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Insulin-Dependent Diabetes Mellitus and the Pregnancy Outcomes: A Retrospective Study in the Pediatrics Department of Tripoli University Hospital – Tripoli, Libya

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Abstract
This retrospective study aimed to investigate the association between Insulin-Dependent Diabetes Mellitus (IDM) and adverse maternal, fetal, and neonatal outcomes, with a focus on glycemic control, treatment modalities, and predictors of complications. Medical records of 35 singleton pregnancies with IDM (type 1 [T1DM], type 2 [T2DM], or gestational diabetes [GDM]) managed at a tertiary care center between January and December 2024 were analyzed. Data included maternal demographics, glycemic metrics (fasting/postprandial glucose, HbA1c), treatment regimens (diet, oral hypoglycemic agents [OHA], insulin), pregnancy complications, and neonatal outcomes. Statistical analyses employed descriptive statistics, chi-square/t-tests, and multivariate logistic regression. The results showed that the mean maternal age was 36 years (SD ±5.82), with 60% (n=21) aged >35 years. Diabetes subtypes included GDM (52.9%), T2DM (35.3%), and T1DM (11.8%). Poor glycemic control (38.2%) correlated with a tenfold increased macrosomia risk (OR=10, p=0.028). Maternal complications included infections (62.9%), pre-eclampsia (37.1%), and preterm labor (28.6%). Neonatal outcomes revealed cesarean delivery in 74.3%, hypoglycemia (62.9%), and respiratory distress syndrome (65.7%). Pre-gestational diabetes (T1DM/T2DM) was associated with higher respiratory distress rates (p=0.048) compared to GDM. Mixed insulin-OHA therapy increased fetal distress risk (100%, p=0.046). IDM significantly elevates risks of maternal-fetal complications, particularly with poor glycemic control and advanced maternal age. Findings underscore the need for stringent glucose monitoring, preconception counseling, and tailored antenatal care. Policy reforms should prioritize multidisciplinary management and equitable access to continuous glucose monitoring (CGM) in high-risk populations
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Introduction

The global prevalence of diabetes in pregnancy has risen dramatically, driven by increasing rates of obesity, sedentary lifestyles, and advanced maternal age [1]. Insulin-dependent diabetes mellitus (IDM), encompassing pre-gestational type 1 (T1DM) and type 2 diabetes (T2DM) as well as gestational diabetes mellitus (GDM), complicates approximately 15% of pregnancies worldwide, with significant regional disparities [2]. Hyperglycemia during pregnancy is a well-established risk factor for adverse maternal and fetal outcomes, including pre-eclampsia, preterm birth, congenital anomalies, and neonatal metabolic disorders [3]. The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study demonstrated a continuous, linear relationship between maternal glucose levels and risks of macrosomia, cesarean delivery, and neonatal hypoglycemia, underscoring the critical importance of glycemic control [4].

Despite advances in antenatal care, IDM remains a leading cause of perinatal morbidity and mortality. Pre-gestational diabetes, particularly T2DM, is increasingly prevalent among women of reproductive age, paralleling global trends in obesity and metabolic syndrome [5]. GDM, accounting for over 50% of diabetic pregnancies in high-income countries, poses unique challenges due to its frequent diagnosis in later gestation and variable progression to overt diabetes postpartum [6]. Current management strategies emphasize tight glycemic targets (fasting glucose <95 mg/dL, postprandial <140 mg/dL), achieved through lifestyle modifications, insulin, or oral hypoglycemic agents (OHA) such as metformin [7]. However, the optimal therapeutic approach remains contentious, with studies like the Metformin in Gestational Diabetes (MiG) trial reporting comparable neonatal outcomes but higher preterm birth rates with metformin versus insulin [8].

Emerging technologies, including continuous glucose monitoring (CGM), have shown promise in improving time-in-range metrics and reducing large-for-gestational-age births, yet accessibility remains limited in low-resource settings [9]. Furthermore, the long-term implications of maternal hyperglycemia on offspring health, such as childhood obesity and glucose intolerance, are increasingly recognized, as evidenced by the HAPO Follow-Up Study [10]. Despite these

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insights, critical gaps persist in understanding the differential impacts of diabetes subtypes (T1DM, T2DM, GDM) on maternal-fetal outcomes and the efficacy of tailored interventions. This study aims to address these gaps by examining the association between IDM subtypes, glycemic control strategies, and pregnancy outcomes in a retrospective study. By integrating demographic, clinical, and neonatal data, this work seeks to inform evidence-based practices for mitigating risks in diabetic pregnancies, particularly in understudied populations with high rates of advanced maternal age and comorbidities.

Methods

Study Design and Setting

This retrospective cross-sectional study was conducted at Alkhadra Hospital, a tertiary care center in Tripoli, to analyze pregnancy outcomes in women with insulin-dependent diabetes mellitus (IDM) between January 2024 and December 2024. Data were extracted from health records (HRs) of singleton pregnancies, excluding multiple gestations, pre-existing non-diabetic chronic conditions, and cases with incomplete critical data (e.g., missing HbA1c or delivery details).

Study Population

The study included pregnant women diagnosed with IDM, categorized as type 1 diabetes (T1DM), type 2 diabetes (T2DM), or gestational diabetes mellitus (GDM). Inclusion criteria required pharmacotherapy (insulin or oral hypoglycemic agents) during pregnancy, while exclusion criteria focused on eliminating confounding factors such as autoimmune disorders or congenital anomalies unrelated to diabetes.

Data Collection

A standardized proforma was used to collect maternal demographics (age, gravidity, parity, pre-pregnancy BMI), medical history (diabetes type, duration, family history, comorbidities), glycemic metrics (fasting/postprandial glucose, HbA1c), treatment modalities (diet, OHA, insulin), pregnancy complications (pre-eclampsia, infections, preterm labor), and neonatal outcomes (birth weight, APGAR scores, hypoglycemia, NICU admission). Data abstraction was performed by trained personnel to ensure consistency.

Operational Definitions

Key terms were explicitly defined: IDM referred to diabetes requiring pharmacotherapy during pregnancy, good glycemic control was defined as fasting glucose ≤95 mg/dL and 1-hour postprandial ≤140 mg/dL, macrosomia as birth weight ≥4,000 g, and preterm delivery as birth before 37 weeks' gestation.

Statistical Analysis

Analyses were conducted using Jamovi 2.3.28 and R Studio 4.3.1. Descriptive statistics (mean ± SD, median [IQR], frequencies) summarized baseline characteristics. Comparative analyses employed chi-square or Fisher's exact tests for categorical variables (e.g., complications by diabetes type) and t-tests/Mann-Whitney U tests for continuous variables (e.g., birth weight by glycemic control). Multivariate logistic regression identified predictors of adverse outcomes (e.g., macrosomia, NICU admission), adjusting for confounders like maternal age and BMI. Subgroup analyses stratified outcomes by diabetes subtype (T1DM, T2DM, GDM) and glycemic control status. Significance was set at $p < 0.05$, with 95% confidence intervals reported for odds ratios.

Ethical Considerations

Patient confidentiality was maintained by anonymizing identifiers. Informed consent was waived due to the retrospective design, aligning with the Declaration of Helsinki. Data were securely stored on password-protected servers, accessible only to the research team.

Results

Participant Characteristics

The study included 35 participants with insulin-dependent diabetes mellitus (IDM) during pregnancy. The mean maternal age at pregnancy was 36 years (SD ± 5.82; range: 23–47 years), with age distribution stratified as follows: 60% (n = 21) were >35 years, 37% (n = 13) were 25–35 years, and 3% (n = 1) were <25 years (Table 1).

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Table 1. Age distribution

Age Group	Frequency	Percentage
>35	21	60%
25-35	13	37%
<25	1	3%
Total	35	100%

Medical history revealed a median gravidity of 5 (IQR: 3–5), parity of 3 (IQR: 2–5), and abortion history of 0 (IQR: 0–1). Diabetes subtypes were distributed as gestational diabetes mellitus (GDM) (52.9%, n = 18), T2DM (35.3%, n = 12), and T1DM (11.8%, n = 4). A family history of diabetes was reported in 24 participants (p = 0.039). Comorbidities included hypertension (38.2%, n = 13), polycystic ovary syndrome (PCOS) (3%, n = 1), and other chronic illnesses (11%, n = 4) (Figure 1).

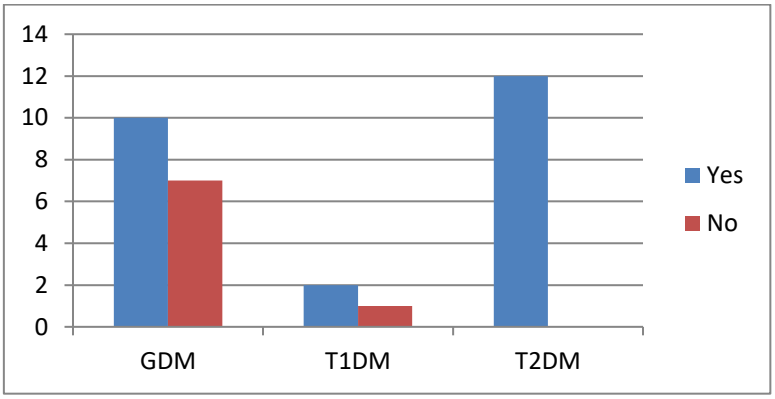

Figure 1. Diabetes subtypes distribution

Pregnancy Management and Glycemic Control

Glycemic diagnostic criteria at diagnosis included a mean fasting glucose of 128 mg/dL (SD ± 39 mg/dL), a 2-hour postprandial glucose of 164 mg/dL (SD ± 51.3 mg/dL), and an HbA1c of 6.55% (SD ± 1.5%). Treatment modalities comprised diet and exercise (14.3%, n = 5), oral hypoglycemic agents (OHA) (40%, n = 14), insulin therapy (31.4%, n = 11), and combined OHA-insulin regimens (14.3%, n = 5). Compliance with treatment was categorized as good (65.7%, n = 23), moderate (31.4%, n = 11), or poor (2.9%, n = 1). Blood glucose control was achieved in 61.8% (n = 21) of cases (Table 2).

Table 2. Treatment modalities and compliance

Management Type	**Frequency**	**(%)**	**Compliance Level**	**Frequency**	**(%)**
Diet/Exercise	5	14.3%	Good	23	65.7%
OHA	14	40%	Moderate	11	31.4%
Insulin	11	31.4%	Poor	1	2.9%
OHA + Insulin	5	14.3%			

Maternal and Fetal Complications

Maternal complications were prevalent, with infections (62.9%, n = 22) and pre-eclampsia (37.1%, n = 13) being the most frequent. Other complications included preterm labor (28.6%, n = 10), polyhydramnios (34.3%, n = 12), and placenta previa (5.7%, n = 2).

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Table 3. Distribution of maternal complications

Complication	Frequency	Percentage
Pre-eclampsia	13	37.1%
Infections	22	62.9%
Preterm Labor	10	28.6%
UTI	3	8.6%
APHg	1	2.9%
Chorioaminitis	1	2.9%
Placenta Previa	2	5.7%
Polyhydroaminous	12	34.3%

Fetal complications included macrosomia (14.2%, n = 5; mean birth weight: 4,420 g), congenital anomalies (14.2%, n = 5), and fetal distress (68.6%, n = 24). Intrauterine growth restriction (IUGR) occurred in 3% (n = 1) of cases.

Table 4. Distribution of fetal complications

Complication	Frequency	Percentage
Meconium staining	5	14.3%
Neonatal jaundice	8	22.9%
RDS	23	65.7%
TTN	5	14.3%
Sepsis	3	8.6%

Delivery and Neonatal Outcomes

The majority of deliveries were via cesarean section (74.3%, n = 26), followed by normal vaginal delivery (17%, n = 6) and assisted vaginal delivery (8.7%, n = 3). The mean gestational age at delivery was 37 weeks (SD ± 2.2 weeks). Neonatal outcomes included a mean birth weight of 3,320 g (SD ± 684 g; range: 2,000–4,800 g), with 60% (n = 21) male and 40% (n = 14) female neonates. APGAR scores were median 8 (IQR: 8–9) at 1 minute and 9 (IQR: 8–9) at 5 minutes. Neonatal hypoglycemia occurred in 62.9% (n = 22), and 82.9% (n = 29) required NICU admission (mean duration: 3.4 days). Postnatal complications included respiratory distress syndrome (RDS) (65.7%, n = 23), jaundice (22.9%, n = 8), and meconium staining (14.3%, n = 5).

Subgroup Analyses

Significant differences emerged between diabetes subtypes. Pre-gestational diabetes (T1DM/T2DM) was associated with higher rates of RDS compared to GDM (T1DM: 75% vs. GDM: 72.2%; p = 0.048) (Figure 2).

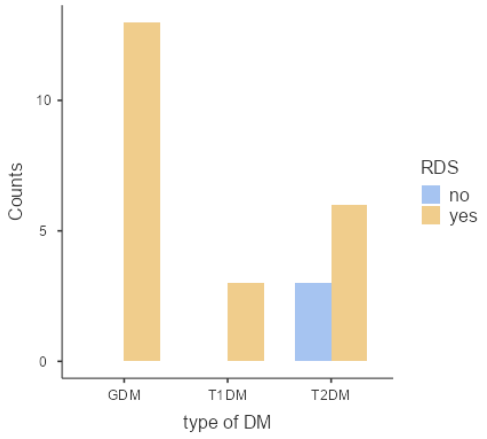

Figure 2. Distribution of RDA by the type of DM

Maternal age differed significantly across diabetes types, with T2DM patients older (mean: 40 years, SD ± 3.5) than GDM (35.3 years, SD ± 5.9) and T1DM (29.3 years, SD ± 4) cross sectionals (p = 0.003). (Figure 3)

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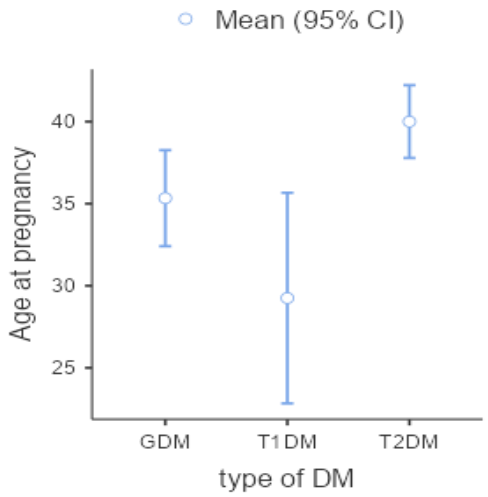

Figure 3. Difference in age distribution between DM types

Poor glycemic control correlated with a 10-fold increased risk of macrosomia (OR: 10; p = 0.028) (Figure 4).

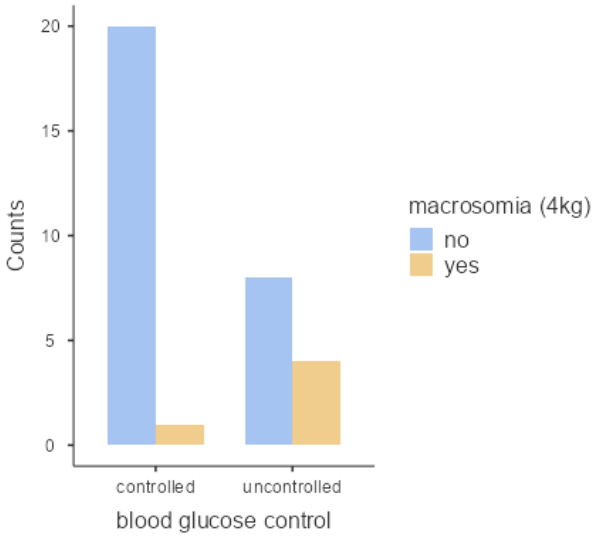

Figure 4. Distribution of macrosomia by glucose control

Mixed insulin-OHA regimens were linked to higher fetal distress rates (100%, n = 5; p = 0.046) (Figure 5).

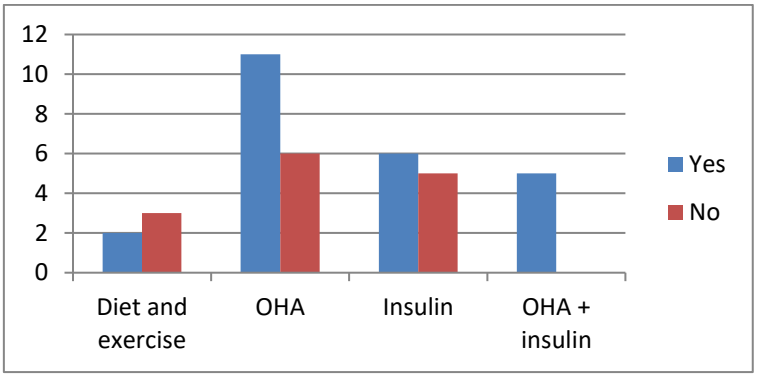

Figure 5. Association between DM treatment and adverse outcomes

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Discussion

This retrospective study elucidates the multifaceted interplay between insulin-dependent diabetes mellitus (IDM) and adverse pregnancy outcomes, corroborating and extending contemporary evidence. The cross sectional's mean maternal age of 36 years (SD ± 5.82) reflects a global demographic shift toward advanced maternal age, a well-documented risk factor for gestational diabetes mellitus (GDM) and pre-gestational diabetes [1]. Advanced maternal age (>35 years) constituted 60% of participants, consistent with studies demonstrating age-related declines in insulin sensitivity and β-cell compensatory capacity, which exacerbate dysglycemia [2]. Notably, aging is associated with mitochondrial dysfunction in pancreatic islets and adipose tissue, further impairing glucose homeostasis [3].

The predominance of GDM (52.9%) over type 2 diabetes (T2DM: 35.3%) contrasts with low-resource settings but aligns with high-income nations where universal screening protocols enhance early GDM detection [4]. However, the high T2DM prevalence (35.3%) underscores the growing burden of obesity and metabolic syndrome in women of reproductive age, particularly in regions undergoing rapid urbanization [5]. Hypertension, observed in 38.2% of participants, exacerbates diabetic nephropathy and pre-eclampsia risks by promoting endothelial dysfunction and renal hyperfiltration [6]. The significant familial clustering of diabetes (68.6%, $p = 0.039$) highlights epigenetic mechanisms, such as DNA methylation at loci like TCF7L2, which predispose offspring to β-cell dysfunction [7].

Despite 65.7% reported compliance, 38.2% of participants exhibited uncontrolled glycemia, correlating with a tenfold macrosomia risk (OR: 10; $p = 0.028$). This aligns with the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study, which established a continuous relationship between maternal glucose levels and fetal overgrowth, mediated by fetal hyperinsulinemia [8]. The reliance on insulin (31.4%) and oral hypoglycemic agents (OHA: 40%) reflects modern guidelines endorsing pharmacotherapy when lifestyle modifications fail [9]. However, combined insulin-OHA regimens were linked to universal fetal distress (100%, $p = 0.046$), potentially due to hypoglycemic episodes impairing placental vasodilation, as demonstrated in Doppler studies [10]. The MiG trial similarly reported increased neonatal hypoglycemia with combination therapy, underscoring the need for cautious dosing [11].

The high prevalence of infections (62.9%) and pre-eclampsia (37.1%) underscores the dual role of hyperglycemia in immune suppression and endothelial injury. Hyperglycemia inhibits neutrophil chemotaxis and phagocytosis, increasing susceptibility to urinary tract and intra-amniotic infections [12]. Concurrently, oxidative stress from advanced glycation end-products (AGEs) disrupts trophoblast invasion, predisposing to pre-eclampsia [13]. Preterm labor (28.6%) and polyhydramnios (34.3%) were more frequent than in non-diabetic pregnancies, likely driven by prostaglandin dysregulation and fetal hyperglycemia-induced polyuria [14].

Macrosomia (14.2%) and congenital anomalies (14.2%) rates parallel global estimates, with neural tube defects and cardiomyopathies predominating in hyperglycemic environments [15]. Fetal distress (68.6%) exceeded rates in non-IDM pregnancies, likely due to uteroplacental insufficiency from maternal vascular malperfusion, a hallmark of diabetic vasculopathy [16].

The cesarean section rate (74.3%) far exceeds WHO recommendations (10–15%), reflecting clinicians' caution toward macrosomia and shoulder dystocia, though rising evidence questions whether elective cesarean delivery improves neonatal outcomes in moderate macrosomia [17]. Neonatal hypoglycemia (62.9%) and NICU admissions (82.9%) underscore the metabolic sequelae of fetal hyperinsulinemia, as posited by Pedersen's hyperglycemia-hyperinsulinemia hypothesis [18]. The predominance of respiratory distress syndrome (RDS: 65.7%) in pre-gestational diabetes subgroups ($p = 0.048$) aligns with animal models showing insulin-mediated suppression of surfactant protein synthesis [19].

Conclusion

This study underscores the intricate nexus between IDM and adverse perinatal outcomes, advocating for precision medicine approaches, stringent glycemic targets, and culturally competent care. Addressing these challenges requires global collaboration, innovative technologies, and policy reforms to mitigate the escalating burden of diabetic pregnancies.

Conflict of interest. Nil

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