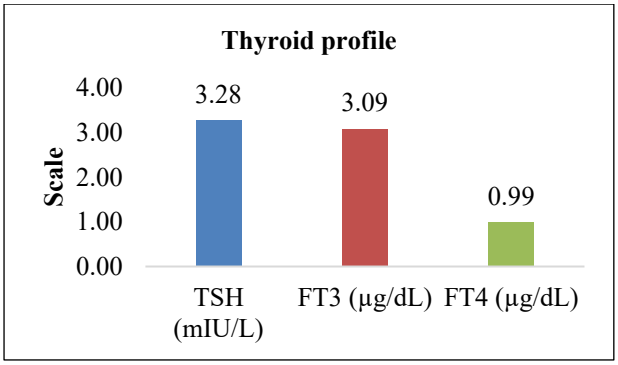

Figure 2: Thyroid profile of pregnant women during the gestational period of less than 12 weeks.

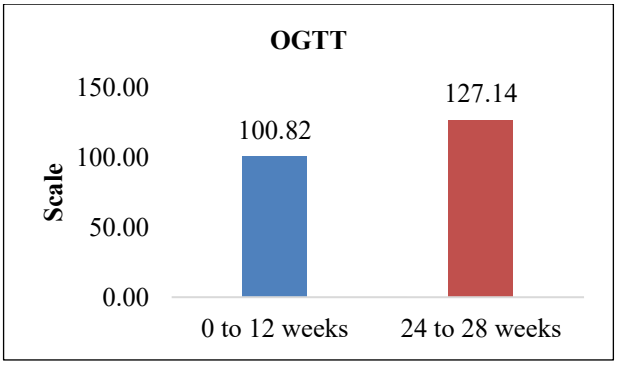

Figure 3: OGTT of pregnant women in the first and second trimesters.

Table 2: Proportion of mothers among the study groups developing GDM at 24 to 28 weeks of gestation.

Subjects (n=100)	Groups				P value[#]
	Euthyroid (n=50)		Hypothyroid (n=50)		
	N	%	N	%	
Non-GDM	40	80.0%	10	20.0%	<0.001*
GDM	10	20.0%	40	80.0%	

[#]Chi-square test; *Statistically significant

Table 3: Delivery outcomes: gestational age at delivery, mode of delivery, and neonatal Apgar score.

Subjects (n=100)	Groups								P value[#]
	Euthyroid (n=50)				Hypothyroid (n=50)				
	Non-GDM (n=40)		GDM (n=10)		Non-GDM (n=10)		GDM (n=40)		
	N	%	N	%	N	%	N	%	
<32 weeks	0	0.0	0	0.0	0	0.0	0	0.0	0.003*
32 to 36 weeks	1	2.5	2	20.0	2	20.0	14	35.0	
>36 weeks	39	97.5	8	80.0	8	80.0	26	65.0	
NVD	22	55.0	4	40.0	8	80.0	11	27.5	0.009*
LSCS	18	45.0	6	60.0	2	20.0	29	72.5	
APGAR score (At 5 min)	7.08	0.89	6.70	1.06	5.50	0.97	5.20	0.85	<0.001*

[#]Chi-square test; *Statistically significant; "Independent t-test

Table 4: Distribution based on maternal-comorbidities and complications among the study groups.

Subjects (n=100)	Groups								P value[#]
	Euthyroid (n=50)				Hypothyroid (n=50)				
	Non-GDM (n=40)		GDM (n=10)		Non-GDM (n=10)		GDM (n=40)		
	N	%	N	%	N	%	N	%	
Anemia	3	7.5	2	20.0	3	30.0	12	30.0	
Fibroid uterus	0	0.0	0	0.0	0	0.0	1	2.5	
GHTN	0	0.0	2	20.0	0	0.0	3	7.5	
IUGR	0	0.0	0	0.0	0	0.0	1	2.5	
Macrosomia	0	0.0	0	0.0	0	0.0	1	2.5	
Oligo-hydramnios	1	2.5	0	0.0	0	0.0	2	5.0	
Poly-hydramnios	0	0.0	0	0.0	0	0.0	1	2.5	
Preeclampsia	0	0.0	1	10.0	0	0.0	3	7.5	
Preterm	1	2.5	0	0.0	0	0.0	10	25.0	
Previous LSCS	2	5.0	0	0.0	0	0.0	0	0.0	
PROM	0	0.0	0	0.0	1	10.0	0	0.0	

Continued.

Subjects (n=100)	Groups								P value[#]
	Euthyroid (n=50)				Hypothyroid (n=50)				
	Non-GDM (n=40)		GDM (n=10)		Non-GDM (n=10)		GDM (n=40)		
	N	%	N	%	N	%	N	%	
Residual polio	0	0.0	0	0.0	0	0.0	1	2.5	
Rh negative	5	12.5	0	0.0	0	0.0	0	0.0	
Tricho-moniasis	0	0.0	0	0.0	0	0.0	1	2.5	
UTI	1	2.5	2	20.0	1	10.0	1	2.5	
None	27	67.5	3	30.0	5	50.0	3	7.5	
Atonic PPH	0	0.0	0	0.0	0	0.0	8	20.0	0.003*
Oligo-hydramnios	1	2.5	0	0.0	0	0.0	2	5.0	
Poly-hydramnios	0	0.0	0	0.0	0	0.0	1	2.5	
Post term	0	0.0	0	0.0	1	10.0	0	0.0	
PROM	1	2.5	0	0.0	0	0.0	3	7.5	
Preeclampsia	0	0.0	0	0.0	0	0.0	1	2.5	
Preterm delivery	0	0.0	2	20.0	1	10.0	9	22.5	
Abruptio placenta	0	0.0	0	0.0	0	0.0	1	2.5	
None	38	95.0	8	80.0	8	80.0	15	37.5	

[#]Chi-square test; *Statistically significant

Table 5: Distribution based on fetal complications and neonatal Intensive Care Unit (NICU) admission among the study groups.

Subjects (n=100)	Groups								P value[#]
	Euthyroid (n=50)				Hypothyroid (n=50)				
	Non-GDM (n=40)		GDM (n=10)		Non-GDM (n=40)		GDM (n=10)		
	N	%	N	%	N	%	N	%	
Hyper-bilirubinemia	2	5.0	0	0.0	1	10.0	3	7.5	
Hypoglycemia	0	0.0	0	0.0	0	0.0	6	15.0	
IUGR	0	0.0	0	0.0	0	0.0	3	7.5	
LBW	0	0.0	1	10.0	0	0.0	2	5.0	0.001*
MSL	1	2.5	0	0.0	1	10.0	4	10.0	
Preterm	0	0.0	0	0.0	0	0.0	3	7.5	
RDS	1	2.5	0	0.0	0	0.0	8	20.0	
None	36	90.0	9	90.0	8	80.0	11	27.5	
Yes	4	10.0	0	0.0	1	10.0	25	62.5	<0.001*
No	36	90.0	10	100.0	9	90.0	15	37.5	

[#]Chi-square test; *Statistically significant

The coexistence of hypothyroidism and GDM increases the risk of preterm delivery and significantly elevates cesarean section rates to 72.5% (p=0.009). Furthermore, this group demonstrated significantly lower 5-minute APGAR scores (p<0.001), indicating compromised neonatal vitality that demands heightened intrapartum surveillance.

Hypothyroid GDM mothers faced a significantly higher comorbidity burden (p<0.001), with only 7.5% remaining condition-free (vs. 67.5% in euthyroid) due to elevated anaemia (30%), preterm delivery (25%), gestational hypertension (7.5%), preeclampsia (7.5%), and unique risks like oligohydramnios (5%). Maternal complications were similarly compounded (p=0.003), with uneventful pregnancies plummeting to 37.5% (vs. 95% in euthyroid) amid rising rates of preterm delivery (22.5%), atonic PPH (20%), and PROM (7.5%).

Fetal complications were significantly higher in the hypothyroid GDM group (p=0.001), as only 27.5% of their neonates were complication-free (vs. 90% in euthyroid controls), exhibiting elevated rates of RDS (20%) and hypoglycemia (15%), meconium-stained liquor and Intrauterine growth restriction (IUGR) in 10% and 7.5%. This dual burden severely compromised outcomes, resulting in notably higher NICU admissions (62.5%) for this subset (p<0.001), supporting early GDM screening in hypothyroid women.

DISCUSSION

Diabetes mellitus stands as a leading non-communicable disease globally, presenting a significant public health burden due to its increasing prevalence and its association with multiple long-term complications. Among women during pregnancy, a unique form Gestational Diabetes Mellitus (GDM) is commonly encountered and ranks among the most prevalent endocrine disorders affecting expectant mothers. Notably, GDM is often preceded or accompanied by thyroid disorders, which are the second most frequent endocrine dysfunctions seen during gestation.

The thyroid gland plays an indispensable role in regulating basal metabolic processes, including the metabolism of carbohydrates, proteins, and lipids. Through the modulation of these pathways, thyroid hormones have a substantial influence on insulin action and glucose homeostasis. In particular, hypothyroidism, characterized by reduced levels of thyroid hormones, can impair insulin-mediated glucose uptake and utilization by peripheral tissues, primarily by lowering metabolic rate and altering pancreatic β-cell function. These changes contribute to a state of increased insulin resistance, especially during pregnancy, where physiological insulin resistance is already heightened as a natural adaptation to support fetal growth.

When this pre-existing insulin resistance is compounded by hypothyroidism, it predisposes the pregnant woman to dysregulated glucose metabolism, significantly increasing the risk of developing GDM. This adverse metabolic interplay is of particular clinical interest as both GDM and hypothyroidism are independently associated with maternal and fetal complications, including pre-eclampsia, macrosomia, preterm delivery, and neonatal hypoglycemia.

Thus, monitoring and managing thyroid function during early pregnancy can be pivotal in preventing or mitigating the risks associated with gestational diabetes and its sequelae. A growing body of evidence suggests that thyroid dysfunction, especially hypothyroidism, is more frequently observed among women diagnosed with GDM, emphasising a potential pathophysiological link between the two conditions[3,5]. Recognising this association, the present prospective cohort study was designed to examine the incidence and outcomes of GDM in pregnant women with and without hypothyroidism.

In the present study, hypothyroid women who developed GDM had a higher mean age of 27.9 years, compared to 23.9 years in those who did not develop GDM (p=0.036). Notably, the 26-30 years age group accounted for the majority (42%) of women presenting with both hypothyroidism and GDM, indicating this bracket as a particularly vulnerable demographic. These results emphasise the role of increasing maternal age as an independent risk factor for the emergence of GDM in the context of thyroid dysfunction. Previous studies support this observation. Yang et al demonstrated a significant positive trend between maternal age and GDM prevalence (p<0.0001).[13] Similarly, Tirosh et al found the most common age range for the coexistence of GDM and hypothyroidism to be 28-38 years.[15] These findings consistently reinforce the influence of age on the development of dual endocrinopathies. In contrast, Prasad et al reported comparable mean ages between their study and control groups (25.38±4.52 vs. 24.31±4.19), but did not perform age-stratified analysis for GDM risk, limiting the strength of their conclusions regarding maternal age as a contributing factor.[3] Taken together, the present and previous studies strongly suggest that as maternal age advances, there is a cumulative risk of impaired glucose regulation and thyroid dysfunction.

Physiological mechanisms such as increased insulin resistance, reduced β-cell reserve, and altered endocrine adaptation with advancing age may heighten susceptibility to GDM, especially in the presence of pre-existing hypothyroidism. Thus, these findings advocate for early and vigilant screening strategies, particularly in older pregnant women, to identify those at risk of this clinically significant double endocrinopathy and to implement timely interventions aimed at improving maternal and fetal outcomes.

In the present study, the distribution of parity revealed that primigravida women were more frequently represented across both euthyroid and hypothyroid groups, with 60.0% of euthyroid non-GDM and hypothyroid non-GDM women were primigravida, while primigravida were recorded in 40.0% of euthyroid GDM and 57.5% of hypothyroid GDM participants. Multigravida status was comparatively more prevalent in the GDM groups, yet the observed differences were not statistically significant (p=0.713). Hence, the present study did not establish parity as a significant predictor or risk factor for the development of GDM in the context of thyroid dysfunction. Tirosh et al reported that 56.6% of women with combined diabetes and hypothyroidism had 2-5 deliveries, while 14.5% had six or more deliveries, compared to 28.9% primigravida, highlighting the association of multiparity with dual endocrinopathy in their cohort (p<0.0001).[15] Although Prasad et al mentioned parity distribution (59% primigravida in controls vs. 48% in hypothyroid women), no statistical analysis was performed.[3] The explanation for the observed trend in previous studies could relate to the cumulative endocrine burden associated with successive pregnancies, which may predispose multigravida women to metabolic dysregulation, insulin resistance, and thyroid dysfunction. Repeated pregnancies might also be associated with delayed maternal age, another known risk factor for GDM and hypothyroidism. However, the lack of statistical association in the present study may reflect the sample size, population characteristics, or differing inclusion criteria, thereby indicating that while multiparity may influence endocrine risk in pregnancy, its role is likely context-dependent and multifactorial.

In the present study, a markedly high proportion of hypothyroid pregnant women 80% developed gestational diabetes mellitus (GDM), compared to only 20% among euthyroid women. This statistically highly significant association ($p<0.001$) indicates a robust link between maternal hypothyroidism and the development of GDM, suggesting the possibility of a clinically relevant dual endocrinopathy during pregnancy. Several previous studies have reported similar associations. Divakar et al observed that 82.7% of women diagnosed with GDM were also hypothyroid ($p<0.0001$), supporting the hypothesis of their frequent coexistence.[2] Gong et al, through a comprehensive meta-analysis, demonstrated an elevated risk of GDM in women with both subclinical (OR = 1.558; 95% CI: 1.292-1.877) and overt hypothyroidism (OR = 1.892; 95% CI: 1.679-2.132), with a pooled odds ratio of 1.749 ($p<0.001$).[5]

Prasad et al found GDM in 8% of hypothyroid women compared to 1% in euthyroid counterparts ($p=0.0349$).[3] Yang et al further investigated this link and noted that GDM incidence significantly decreased from 17.25% to 11.62% across increasing FT4 quartiles ($p<0.0001$), indicating an inverse correlation between FT4 levels and GDM risk.[13] In terms of prevalence, Parveen et al reported hypothyroidism among 33.3% of women with GDM, closely approximating the findings of the current study.[16] Nevertheless, the broader literature aligns with the present findings. Fatima et al demonstrated a significant positive correlation between elevated TSH levels and maternal glucose concentrations, reinforcing the notion that even subclinical hypothyroidism may disrupt glucose metabolism.[14] A meta-analysis involving ten cohort studies also found that GDM risk increased significantly when TSH levels exceeded 4.0 mIU/L, regardless of thyroid autoantibody status. Interestingly, when TSH was below 4.0 mIU/L, GDM risk appeared influenced by the presence of thyroid autoantibodies, suggesting a potential immunological mechanism. Collectively, this body of evidence underscores the clinical significance of early pregnancy thyroid function screening. Early identification of hypothyroidism in pregnancy could serve as a preventive strategy to mitigate GDM risk, allowing timely intervention and potentially improving both maternal and fetal outcomes.

In the present study, gestational age at the time of delivery was stratified into three categories: 32-36 weeks, >36-40 weeks, and >40 weeks. The majority of euthyroid non-GDM, euthyroid GDM, and hypothyroid non-GDM women delivered at term (>36-40 weeks). However, 35.0% of hypothyroid GDM women delivered preterm between 32-36 weeks, which was the highest among all groups. The mean gestational age was lowest in the hypothyroid GDM group (37.33±2.06 weeks), followed by euthyroid GDM (38.30±0.48 weeks), hypothyroid non-GDM (38.80±1.40 weeks), and highest in euthyroid non-GDM (38.97±1.22 weeks). This difference in gestational age categories was found to be statistically significant ($p = 0.003$). These findings suggest that coexistent hypothyroidism and GDM may predispose women to a higher risk of preterm delivery. The observations from the present study are supported by Yang et al noted an increasing incidence of GDM with earlier gestation at diagnosis and delivery.[13] Tirosh et al, who reported that women with dual endocrinopathy had a mean gestational age of 38.3±2.3 weeks, significantly lower than 39.2±2.3 weeks in healthy pregnancies ($p<0.0001$), with 14.0% of them delivering preterm.[15] Similarly, Amudha et al recorded 18.8% preterm births in the group with both diabetes and hypothyroidism.[17] Sahu et al also found a higher incidence of preterm labor and intrauterine growth restriction in overt hypothyroid women.[18] These findings collectively emphasize that dual endocrinopathy may interfere with the normal gestational course, potentially through mechanisms such as placental insufficiency, endocrine imbalance, or heightened obstetric risk, leading to early onset of labour or medically indicated preterm delivery.

The present study's statistically significant association between lower gestational age and hypothyroid GDM status reinforces the necessity for enhanced prenatal surveillance and timely intervention in such high-risk pregnancies.

In the present study, mode of delivery differed significantly across the groups, with the highest cesarean section (LSCS) rate observed among hypothyroid GDM women (72.5%), compared to 55.0% in hypothyroid non-GDM, 45.0% in euthyroid GDM, and 45.0% in euthyroid non-GDM groups. Vaginal delivery was most common in euthyroid non-GDM women (55.0%) and least in hypothyroid GDM women (27.5%). The association between mode of delivery and endocrine status was statistically significant ($p=0.009$), indicating that dual endocrinopathy substantially increases the likelihood of operative delivery. This finding is well supported by previous studies. Tirosh et al demonstrated that 44.4% of women with both hypothyroidism and diabetes underwent cesarean section, which was significantly higher than the general population, and multivariate analysis confirmed dual endocrinopathy as an independent risk factor for cesarean delivery (OR = 3.46).[15]

Amudha et al reported LSCS rates of 48.0% in the dual pathology group, 36.2% in diabetes-only, and 30.8% in hypothyroidism-only groups, highlighting the additive effect of coexistent conditions.[17] Yang et al also showed a significantly increased cesarean rate of 15.46% in GDM women compared to 11.75% in non-GDM women ($p<0.0001$).[13] Sahu et al observed an elevated rate of cesarean section due to fetal distress in subclinical hypothyroid women (24%, $p=0.04$).[18] Parveen et al echoed similar observations in their discussion, attributing increased LSCS rates to complications arising from dual endocrinopathy.[16] The elevated cesarean rates observed in hypothyroid GDM pregnancies can be attributed to several factors.

These include poor glycemic control, fetal macrosomia, pre-eclampsia, oligohydramnios/polyhydramnios, and a higher incidence of non-reassuring fetal heart rate patterns, all of which are more common in endocrine-compromised pregnancies. Hypothyroidism, by affecting uterine contractility and prolonging labor, further compounds this risk. Collectively, the present study and corroborating evidence from previous studies emphasize the need for careful intrapartum monitoring and individualized delivery planning in high-risk groups such as those with combined GDM and hypothyroidism.

In the present study, a significantly lower APGAR score at 5 minutes was observed in neonates born to mothers with hypothyroid GDM. Notably, 100% of neonates in the hypothyroid GDM group had 5-minute APGAR scores less than 7, with a mean score of 5.20±0.85. In contrast, the mean APGAR score was 7.08±0.89 in the euthyroid non-GDM group, 6.10±0.32 in the euthyroid GDM group, and 6.80±0.63 in the hypothyroid non-GDM group. The difference across groups was found to be highly statistically significant ($p<0.001$), indicating a direct adverse impact of combined gestational diabetes and hypothyroidism on immediate neonatal adaptation. Among the previous studies, Sahu et al reported that the percentage of neonates with low APGAR scores (<7 at 1 minute) was 12.9% in subclinical hypothyroid, 11.1% in overt hypothyroid, and 5.3% in the control group.[18] Though this trend was not statistically significant, it indicated poorer neonatal outcomes in hypothyroid pregnancies. Similarly, Tirosh et al documented that 1.8% of neonates in the combined hypothyroid and diabetic group had 5-minute APGAR scores <7, although the comparison did not reach statistical significance.[15]

The low APGAR scores seen in hypothyroid GDM pregnancies may be explained by several interrelated pathophysiological mechanisms. Hypothyroidism is associated with impaired placental function, reduced uteroplacental perfusion, and fetal hypoxia, while GDM contributes to macrosomia, metabolic acidosis, and delayed lung maturity, increasing the likelihood of birth asphyxia. The combination of these endocrine disorders may potentiate perinatal compromise, leading to poor neonatal responsiveness immediately after birth. The significantly lower scores in the present study, when compared to the more modest trends seen in previous studies, may be due to differences in sample size, population characteristics, or neonatal resuscitation protocols. Nonetheless, the cumulative evidence suggests that coexisting GDM and hypothyroidism pose a tangible risk to neonatal vitality, underscoring the importance of timely screening, intra-partum monitoring, and neonatal support in such high-risk deliveries.

In the present study, maternal comorbidities were significantly more prevalent among women with hypothyroid GDM. Only 7.5% of these women had no comorbidities, compared to 67.5% in the euthyroid non-GDM group, indicating a stark difference. The most common comorbidities observed in the hypothyroid GDM group were anaemia (30.0%), preterm delivery (25.0%), gestational hypertension (10.0%), preeclampsia (10.0%), and Oligohydramnios (5.0%), with a highly significant association ($p<0.001$). In contrast, in the euthyroid non-GDM group, 67.5% had no comorbidities, and the remainder had minimal isolated conditions, underlining the compounded risk imposed by dual endocrinopathy. These findings are supported by several previous studies. Parveen et al also acknowledged the presence of gestational complications like preeclampsia, abruption, and preterm labour among women with thyroid dysfunction and GDM, although without quantification.[16] Tirosh et al reported significantly higher rates of preeclampsia (14.0%), chronic hypertension (11.1%), infertility treatment (11.1%), and history of abortions (8.8%) in women with coexisting diabetes and hypothyroidism.[15] Similarly, Amudha et al documented high rates of severe preeclampsia (28.6%), gestational hypertension (14.3%), polyhydramnios (35.7%), placental abruption (21.4%), and PPH (32%) in the dual endocrinopathy group.[17] Sahu et al observed a strong association between overt hypothyroidism and pregnancy-induced hypertension (20.7%, $p=0.04$).[18]

The higher burden of maternal comorbidities in hypothyroid GDM pregnancies may be attributed to shared pathophysiological mechanisms, including endothelial dysfunction, oxidative stress, and chronic low-grade inflammation, all of which predispose to hypertensive disorders, anaemia, and placental abnormalities. Additionally, both conditions independently affect vascular function and uteroplacental perfusion, further escalating obstetric risk. Hence, the present study, consistent with the evidence from previous studies, underscores the compounded morbidity risk when GDM coexists with thyroid dysfunction, necessitating comprehensive antenatal care and timely intervention.

In the present study, maternal complications were observed with greater frequency in the hypothyroid GDM group (62.5%). Among these women, only 37.5% had no complications, compared to 77.5% in euthyroid non-GDM, 60.0% in euthyroid GDM, and 20% in hypothyroid non-GDM groups. The most frequently noted maternal complications in the hypothyroid GDM group were preterm delivery (22.5%), atonic postpartum haemorrhage (20.0%), severe preeclampsia (10.0%), and placental abruption (5.0%), with the group showing a statistically significant difference in maternal complication rates ($p=0.003$).[12] These findings emphasize the heightened risk of maternal morbidity when gestational diabetes mellitus coexists with thyroid dysfunction. Several previous studies echo these findings. Parveen et al also discussed a higher prevalence of complications like preeclampsia and abruption in women with dual endocrinopathy.[16] Tirosh et al reported that 14.0% of women with dual endocrinopathy had preeclampsia, and noted increased rates of labour induction (39.2%) and amniotic fluid infection (1.8%).[15] Amudha et al found severe preeclampsia in 28.6%,

gestational hypertension in 14.3%, placental abruption in 21.4%, and PPH in 32.0% of women with both diabetes and hypothyroidism.[17] Sahu et al found that pregnancy-induced hypertension occurred in 20.7% of overt hypothyroid women (p=0.04) and recorded significant occurrences of IUGR and intrauterine fetal demise, reflecting systemic maternal compromise.[18]

These elevated complication rates can be attributed to the interplay of metabolic, vascular, and hormonal disturbances that occur when GDM and hypothyroidism coexist. Hypothyroidism impairs vascular compliance and endothelial function, while GDM exacerbates placental dysfunction and inflammatory pathways, together increasing the risk of hypertensive disorders, placental separation, and uterine atony. Moreover, hormonal dysregulation can affect myometrial contractility, increasing the risk of hemorrhage. The findings of the present study, supported robustly by data from previous studies, highlight that coexisting GDM and hypothyroidism significantly elevate maternal risk, necessitating early detection, multidisciplinary antenatal management, and preparedness for obstetric complications during delivery.

In the present study, fetal complications were most frequently observed in the hypothyroid GDM group, with only 27.5% of neonates born to these mothers being complication-free, compared to 92.5% in euthyroid non-GDM, 60.0% in euthyroid GDM, and 75.0% in hypothyroid non-GDM groups. The most common complications in the hypothyroid GDM group were respiratory distress syndrome (20.0%), neonatal hypoglycemia (15.0%), intrauterine growth restriction (7.5%), birth asphyxia (5.0%), and meconium aspiration syndrome (2.5%). The difference across groups was statistically significant (p=0.001), indicating that dual endocrinopathy is strongly associated with poor fetal outcomes. The results of the present study are supported by multiple previous studies. Tirosh et al found a significantly higher incidence of adverse fetal outcomes among women with both diabetes and hypothyroidism, reporting low birth weight (<2.5 kg) in 10.5%, small for gestational age (SGA) in 2.3%, and large for gestational age (LGA) in 21.6%. Additionally, preterm births between 32-34 weeks occurred in 2.3%, and fetal mortality in 0.6% of this group.[15] Sahu et al reported IUGR in 13.8% and intrauterine fetal demise (IUFD) in 13% of overt hypothyroid pregnancies (p=0.0004), along with increased neonatal complications.[18] Amudha et al found that 7.1% of women with dual pathology had IUFD, and 17.5% of neonates were macrosomic, indicating both ends of the fetal growth spectrum were affected.[17] Yang et al and Parveen et al also discussed increased fetal compromise in association with maternal endocrinopathies.[13,16] These findings may be attributed to the deleterious effects of both GDM and hypothyroidism on placental function, fetal metabolism, and oxygen delivery. GDM is associated with fetal hyperinsulinemia and altered glucose homeostasis, increasing the risk of macrosomia and neonatal hypoglycemia. Meanwhile, maternal hypothyroidism can impair neuronal development, reduce fetal oxygenation, and contribute to growth restriction. The combined burden of both disorders leads to a high-risk intrauterine environment, with compounded effects on fetal growth, lung maturity, and metabolic regulation. Therefore, as evidenced by the present study and corroborated by previous literature, coexistent GDM and hypothyroidism significantly elevate the risk of fetal morbidity and necessitate enhanced fetal surveillance and timely perinatal care.

In the present study, NICU admissions were markedly higher among neonates born to mothers with hypothyroid GDM. Specifically, 62.5% of neonates in the hypothyroid GDM group required NICU admission, compared to only 10.0% in the hypothyroid non-GDM group, 10.0% in the euthyroid non-GDM group, and 0% in the euthyroid GDM group. This difference was statistically significant (p<0.001), highlighting a strong association between dual endocrinopathy and the need for intensive neonatal care. The majority of NICU admissions in this group were due to respiratory distress, hypoglycemia, prematurity, and birth asphyxia, which are known complications of maternal GDM and hypothyroidism. Among the previous studies, Sahu et al also found that 11.1% of neonates born to overt hypothyroid mothers and 12.9% in the subclinical group required NICU admission, compared to 5.1% in the control group, though statistical significance was noted primarily in the hypothyroid group.[18] Tirosh et al did not explicitly report NICU admission rates, but the high prevalence of preterm births (14.0%), low birth weight (10.5%), and LGA (21.6%) in the dual endocrinopathy group suggests a higher likelihood of NICU requirement.[15]

The elevated NICU admission rates in the present study can be attributed to the synergistic effects of maternal hypothyroidism and gestational diabetes, both of which independently contribute to neonatal complications. Hypothyroidism may impair fetal lung maturation and neurological development, while GDM predisposes to neonatal hypoglycemia, macrosomia, and respiratory distress. The coexistence of these two conditions amplifies fetal vulnerability, necessitating closer postnatal monitoring and intensive care. The findings of the present study, along with supportive evidence from previous studies, underscore the importance of early identification and comprehensive management of endocrine disorders in pregnancy to reduce NICU admissions and improve neonatal outcomes.

The single-centre study methodology maximised internal validity and protocol adherence, delivering foundational, highly robust, and precise estimates for the primary outcome of population prevalence. This methodology is ideally scaled for rigorous and conclusive hypothesis evaluation, establishing validated findings that necessitate future multi-centre studies with expanded cohorts the essential next phase required to comprehensively validate

and expand these high-quality findings across diverse populations.

CONCLUSION

The study conclusively demonstrates a strong association between first-trimester hypothyroidism and the subsequent development of gestational diabetes mellitus (GDM) [80%], thereby emphasizing the occurrence of GDM among hypothyroid pregnant women. The coexistence of hypothyroidism and gestational diabetes mellitus (GDM) is a clinically significant entity in pregnancy, associated with a spectrum of maternal and neonatal complications. Thus, early recognition of modifiable risk factors remains pivotal in mitigating these risks. Integration of pre-conception counselling with universal early screening strategies for thyroid as well as for GDM can facilitate timely diagnosis and intervention. A multidisciplinary approach encompassing obstetricians, endocrinologists, physicians, and neonatologists is essential for delivering holistic care and hence plays a key role in optimising maternal and neonatal outcomes.

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