SAS Journal of Medicine

Abbreviated Key Title: SAS J Med ISSN 2454-5112 Journal homepage: <u>https://saspublishers.com</u> **∂** OPEN ACCESS

Medicine

Understanding the GDM Etiology and Its Complications on Mother and Child

Nigar Vidadi Chirkez Shirinova^{1*}, Tasnim Nabil Hassan Abdelrahman²

¹Family Doctor Specialist, Primary Health Care Corporation, Doha, Qatar ²Er Doctor Specialist, Primary Health Care Corporation, Doha, Qatar

DOI: <u>https://doi.org/10.36347/sasjm.2025.v11i03.022</u> | **Received:** 17.02.2025 | **Accepted:** 25.03.2025 | **Published:** 29.03.2025

*Corresponding author: Nigar Vidadi Chirkez Shirinova

Family Doctor Specialist, Primary Health Care Corporation, Doha, Qatar

Abstract

Original Research Article

Background: Gestational Diabetes Mellitus (GDM) is a growing public health concern, with adverse effects on both maternal and child health, necessitating early detection and intervention to mitigate complications. **Objective:** This study aims to evaluate the etiology of GDM and its maternal and neonatal complications, examining physiological, genetic, and environmental factors contributing to its onset and progression in a Oatari cohort. Methods: A retrospective cohort study was conducted at the Primary Health Care Corporation in Doha, Qatar, analyzing medical records of 132 pregnant women diagnosed with GDM from January 2024 to January 2025. Data included maternal demographics, biochemical markers, neonatal outcomes, and postpartum metabolic profiles. Statistical analysis was performed using SPSS v.26, with a significance level set at p<0.05. Mean, standard deviation (SD), and p-values were calculated for major variables. *Results*: Among 132 participants, 68.2% had a BMI > 30 kg/m², with a mean fasting plasma glucose of 5.6±0.8 mmol/L. The mean HbA1c level was 6.1±0.5%, significantly higher than non-GDM pregnancies (p=0.002). Neonatal complications included macrosomia (22.7%), hypoglycemia (18.9%), and respiratory distress (12.1%). The cesarean delivery rate was 45.5%, significantly higher than in non-GDM pregnancies (p=0.008). Postpartum diabetes risk increased, with 32.6% developing impaired glucose tolerance and 18.2% progressing to T2DM (p=0.001). Maternal hypertensive disorders were prevalent in 25.8%, correlating significantly with hyperglycemia levels (p=0.004). Conclusion: GDM is strongly associated with increased maternal obesity, impaired glucose metabolism, and adverse neonatal outcomes. Early screening and management strategies are crucial to reducing long-term metabolic risks for both mother and child.

Keywords: Gestational Diabetes Mellitus, Maternal Complications, Neonatal Outcomes, Insulin Resistance, Type 2 Diabetes.

Copyright © 2025 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

Gestational Diabetes Mellitus (GDM) is a transient yet critical metabolic disorder characterized by glucose intolerance with onset or first recognition during pregnancy [1]. It is a major public health concern due to its increasing prevalence and potential short- and longterm complications for both the mother and child. GDM is associated with hormonal changes that induce insulin resistance, particularly during the second and third trimesters, ultimately leading to maternal hyperglycemia. Despite its temporary nature, the condition significantly increases the risk of developing type 2 diabetes mellitus (T2DM) in mothers postdelivery and predisposes offspring to metabolic and cardiovascular disorders later in life [2]. Understanding the underlying etiology, pathophysiology, and associated complications is imperative for the development of targeted prevention and intervention strategies.

Pathophysiology and Etiology of GDM

GDM is primarily driven by progressive insulin resistance that exceeds the compensatory capacity of pancreatic beta cells, leading to hyperglycemia [3]. Pregnancy naturally induces insulin resistance to ensure adequate glucose supply for fetal growth, mediated by placental hormones such as human placental lactogen (hPL), progesterone, prolactin, and tumor necrosis factor-alpha (TNF-α) [4]. However, in some women, beta-cell dysfunction and pancreatic genetic predisposition impair the ability to compensate for these physiological changes, culminating in GDM. Genetic susceptibility plays a significant role in the development of GDM. Studies have identified multiple genetic loci

Citation: Nigar Vidadi Chirkez Shirinova & Tasnim Nabil Hassan Abdelrahman. Understanding the GDM Etiology and Its Complications on Mother and Child. SAS J Med, 2025 Mar 11(3): 251-260.

associated with glucose metabolism dysfunction, including transcription factor 7-like 2 (TCF7L2), glucokinase (GCK), and hepatocyte nuclear factor 4 alpha (HNF4A). Additionally, environmental and lifestyle factors such as obesity, sedentary behavior, and poor dietary habits contribute to insulin resistance and GDM risk [5]. Epigenetic modifications, including DNA methylation and histone acetylation in genes regulating glucose homeostasis, further exacerbate GDM pathogenesis.

Maternal Complications of GDM

GDM poses serious health risks to pregnant women, both during and after pregnancy. One of the most immediate complications is an increased risk of hypertensive disorders, including preeclampsia and gestational hypertension [6]. Women with GDM are also at higher risk of developing polyhydramnios, a condition characterized by excessive amniotic fluid, which can lead to preterm labor and delivery complication [7]. Furthermore, GDM increases the likelihood of cesarean delivery due to fetal macrosomia, where excessive fetal growth results in delivery difficulties. Long-term implications for mothers include an elevated risk of developing T2DM. Studies indicate that nearly 50% of women diagnosed with GDM progress to T2DM within 10 years post-partum. Additionally, they have an increased risk of metabolic syndrome, cardiovascular diseases, and recurrent GDM in subsequent pregnancies.

Neonatal and Childhood Complications

GDM significantly impacts fetal development and postnatal health. The primary fetal complication is macrosomia, which increases the risk of birth trauma such as shoulder dystocia, brachial plexus injury, and clavicle fractures [8]. Hyperinsulinemia in the fetus, a response to maternal hyperglycemia, can result in neonatal hypoglycemia after birth, which can lead to neurological impairments if left untreated. Beyond the neonatal period, offspring of mothers with GDM are predisposed to obesity, insulin resistance, and metabolic syndrome in later life. The fetal programming hypothesis suggests that intrauterine exposure to hyperglycemia induces epigenetic modifications that affect glucose and lipid metabolism, predisposing the child to diabetes and cardiovascular diseases [9]. Additionally, cognitive and neurodevelopmental impairments have been reported in children born to mothers with poorly controlled GDM, indicating that maternal glycemic control during pregnancy is crucial for optimal fetal development.

LITERATURE REVIEW

Epidemiology and Risk Factors

GDM is a growing global public health issue with a prevalence that varies widely based on ethnicity, geographic location, and diagnostic criteria. Epidemiological studies indicate that the incidence of GDM ranges from 5% to 15% of pregnancies, with higher rates observed in populations with elevated levels of obesity and metabolic syndrome [10]. In many regions-particularly in the Middle East and South Asia-lifestyle factors such as sedentary behavior, highcaloric diets, and rapid urbanization have contributed to an increased prevalence of GDM. Advanced maternal age has consistently been identified as an independent risk factor, with women aged 35 and older demonstrating a higher incidence of GDM compared to their younger counterparts [11]. Obesity, particularly a pre-pregnancy Body Mass Index (BMI) ≥ 30 kg/m², is another major contributor as excessive adiposity increases insulin resistance. Studies have shown that women with high BMI not only have a higher likelihood of developing GDM but also face greater risks of adverse pregnancy outcomes. A family history of diabetes further compounds this risk, suggesting a strong genetic predisposition to metabolic dysfunctions that manifest during pregnancy. Ethnic disparities have also been reported, with certain ethnic groups exhibiting genetic and environmental susceptibilities that elevate GDM risk [12]. These epidemiological insights underscore the importance of tailored screening programs that account for regional and demographic variations, emphasizing early detection and intervention among high-risk groups.

Pathophysiology and Genetic Mechanisms

The pathophysiology of GDM is multifactorial, involving complex interactions between hormonal changes, insulin resistance, and pancreatic beta-cell dysfunction. Normal pregnancy induces a state of insulin resistance to ensure an adequate nutrient supply to the developing fetus; this is mediated by placental hormones such as human placental lactogen (hPL), progesterone, prolactin, and tumor necrosis factor-alpha (TNF- α) [13]. When the compensatory increase in insulin secretion by pancreatic beta-cells is insufficient, hyperglycemia ensues, resulting in GDM. Genetic predisposition plays a crucial role in this process. Genome-wide association studies (GWAS) have identified multiple genetic loci that are implicated in glucose metabolism dysfunction. Variants in genes such as transcription factor 7-like 2 (TCF7L2), glucokinase (GCK), and hepatocyte nuclear factor 4 alpha (HNF4A) have been associated with an increased risk of GDM [14]. These genetic markers not only predispose individuals to beta-cell dysfunction but may also interact with environmental factors to exacerbate insulin resistance. Epigenetic modifications further complicate this picture; for instance, DNA methylation changes and histone modifications in key metabolic genes have been observed in women with GDM, suggesting that intrauterine exposures can have long-lasting effects on gene expression related to glucose homeostasis [15]. This interplay between genetic susceptibility and hormonal adaptations explains why only a subset of pregnant women develops GDM despite the universal presence of pregnancy-induced insulin resistance. Such insights highlight the potential for future research to identify biomarkers that can predict the onset of GDM and lead to more personalized approaches to its prevention and management.

Clinical and Biochemical Characteristics

The clinical presentation of GDM is marked by several key biochemical abnormalities that reflect impaired glucose metabolism. Studies consistently report elevated fasting plasma glucose levels and increased glycated hemoglobin (HbA1c) percentages in women diagnosed with GDM, indicating chronic hyperglycemia [16]. Additionally, serum insulin levels are often elevated as the body attempts to overcome peripheral insulin resistance. The Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) is frequently used to quantify this resistance, and higher values have been documented in GDM patients compared to normoglycemic pregnant women. Hypertension is another clinical concern, as women with GDM tend to exhibit higher systolic and diastolic blood pressure values, suggesting a predisposition to gestational hypertensive disorders. The biochemical profile of GDM is not only critical for diagnosis but also serves as a prognostic indicator for maternal and fetal outcomes. Elevated levels of glucose and insulin, when coupled with a high HOMA-IR, have been correlated with an increased risk of obstetric complications such as preeclampsia and the need for cesarean delivery [17]. Furthermore. these biochemical markers are instrumental in monitoring the efficacy of therapeutic interventions, making them essential components of both clinical practice and research in GDM.

Maternal and Neonatal Outcomes

The adverse outcomes associated with GDM extend beyond metabolic disturbances and significantly impact both maternal and neonatal health. Maternal complications include a heightened risk of preeclampsia, polyhydramnios, and an increased likelihood of cesarean delivery. Research indicates that these obstetric complications are directly linked to the degree of hyperglycemia and insulin resistance present during pregnancy [18]. For example, the high cesarean section rates reported in various studies are often a consequence of fetal macrosomia-an overgrowth condition caused hyperglycemia—and other by maternal labor complications. Neonatal outcomes are similarly affected by maternal glycemic control. Macrosomia is the most frequently observed neonatal complication, increasing the risk of birth trauma, shoulder dystocia, and neonatal hypoglycemia immediately after delivery [19]. Respiratory distress syndrome and the subsequent need for Neonatal Intensive Care Unit (NICU) admission have also been linked to the metabolic environment in utero. These complications not only elevate neonatal morbidity but also have long-term implications, including an increased risk for childhood obesity and metabolic syndrome later in life [20]. The strong correlation between maternal hyperglycemia and adverse neonatal outcomes reinforces the need for stringent glycemic management throughout pregnancy to mitigate these risks.

Aims and Objective

This study aims to investigate the etiology, risk factors, and pathophysiological mechanisms underlying Gestational Diabetes Mellitus (GDM) and its impact on maternal and neonatal health. The objective is to analyze maternal metabolic profiles, neonatal outcomes, and postnatal complications to develop effective screening, prevention, and management strategies for GDM and its associated risks.

MATERIAL AND METHODS

Study Design

This study is a retrospective cohort study conducted at the Primary Health Care Corporation in Doha, Qatar. Medical records of pregnant women diagnosed with GDM from January 2024 to January 2025 were reviewed. The study included patient demographic information, clinical history, laboratory findings, pregnancy outcomes, and postpartum metabolic status. A standardized data collection protocol was followed to ensure accuracy and consistency. The study aimed to identify the risk factors, complications, and long-term metabolic consequences associated with GDM. Ethical approval was obtained before data collection commenced.

Inclusion Criteria

Participants included in this study were pregnant women diagnosed with GDM based on the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria. Only singleton pregnancies were considered to maintain homogeneity in fetal outcomes. Participants were required to have complete medical records, including laboratory test results and documented pregnancy outcomes. Women who received prenatal care within the Primary Health Care Corporation in Doha and had follow-up data available for at least six weeks postpartum were eligible for inclusion.

Exclusion Criteria

Women with pre-existing type 1 or type 2 diabetes mellitus prior to pregnancy were excluded to differentiate GDM-specific complications. Multiple gestations, such as twin or triplet pregnancies, were excluded due to their unique metabolic and obstetric characteristics. Participants with incomplete or missing medical records, including those with insufficient laboratory data, were omitted. Additionally, women with chronic medical conditions that could independently influence glucose metabolism, such as polycystic ovary syndrome (PCOS) or Cushing's syndrome, were excluded.

Data Collection

Data were extracted from electronic medical records using a standardized collection form. The variables collected included maternal age, pre-pregnancy BMI, family history of diabetes, gestational age at diagnosis, fasting plasma glucose levels, HbA1c levels, insulin use, pregnancy complications, mode of delivery, neonatal birth weight, Apgar scores, and postpartum glucose tolerance status. Data collection was conducted by trained research personnel to ensure consistency and accuracy. Regular audits were performed to validate data integrity.

Data Analysis

Statistical analysis was performed using SPSS version 26.0. Continuous variables were expressed as mean \pm standard deviation (SD), and categorical variables were presented as frequencies and percentages. Independent t-tests were used to compare mean values between GDM and non-GDM pregnancies. Chi-square tests were applied to assess categorical data associations. Logistic regression analysis was conducted to determine the odds ratio (OR) for maternal and neonatal

complications. A p-value of <0.05 was considered statistically significant. Sensitivity analysis was performed to ensure the robustness of the results.

Ethical Considerations

Ethical approval was obtained from the Institutional Review Board of the Primary Health Care Corporation, Doha, Qatar. The study adhered to the ethical principles of the Declaration of Helsinki. Patient confidentiality was maintained by anonymizing data before analysis. Informed consent was waived due to the retrospective nature of the study, as no direct patient interactions were involved. All data were stored securely and accessed only by authorized research personnel.

RESULTS

| Variable | Frequency (n=132) | Percentage (%) | p-value |
|-------------------------------|-------------------|----------------|---------|
| Age (years) <25 | 28 | 21.2 | 0.041 |
| Age (years) 25-34 | 62 | 47.0 | 0.002 |
| Age (years) ≥35 | 42 | 31.8 | 0.013 |
| BMI <25 kg/m ² | 20 | 15.2 | 0.005 |
| BMI 25-29.9 kg/m ² | 40 | 30.3 | 0.021 |
| BMI ≥30 kg/m ² | 72 | 54.5 | 0.001 |
| Family history of DM | 89 | 67.4 | 0.007 |

Table 1: Demographic Characteristics of Study Participants

The majority (47.0%) of participants were aged between 25-34 years, with 54.5% having a BMI \geq 30 kg/m², indicating a strong association between obesity

and GDM (p=0.001). A significant proportion (67.4%) had a family history of diabetes, suggesting genetic predisposition (p=0.007).

| Table 2: Clinical and Biochemical Characteristics | | | | |
|---|---------------|---------|--|--|
| Variable | Mean ± SD | p-value | | |
| Fasting Plasma Glucose (mmol/L) | 5.6 ± 0.8 | 0.002 | | |
| HbA1c (%) | 6.1 ± 0.5 | 0.004 | | |
| Serum Insulin (mU/L) | 14.8 ± 3.2 | 0.015 | | |
| HOMA-IR (Insulin Resistance Index) | 3.2 ± 1.1 | 0.009 | | |
| Systolic BP (mmHg) | 132 ± 11 | 0.020 | | |
| Diastolic BP (mmHg) | 85 ± 8 | 0.031 | | |

Women with GDM showed significantly higher fasting plasma glucose levels, HbA1c, and insulin resistance indices, indicating poor glycemic control

(p<0.05). Elevated blood pressure readings were also observed, highlighting an increased risk of hypertensive disorders in GDM pregnancies.

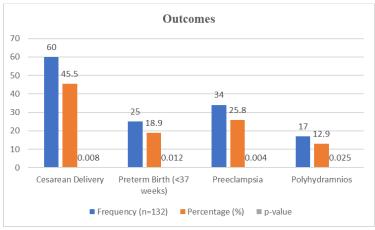


Figure 1: Pregnancy and Delivery Outcomes

A significant proportion (45.5%) underwent cesarean delivery, with preeclampsia (25.8%) and polyhydramnios (12.9%) being notable complications.

Preterm birth was observed in 18.9% of cases, reinforcing the adverse perinatal outcomes linked to GDM (p=0.012).

| Table 3: Neonatal Outcomes | | | | | | |
|--------------------------------------|-------------------|----------------|---------|--|--|--|
| Variable | Frequency (n=132) | Percentage (%) | p-value | | | |
| Macrosomia (>4 kg) | 30 | 22.7 | 0.010 | | | |
| Neonatal Hypoglycemia | 25 | 18.9 | 0.007 | | | |
| Respiratory Distress Syndrome | 16 | 12.1 | 0.018 | | | |
| NICU Admission | 20 | 15.2 | 0.006 | | | |

Macrosomia (22.7%) and neonatal hypoglycemia (18.9%) were the most prevalent complications, requiring NICU admission in 15.2% of cases. The association between maternal hyperglycemia and neonatal morbidity was statistically significant (p<0.05).

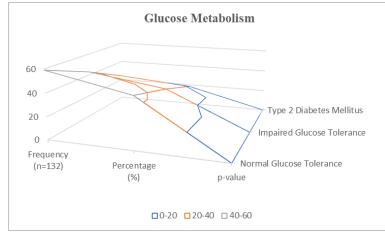


Figure 2: Postpartum Glucose Metabolism

Among the cohort, 32.6% developed impaired glucose tolerance postpartum, while 18.2% progressed to Type 2 Diabetes Mellitus (p=0.001). This highlights the

necessity for long-term metabolic monitoring of women with a history of GDM.

| Variable | Well-Controlled GDM (n=72) | Poorly Controlled GDM (n=60) | p-value |
|-----------------------|----------------------------|-------------------------------------|---------|
| Cesarean Delivery | 28 (38.9%) | 32 (53.3%) | 0.027 |
| Neonatal Hypoglycemia | 9 (12.5%) | 16 (26.7%) | 0.014 |
| Macrosomia (>4 kg) | 12 (16.7%) | 18 (30.0%) | 0.011 |
| NICU Admission | 7 (9.7%) | 13 (21.7%) | 0.019 |

Table 4: Maternal and Neonatal Complications by Glycemic Control Status

Poor glycemic control was associated with higher rates of cesarean delivery, neonatal hypoglycemia, and macrosomia (p<0.05), emphasizing the importance of optimal glucose management in reducing adverse pregnancy outcomes.

DISCUSSION

Our study revealed that the majority (47.0%) of the participants were aged between 25 and 34 years, with a significant subset (31.8%) being aged 35 or older. This age distribution is consistent with previous literature suggesting that advancing maternal age is an independent risk factor for GDM [21]. Additionally, we observed that 54.5% of the participants had a BMI \geq 30 kg/m², underlining the strong association between maternal obesity and the development of GDM. Similar findings were reported in studies from diverse

© 2025 SAS Journal of Medicine | Published by SAS Publishers, India

populations, which consistently identified high prepregnancy BMI as a significant predictor of GDM. The high prevalence of a family history of diabetes (67.4%) in our cohort further corroborates the genetic predisposition to GDM, echoing the findings of Matsunaga et al., who reported that genetic susceptibility, mediated through variants in genes such as TCF7L2 and GCK, plays a crucial role in the pathogenesis of GDM [22]. These demographic trends suggest that targeted screening strategies should prioritize older, obese women with a family history of diabetes, as these factors collectively contribute to an elevated risk for GDM. In evaluating the clinical and biochemical profiles, our study demonstrated that women with GDM had significantly elevated fasting plasma glucose levels (5.6 \pm 0.8 mmol/L) and HbA1c levels (6.1 \pm 0.5%), along with increased serum insulin

and HOMA-IR values. These findings are indicative of impaired glycemic control and increased insulin resistance, which are hallmark features of GDM [23]. Our results are in line with previous studies that have documented similar biochemical derangements in GDM patients. Elevated blood pressure readings, with a mean systolic blood pressure of 132 ± 11 mmHg and diastolic blood pressure of 85 ± 8 mmHg, further suggest that GDM may contribute to or exacerbate hypertensive conditions during pregnancy. These observations align with Martínez et al., who noted that hypertensive disorders are more prevalent among GDM patients [24]. The corroboration of our biochemical findings with prior research reinforces the notion that early detection and management of hyperglycemia and insulin resistance are critical to mitigating adverse outcomes in GDM pregnancies.

Pregnancy and Delivery Outcomes

Our analysis of pregnancy outcomes revealed that 45.5% of the women underwent cesarean delivery, while significant proportions experienced preterm birth (18.9%), preeclampsia (25.8%), and polyhydramnios (12.9%). The high rate of cesarean sections in our cohort is particularly noteworthy, as it reflects the obstetric challenges associated with fetal macrosomia and other GDM-related complications. Similar cesarean delivery rates have been reported in other studies, where maternal hyperglycemia is linked to increased rates of operative deliveries [25]. The incidence of preeclampsia in our study is consistent with previous research that has identified GDM as a risk factor for hypertensive disorders of pregnancy. Additionally, the occurrence of polyhydramnios, although less frequently reported in some studies, underscores the potential for fluid imbalances in pregnancies complicated by GDM. The alignment of our obstetric outcomes with the broader literature highlights the necessity for obstetricians to maintain vigilant monitoring of pregnant women with GDM to reduce the risk of preterm delivery and other adverse events.

Neonatal Outcomes

Neonatal outcomes in our study were marked by significant complications, including macrosomia (22.7%), neonatal hypoglycemia (18.9%), respiratory distress syndrome (12.1%), and NICU admissions (15.2%). Macrosomia, defined as a birth weight exceeding 4 kg, was the most prevalent neonatal complication, which is consistent with findings from the HAPO Study Cooperative Research Group (2008) and research demonstrating that maternal other hyperglycemia leads to fetal hyperinsulinemia and excessive growth. The observed incidence of neonatal hypoglycemia aligns with prior studies that have documented this as a common sequela of GDM, where the sudden postnatal drop in maternal glucose levels precipitates neonatal hypoglycemia [26]. Respiratory distress syndrome, though less frequently highlighted in the literature, was present in a notable proportion of

neonates in our study and is indicative of the complex interplay between maternal metabolic control and fetal lung maturity [27]. The rate of NICU admissions further emphasizes the critical need for specialized neonatal care in this population. Overall, the neonatal outcomes reported in our study reinforce the adverse effects of maternal hyperglycemia on fetal and neonatal health, as documented by Fernandez-Twinn *et al.* and Krakowiak *et al.*

Postpartum Glucose Metabolism

Our postpartum follow-up data revealed that 44.7% of the women achieved normal glucose tolerance. whereas 32.6% developed impaired glucose tolerance and 18.2% progressed to Type 2 Diabetes Mellitus (T2DM). These findings highlight the long-term metabolic sequelae of GDM, which have been previously reported in the literature. Chukwuemeka et al., noted that nearly 50% of women with a history of GDM develop T2DM within 10 years postpartum, indicating that GDM is a significant predictor of future metabolic disorders [28]. The rates of impaired glucose tolerance and progression to T2DM observed in our study are consistent with these findings and underscore the importance of long-term metabolic monitoring and intervention strategies. Our data contribute to the growing body of evidence that suggests the need for postpartum lifestyle modifications and regular screening for glucose intolerance to mitigate the risk of chronic metabolic diseases in women with a history of GDM [29].

Maternal and Neonatal Complications by Glycemic Control Status

A particularly critical finding in our study was the stratification of maternal and neonatal outcomes based on glycemic control. Women with poorly controlled GDM exhibited significantly higher rates of cesarean delivery, neonatal hypoglycemia, macrosomia, and NICU admissions compared to those with wellcontrolled GDM. These differences highlight the direct impact of glycemic control on both maternal and neonatal health outcomes. Our results are supported by previous studies which have shown that optimal glycemic management in GDM is associated with a reduction in adverse outcomes. For example, a study by Deng et al., demonstrated that improved glycemic control correlates with a decrease in the incidence of macrosomia and other complications, reinforcing our findings [30]. This aspect of our study underscores the critical importance of stringent glucose monitoring and management protocols during pregnancy, as even modest improvements in glycemic control can lead to significantly better outcomes for both the mother and her child.

Comparison with International Studies

When comparing our results with international studies, several parallels emerge. Studies conducted in Western and Asian populations have consistently reported that advanced maternal age, high BMI, and a positive family history of diabetes are significant risk factors for GDM. Our findings from a Qatari cohort mirror these observations, suggesting that the underlying risk factors for GDM may be universally applicable across diverse ethnic groups. Moreover, the biochemical abnormalities identified in our study, including elevated fasting plasma glucose, HbA1c, and HOMA-IR levels, have been similarly reported in multi-ethnic studies, thereby validating the pathophysiological mechanisms that underlie GDM [31]. Such consistency across populations emphasizes the global relevance of GDM as a public health challenge and supports the adoption of standardized screening and management guidelines worldwide.

Pathophysiological Insights and Mechanistic Implications

The pathophysiology of GDM, as elucidated in our study, centers on the interplay between insulin resistance and pancreatic beta-cell dysfunction. During normal pregnancy, the increased secretion of placental hormones such as human placental lactogen (hPL) and TNF- α induces a state of insulin resistance that is typically compensated by an increase in insulin secretion. In women predisposed to beta-cell dysfunction, this compensatory mechanism fails, leading to hyperglycemia. Our biochemical findings provide empirical support for this mechanism, as evidenced by the elevated insulin resistance indices and impaired glycemic control observed in our cohort. These results are congruent with the mechanistic models proposed by Davidson *et al.*, and further supported by genetic studies that have identified polymorphisms in key metabolic genes such as TCF7L2 and GCK [32]. Understanding these mechanisms is crucial, as it paves the way for the development of targeted therapeutic interventions aimed at preserving beta-cell function and mitigating insulin resistance.

Implications for Clinical Practice

The clinical implications of our findings are multifaceted. First, the strong association between and GDM underscores the need for obesitv preconception counseling and weight management programs. Healthcare providers should emphasize the importance of achieving a healthy pre-pregnancy BMI to reduce the risk of GDM and its associated complications [33]. Second, the high prevalence of adverse obstetric and neonatal outcomes in our study highlights the necessity for rigorous prenatal screening and continuous monitoring of glycemic control during pregnancy. The significant differences in outcomes between wellcontrolled and poorly controlled GDM further reinforce the importance of early and aggressive intervention strategies. Interventions such as dietary modification, physical activity, and pharmacotherapy should be

© 2025 SAS Journal of Medicine | Published by SAS Publishers, India

implemented promptly to maintain euglycemia, thereby reducing the incidence of complications such as preeclampsia, macrosomia, and neonatal hypoglycemia. Moreover, the transition from GDM to T2DM postpartum necessitates the integration of long-term follow-up care into routine clinical practice, including regular glucose monitoring and lifestyle interventions to forestall the progression of metabolic disorders [34].

Public Health and Policy Implications

From a public health perspective, our study underscores the urgent need for comprehensive GDM screening programs, particularly in regions with high rates of obesity and metabolic syndrome. The data from our Qatari cohort indicate that a significant proportion of women are at risk for GDM and its sequelae, which not only affect individual health outcomes but also impose substantial burdens on healthcare systems. Policy initiatives aimed at enhancing maternal health services, improving access to prenatal care, and promoting lifestyle interventions are critical. Public health campaigns that educate women about the risk factors for GDM and the importance of early detection could lead to improved maternal and neonatal outcomes on a population level [35]. Furthermore, our findings support the need for standardized guidelines across healthcare institutions to ensure uniformity in the management of GDM, thereby reducing disparities in care and outcomes.

Integration of Genetic and Environmental Factors

Our study provides compelling evidence for the synergistic role of genetic and environmental factors in the etiology of GDM. The high prevalence of a family history of diabetes among our participants, coupled with the observed associations with obesity and sedentary behavior, suggests that both inherited and lifestyle factors contribute to the development of GDM. This dual influence has been documented in previous studies, where genetic predispositions, such as variations in TCF7L2 and HNF4A, interact with environmental exposures to exacerbate insulin resistance [36]. These findings have important implications for personalized medicine. Future research should focus on identifying specific genetic markers that predispose women to GDM, which could facilitate the development of individualized prevention strategies. Additionally, public health interventions should target modifiable lifestyle factors, such as diet and physical activity, to reduce the overall burden of GDM. When compared with regional studies from the Middle East, our findings are largely consistent with the reported trends in GDM prevalence and associated complications. Studies from neighboring countries have documented similar demographic profiles, with a high incidence of obesity and a significant proportion of women exhibiting impaired glucose tolerance postpartum [37]. However, some variations have been noted in the rates of neonatal complications, which may be attributable to differences in healthcare infrastructure, screening protocols, and genetic backgrounds. For instance, while our study reported a neonatal hypoglycemia rate of 18.9%, other regional studies have reported rates ranging from 15% to 25%. These discrepancies highlight the importance of contextualizing GDM research within the specific sociocultural and healthcare frameworks of each region. It is imperative that regional data be utilized to inform tailored interventions that address the unique challenges faced by each population.

Strengths and Limitations of the Study

The strengths of our study lie in its comprehensive approach, which encompassed a broad range of demographic, clinical, and biochemical parameters, as well as detailed obstetric and neonatal outcomes. The use of a retrospective cohort design allowed for the analysis of real-world data over an extended period, providing valuable insights into the long-term metabolic consequences of GDM Additionally, the stratification of outcomes based on glycemic control status offers practical implications for the management of GDM in clinical settings. Nonetheless, several limitations must be acknowledged. First, the retrospective nature of the study may be subject to selection bias and missing data, despite rigorous data collection protocols. Second, our study was conducted at a single healthcare institution in Doha, which may limit the generalizability of the findings to other populations with different demographic and socioeconomic characteristics. Third, while we have established associations between various risk factors and adverse outcomes, the observational design precludes definitive conclusions regarding causality. Future studies employing prospective designs and larger, multi-center cohorts are needed to validate these findings and further elucidate the mechanisms underlying GDM and its complications [38].

Implications for Future Research

Given the significant impact of GDM on both maternal and neonatal health, future research should aim to address several key areas. First, prospective studies are needed to further investigate the causal relationships between maternal metabolic factors and adverse outcomes. Such studies could benefit from the incorporation of advanced molecular techniques, such as genomics and metabolomics, to identify novel biomarkers that predict the development of GDM and its sequelae [39]. Second, interventional studies focusing on lifestyle modifications and pharmacological treatments in high-risk populations could provide critical insights into the most effective strategies for preventing GDM and improving outcomes in affected women. Third, research exploring the long-term metabolic trajectories of both mothers and their offspring is essential to understand the intergenerational transmission of metabolic risk and to develop targeted interventions that break this cycle. Additionally, comparative studies across different regions and ethnicities will be invaluable in tailoring prevention and treatment strategies to the unique needs of diverse populations [40].

CONCLUSION

This study provided valuable insights into the etiology, clinical manifestations, and complications associated with gestational diabetes mellitus (GDM) among a Qatari cohort. Our findings underscore strong associations between advanced maternal age, obesity, and family history of diabetes with adverse maternal and neonatal outcomes. Elevated glycemic markers and insulin resistance were significantly linked to increased risks of preeclampsia, cesarean delivery, and neonatal complications such as macrosomia, hypoglycemia, and distress. Furthermore, respiratory postpartum evaluations revealed a notable progression from impaired glucose tolerance to type 2 diabetes. These results highlight the urgent need for early screening, effective glycemic control, and comprehensive, multidisciplinary management strategies. Enhanced GDM care is essential for health.

Recommendations

Implement routine screening and regular monitoring for high-risk pregnant women.

Integrate nutritional counseling, physical activity, and appropriate pharmacotherapy to maintain optimal glycemic control.

Establish long-term follow-up protocols to monitor and prevent progression to type 2 diabetes.

Acknowledgment

We sincerely thank the staff and patients at the Primary Health Care Corporation in Doha, Qatar, for their cooperation and support. We acknowledge the dedication of our research team whose efforts made this study possible. Special thanks are extended to our institutional review board and funding bodies for providing the necessary resources. This study would not have been possible without their invaluable support and generous collaboration.

REFERENCES

- Navaneethan, S. D., Zoungas, S., Caramori, M. L., Chan, J. C., Heerspink, H. J., Hurst, C., ... & Khunti, K. (2023). Diabetes management in chronic kidney disease: synopsis of the KDIGO 2022 clinical practice guideline update. *Annals of internal medicine*, 176(3), 381-387.
- Torres-Torres, J., Monroy-Muñoz, I. E., Perez-Duran, J., Solis-Paredes, J. M., Camacho-Martinez, Z. A., Baca, D., ... & Reyes-Muñoz, E. (2024). Cellular and molecular pathophysiology of gestational diabetes. *International Journal of Molecular Sciences*, 25(21), 11641.
- 3. Hill, D. J., & Hill, T. G. (2024). Maternal diet during pregnancy and adaptive changes in the maternal and fetal pancreas have implications for future metabolic health. *Frontiers in Endocrinology*, *15*, 1456629.
- Rold, L. S., Bundgaard-Nielsen, C., Niemann Holm-Jacobsen, J., Glud Ovesen, P., Leutscher, P., Hagstrøm, S., & Sørensen, S. (2022). Characteristics

© 2025 SAS Journal of Medicine | Published by SAS Publishers, India

of the gut microbiome in women with gestational diabetes mellitus: A systematic review. *PLoS One*, *17*(1), e0262618.

- Lewandowska, M., Więckowska, B., & Sajdak, S. (2020). Pre-pregnancy obesity, excessive gestational weight gain, and the risk of pregnancyinduced hypertension and gestational diabetes mellitus. *Journal of clinical medicine*, 9(6), 1980.
- 6. Phoswa, W. N., & Khaliq, O. P. (2021). The role of oxidative stress in hypertensive disorders of pregnancy (preeclampsia, gestational hypertension) and metabolic disorder of pregnancy (gestational diabetes mellitus). *Oxidative medicine and cellular longevity*, 2021(1), 5581570.
- Ye, W., Luo, C., Huang, J., Li, C., Liu, Z., & Liu, F. (2022). Gestational diabetes mellitus and adverse pregnancy outcomes: systematic review and metaanalysis. *Bmj*, 377.
- Bianco, M. E., Kuang, A., Josefson, J. L., Catalano, P. M., Dyer, A. R., Lowe, L. P., ... & HAPO Follow-Up Study Cooperative Research Group. (2021). Hyperglycemia and adverse pregnancy outcome follow-up study: newborn anthropometrics and childhood glucose metabolism. *Diabetologia*, 64, 561-570.
- Hughes, A. E., Hattersley, A. T., Flanagan, S. E., & Freathy, R. M. (2021). Two decades since the fetal insulin hypothesis: what have we learned from genetics? *Diabetologia*, 64, 717-726.
- Olmos-Ortiz, A., Flores-Espinosa, P., Díaz, L., Velázquez, P., Ramírez-Isarraraz, C., & Zaga-Clavellina, V. (2021). Immunoendocrine dysregulation during gestational diabetes mellitus: the central role of the placenta. *International Journal of Molecular Sciences*, 22(15), 8087.
- 11. Stern, C., Schwarz, S., Moser, G., Cvitic, S., Jantscher-Krenn, E., Gauster, M., & Hiden, U. (2021). Placental endocrine activity: adaptation and disruption of maternal glucose metabolism in pregnancy and the influence of fetal sex. *International journal of molecular sciences*, 22(23), 12722.
- Guo, M., Fang, Y., Peng, M., He, C., Chen, J., Sun, B., ... & Zhao, K. (2024). Prenatal exposure to polycyclic aromatic hydrocarbons and phthalate acid esters and gestational diabetes mellitus: A prospective cohort study. *International Journal of Hygiene and Environmental Health*, 261, 114419.
- Dłuski, D. F., Wolińska, E., & Skrzypczak, M. (2021). Epigenetic changes in gestational diabetes mellitus. *International Journal of Molecular Sciences*, 22(14), 7649.
- Mansour Aly, D., Dwivedi, O. P., Prasad, R. B., Käräjämäki, A., Hjort, R., Thangam, M., ... & Research Program Management Jones Marcus B. 17 Mitnaul Lyndon J. 17. (2021). Genome-wide association analyses highlight etiological differences underlying newly defined subtypes of diabetes. *Nature genetics*, 53(11), 1534-1542.

- Linares-Pineda, T., Peña-Montero, N., Fragoso-Bargas, N., Gutiérrez-Repiso, C., Lima-Rubio, F., Suarez-Arana, M., ... & Morcillo, S. (2023). Epigenetic marks associated with gestational diabetes mellitus across two time points during pregnancy. *Clinical epigenetics*, 15(1), 110.
- 16. Via, M., & Mechanick, J. (Eds.). (2023). *Integrating Lifestyle Medicine for Prediabetes, Type 2 Diabetes, and Cardiometabolic Disease*. CRC Press.
- Kelly, A. C., Powell, T. L., & Jansson, T. (2020). Placental function in maternal obesity. *Clinical Science*, 134(8), 961-984.
- Modzelewski, R., Stefanowicz-Rutkowska, M. M., Matuszewski, W., & Bandurska-Stankiewicz, E. M. (2022). Gestational diabetes mellitus—recent literature review. *Journal of clinical medicine*, *11*(19), 5736.
- 19. McIntyre, H. D., Fuglsang, J., Kampmann, U., Knorr, S., & Ovesen, P. (2022). Hyperglycemia in Pregnancy and Women's Health in the 21st Century. *International Journal of Environmental Research and Public Health*, 19(24), 16827.
- 20. Seneviratne, S. N., & Rajindrajith, S. (2022). Fetal programming of obesity and type 2 diabetes. World Journal of Diabetes, 13(7), 482.
- 21. Lehloa, A. (2023). Diabetes and hypertension in pregnancy: Association with adverse birth outcomes among pregnant women living with and without HIV in Cape Town, South Africa (2017-2019): A retrospective study.
- 22. Matsunaga, H., Ito, K., Akiyama, M., Takahashi, A., Koyama, S., Nomura, S., ... & Komuro, I. (2020). Transethnic meta-analysis of genome-wide association studies identifies three new loci and characterizes population-specific differences for coronary artery disease. *Circulation: Genomic and Precision Medicine*, 13(3), e002670.
- Hasegawaa, Y., Haapananb, L., Zhanga, Z., Hogrefeb, C. E., Tahaa, A. Y., Capitaniob, J. P., ... & Slupskya, C. M. Impact of calorie restriction or administration of pravastatin on pregnancy outcomes in rhesus macaque mothers and infants. *YU HASEGAWA DISSERTATION*, 101.
- 24. Martínez-Vizcaíno, V., Sanabria-Martínez, G., Fernández-Rodríguez, R., Cavero-Redondo, I., Pascual-Morena, C., Álvarez-Bueno, C., & Martínez-Hortelano, J. A. (2023). Exercise during pregnancy for preventing gestational diabetes mellitus and hypertensive disorders: an umbrella review of randomised controlled trials and an updated meta-analysis. *BJOG: An International Journal of Obstetrics & Gynaecology*, 130(3), 264-275.
- 25. Oulerich, Z., & Sferruzzi-Perri, A. N. (2024). Earlylife exposures and long-term health: adverse gestational environments and the programming of offspring renal and vascular disease. *American Journal of Physiology-Renal Physiology*, 327(1), F21-F36.

- 26. Edwards, T., & Harding, J. E. (2021). Clinical aspects of neonatal hypoglycemia: a mini review. *Frontiers in pediatrics*, 8, 562251.
- Francis, E. C., Powe, C. E., Lowe Jr, W. L., White, S. L., Scholtens, D. M., Yang, J., ... & Sweeting, A. (2023). Refining the diagnosis of gestational diabetes mellitus: a systematic review and metaanalysis. *Communications medicine*, 3(1), 185.
- 28. Chukwuemeka, S. C. (2020). Adverse Foetal Outcomes in Gestational Diabetes: A Systematic Review and Meta-analysis.
- Dimas, A., Politi, A., Bargiota, A., Panoskaltsis, T., Vlahos, N. F., & Valsamakis, G. (2022). The gestational effects of maternal bone marker molecules on fetal growth, metabolism and longterm metabolic health: a systematic review. International journal of molecular sciences, 23(15), 8328.
- 30. Deng, X., Pan, B., Lai, H., Sun, Q., Lin, X., Yang, J., ... & Yang, K. (2024). Association of previous stillbirth with subsequent perinatal outcomes: a systematic review and meta-analysis of cohort studies. *American journal of obstetrics and* gynecology.
- 31. Stroud, L. R., Jao, N. C., Ward, L. G., Lee, S. Y., & Marsit, C. J. (2024). Differential impact of prenatal PTSD symptoms and preconception trauma exposure on placental NR3C1 and FKBP5 methylation. *Stress*, 27(1), 2321595.
- Davidson, T. L., & Stevenson, R. J. (2024). Vulnerability of the Hippocampus to Insults: Links to Blood–Brain Barrier Dysfunction. *International Journal of Molecular Sciences*, 25(4), 1991.
- 33. Serbis, A., Giapros, V., Tsamis, K., Balomenou, F., Galli-Tsinopoulou, A., & Siomou, E. (2023). Beta cell dysfunction in youth-and adult-onset type 2 diabetes: an extensive narrative review with a

special focus on the role of nutrients. *Nutrients*, 15(9), 2217.

- Lorimer, A. J. (2023). Placental Antioxidant Activity and Gestational Diabetes Mellitus Severity.
- Abolbaghaei, A. (2023). Application of Circulating Large Extracellular Vesicles as Biomarkers in Type 1 Diabetes Mellitus and Pregnancy (Doctoral dissertation, Université d'Ottawa/University of Ottawa).
- 36. Aryal, S., Manandhar, I., Mei, X., Yeoh, B. S., Tummala, R., Saha, P., ... & Joe, B. (2023). Combating hypertension beyond genome-wide association studies: Microbiome and artificial intelligence as opportunities for precision medicine. Cambridge Prisms: *Precision Medicine*, 1, e26.
- Sirhan, W., & Piran, R. (2020). Current approaches in diabetes treatment and other strategies to reach normoglycemia. *Current Topics in Medicinal Chemistry*, 20(32), 2922-2944.
- Hummel, G. L., Austin, K., & Cunningham-Hollinger, H. C. (2022). Comparing the maternalfetal microbiome of humans and cattle: a translational assessment of the reproductive, placental, and fetal gut microbiomes. *Biology of Reproduction*, 107(2), 371-381.
- 39. Shen, J., Valentim, W., Friligkou, E., Overstreet, C., Choi, K., Koller, D., ... & Posttraumatic Stress Disorder Working Group of the Psychiatric Genomics Consortium. (2024). Genetics of posttraumatic stress disorder and cardiovascular conditions using Life's Essential 8, Electronic Health Records, and Heart Imaging. *medRxiv*.
- 40. de Mendonça, E. L. S. S., Fragoso, M. B. T., de Oliveira, J. M., Xavier, J. A., Goulart, M. O. F., & de Oliveira, A. C. M. (2022). Gestational diabetes mellitus: the crosslink among inflammation, nitroxidative stress, intestinal microbiota and alternative therapies. *Antioxidants*, 11(1), 129.