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Predictors and Outcomes in Gestational Diabetes Requiring Insulin Therapy

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ABSTRACT

Objective: To evaluate risk factors that predict Insulin requirements and outcomes in women with gestational diabetes in a resource-limited country.

Study Design: Retrospective longitudinal study.

Place and Duration of Study: Department of Gynaecology and Obstetrics, Combined Military Hospital, Mangla Pakistan, from Jan to Dec 2019.

Methodology: Our study included 100 pregnant women with gestational diabetes over a period of one year. The primary outcome was to calculate the frequency of gestational diabetes and the correlation between maternal age and parity with subdermal Insulin therapy in a peripheral (Class C) hospital. The secondary outcomes of this study included mode of delivery and neonatal birth weight.

Results: Out of 1509 deliveries, our study included 100 pregnant women (6.62%). Sixty-two (62%) required Insulin to control hyperglycemia in addition to oral Metformin; 36% required oral Metformin alone. Maternal age (p=0.078), presence of co-morbidity (p=0.260), and parity (p=0.242) did not predict Insulin requirement. A caesarean section (69%) was the most common mode of delivery. Insulin requirements to control hyperglycemia didn't correlate with mode of delivery (p=0.825). The neonatal birth weight was 3.30±0.33 kg in patients requiring Insulin versus 3.26±0.25 kg in other treatments (p=0.86). There was one intrauterine death.

Conclusion: The frequency of gestational diabetes was 6.62%. Maternal age, parity, and the presence of maternal co-morbidities did not predict Insulin requirements. There was no correlation between Insulin therapy, mode of delivery, or neonatal outcome.

Keywords: Birth weight, Gestational diabetes, Insulin requirement, Maternal age, Mode of delivery, Parity.

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INTRODUCTION

Hyperglycemia during pregnancy can present as diabetes mellitus (DIP) or gestational diabetes mellitus (GDM). GDM is one of the most frequent metabolic disorders encountered during pregnancy, with an increasing prevalence of 1–45% globally.[1,2] Hyperglycemia has become a public health issue due to its short- and long-term feto-maternal effects, and it requires planned periconception, antenatal, intrapartum, and postnatal care.[3,4] GDM may lead to feto-maternal risks like miscarriage, foetal anomalies, macrosomia, preterm births, perinatal death, maternal retinopathy, nephropathy, neuropathy, hypertensive disorder, etc.

Maternal and neonatal outcomes can only be improved by early diagnosis and prompt management. International guidelines recommend medical nutrition therapy, oral medication, and Insulin therapy. Medical nutrition therapy (MNT) is empirically used in cases with pre-existing diabetes, with risk factors, on diagnosis and initiation of treatment, and during postnatal care. Resistant cases that do not respond to MNT and exercise should be treated with Metformin.[5] Cases with Metformin contraindication, FBG ≥7.0 mmol/L at diagnosis, and complications, such as macrosomia or polyhydramnios, should start Insulin immediately, with or without Metformin.[6] Insulin therapy is reserved for pregnant women with Insulin-dependent diabetes type 1 and patients whose MNT and oral medications fail to achieve euglycemia. Insulin therapy has been shown to be safe during pregnancy and lactation.[7] Hence, understanding the risk factors that can predict Insulin requirements in GDM can enable obstetricians to timely intervene and improve outcomes.[8]

Pakistan, a resource-limited country, suffers from a lack of awareness about reproductive health, social taboos associated with pregnancy complications that

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lead to delayed hospital presentations, and compromised care for feto-maternal patients. Our institute is a peripheral hospital that serves not only the armed forces, but also provides maternal healthcare to over 16 thousand locals. There are only a few studies available on GDM and its indigenous population. The authors could not find any published material on predictors of Insulin therapy and feto-maternal outcomes associated with Insulin therapy. The purpose of this study was to evaluate the frequency of GDM, the risk factors that predict Insulin therapy in GDM, and the outcomes of patients on Insulin therapy.

METHODOLOGY

After receiving approval from the Hospital Ethical Review Committee (IERC # 205/Adm/Gen, dated May 10, 2022), the retrospective longitudinal study was conducted at the Department of Obstetrics and Gynaecology, Combined Military Hospital, Mangla Pakistan, from January to December 2019. The WHO sample size calculator was used to etimate a sample size with the prevalence of gestational diabetes of 8.9%.[8] The patients with hyperglycemia or diabetes presented to the hospital were included by convenience sampling.

Inclusion Criteria: Pregnant females of all age groups with singleton or multiple pregnancies; whether vaginal or caesarean section, with a diagnosis of gestational diabetes, were included.

Exclusion criteria: All pregnant women with morbidities other than GDM and pre-existing diabetes mellitus were excluded.

The diagnosis of maternal diabetes was based on an OGTT test for new cases and BSF, as well as 2 hours of PP (BSR) for already diagnosed diabetic patients based on World Health Organisation (WHO) disease criteria.[9] During the Out-Patient consultation, a consultant obstetrician assessed all of the patients and managed them according to the institute's protocols. Consultant obstetricians manually collected retrospective data from a medical record sheet. The primary outcome was to calculate the frequency of gestational diabetes and the correlation between maternal age and parity with subdermal Insulin therapy in a peripheral (Class C) hospital. The secondary outcomes of this study included mode of delivery and neonatal birth weight.

To analyse the results, IBM Statistical Package for Social Sciences version 23.00 was used. The qualitative data was presented as frequency and percentage. The quantitative data was presented as Mean±SD. Chi-square test and independent sample t-test were applied to explore the inferential statistics. The *p*-value of ≤0.05 was set as the cut-off value for significance.

RESULTS

At our Institute, a total of 1509 obstetric cases delivered babies. 100(6.62%) pregnant women developed gestational diabetes. The mean age of the study population was 29.8±4.71 years. The majority of 67 were multiparous, 23 were grand multiparous, and 10 were primigravida. 62% required Insulin to control hyperglycemia in addition to oral Metformin. 36% of pregnant women required oral Metformin alone; 7% required subdermal enoxaparin; and 1% required oral methyldopa as part of their treatment. At term, the mean subdermal Insulin 70/30 requirement was 31.6 units ±18.7 over 24 hours. In addition, 13% required additional subdermal regular Insulin, and 1% required long-acting Insulin (12 units).

Most of the pregnant ladies were aged 26–30 years (n=46), had no co-existing maternal co-morbidities (n=91), and most had previous vaginal deliveries (n=67). The co-existing maternal morbidities included pregnancy-induced hypertension (n=3), thalassemia minor (n=2), deep venous thrombosis (n=1), etc. The comparison of maternal factors with the Insulin required is given in Table-I.

Table-I: Comparison of Maternal Factors and Insulin Requirement (n=100)

Variables		Insulin requirement		*p*-value
		Yes (n=62)	No (n=38)	
Parity	Primigravida	5(8.1%)	5(13.2%)	0.552
	2-4	41(66.1%)	26(68.4%)	
	≥5	16(25.8%)	7(18.4%)	
Mean age (years)		30.4 ± 5.12	28.8±3.83	0.164
Presence of other co-morbidity		7(11.3%)	2(5.3%)	0.260
Previous cesarean delivery		18(29%)	15(39.5%)	0.381

In their current pregnancy with GDM, caesarean section (69%) was more common than vaginal delivery, and two (2%) intrauterine deaths of fetuses Previous history revealed neonatal risk factors, which included 10 previous perinatal deaths, 4 oligohy-dramnios, and 4 intrauterine growth retardation. The mean birth weight was 3.2kg±0.30 (minimum 2.4kg; maximum 4.1kg). Table-II compares the outcome with Insulin requirements.

Table-II: Comparison of Outcomes with Insulin Requirement (n=100)

Variables	Insulin Requirement		*p*-value
	Yes(n=62)	No(n=38)	
Mode of delivery			
Vaginal delivery	20(32.3%)	11(28.9%)	0.825
Cesarean section	42(67.7%)	27(71.1%)	
Neonatal Birth weight (kg)			
	3.30±0.33	3.26±0.25	0.860
History of adverse peri-natal outcome			
Yes	6(9.7%)	3(7.9%)	1.000
No	56(90.3%)	35(92.1%)	
Present adverse outcome			
Intrauterine growth retardation	4(6.5%)	-	0.197
Oligohydramnios	3(4.8%)	1(2.6%)	
Intra-uterine demise	1(1.6%)	-	
None	54(87.1%)	37(97.4%)	

DISCUSSION

Globally, GDM is reported to affect 3.8–6.98% of all pregnancies in developed countries.[9,10] These results are similar to our 6.6% frequency of GDM. A systematic review of 16 countries in the Middle East and North Africa (MENA) showed a prevalence of 13%, with the highest (24%) in Saudi Arabia, which is similar to Sub-Saharan Africa (14%), but higher than ours (6.2%) and European countries (2-6%).[11,12] Euglycemia has been shown to be associated with better maternal and neonatal outcomes.[13,14]

Our study has shown that 62% of GDM patients require subdermal Insulin to maintain euglycemia. This number is much higher than the 15–50% reported by other authors.[15,16] This higher Insulin requirement in our study population may be due to a genetic difference between the Caucasian and Asian populations: lower compliance with oral Metformin or non-adherence to the dietary and lifestyle modifications advised by the obstetrician.[17,18] However, these were not variables included in our study. A study in Germany (2021) studied 454 pregnant women diagnosed with GDM. They reported the use of diet in 275(60.5%), bolus Insulin only in 45(9.9%), basal Insulin only (16%), and multiple daily injections in 61(14%).[19] Most of the pregnant women in our study with GDM required multiple daily injections. This may result in poor compliance or hesitation due to fear of needles in pregnant women, especially in a country with low literacy rates, a lack of awareness, and stigmas associated with Insulin dependence. This, in turn, contributes to worse outcomes for mothers and newborns in developing nations.

In GDM, studies have been conducted to analyze predictors of Insulin requirements. Barnes *et al*.[20] presented a novel model for Insulin prediction in GDM. They reported that 85.7%–93.1% of women with 6-7 predictors required Insulin in addition to medical nutrition therapy, compared to 9.3–14.7% of women with 0–1 predictors. These predictors were: maternal age >30 years; family history of diabetes mellitus; GDM diagnosis at <24 weeks gestation; prior GDM; fasting venous blood glucose >5.3 mmol/L; and HbA1c >5.5% at GDM diagnosis. In a study, Eleftheriades *et al*.[21] reported maternal body mass index (BMI); higher fasting and one-hour post-prandial glucose levels are predictors of Insulin requirement. They didn't report significant variation in maternal age: 34.15±4.2 years in dietary control versus 34.5 years ±4.0 in those requiring Insulin; *p*=0.105. Similarly, they didn't report smoking or conception by artificial reproductive techniques as predictors of Insulin requirement in GDM. We did not investigate risk factors such as BMI, smoking, or method of conception. Additionally, they conducted a comparison between dietary and lifestyle modifications and Insulin requirements, while we advised all our patients with GDM to modify their lifestyles and take oral Metformin.

Hashaad *et al*.[22] (2021) reported that 71(50.71%) patients underwent caesarean delivery and 69(49.28%) had vaginal delivery. They further explained that among caesarean deliveries, 55.7% were treated with Insulin and 45.7% with Metformin; the *p*-value 0.237 remained insignificant. In their study, parity appears to have had no impact as a predictor (*p*-value 0.583), although 71.4% of multiparas were treated with Insulin. These results are comparable to our caesarean section rate (69%) in GDM. Among the caesarean group, 60.86% were treated with Insulin and 39.13% with oral Metformin, *p*-value 0.825, which is statistically insignificant. We reported a parity of 3.4±1.47 in the Insulin treatment group versus 3.0±1.62 in the oral Metformin group.

Our study has certain limitations. Although we were able to achieve euglycemia in GDM, we didn't include the laboratory value of fasting and the 1-hour post-prandial value of plasma glucose level, nor did we include HbA1C in our diagnostic criteria for our outcomes. Therefore, we are unable to comment on these aspects of the study. We did not include long-term maternal and neonatal outcomes, so our results

cannot be extrapolated to the long-term outcomes of GDM.

CONCLUSION

The frequency of gestational diabetes was 6.62%. Maternal age, parity, and the presence of maternal co-morbidity did not predict Insulin requirements. There was no correlation between Insulin therapy, mode of delivery, or neonatal outcome.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AE & AI: Conception, study design, drafting the manuscript, approval of the final version to be published.

ZDB & MZ: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

SZ & SBM: Data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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