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Glibenclamide versus insulin in treatment of gestational diabetes mellitus - a randomised controlled trial

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Abstract

Background: One of the most serious consequences of pregnancy is Gestational diabetes mellitus (GDM). It has a negative impact on the mother and the newborn. Maintaining normal blood glucose levels in GDM lowers morbidity for both mother and infant. The first therapy for GDM consists of diet and exercise. If these approaches fail to reach glycemic objectives, medical management should be instituted, which may include insulin or oral hypoglycemic medications.

Aim of the work: To determine the glibenclamide versus insulin efficacy in achieving the adequate glycemic control.

Methods: This randomized control study was conducted on 120 pregnant women with gestational ages ranging from 20 to 37 weeks at Ain Shams University Maternity Hospital between July 2018 and June 2019, using inclusion and exclusion criteria.

Results: Regarding to the glycemic control, there was no significant difference in mean glucose levels at enrollment time before treatment between the two groups as fasting glucose levels were 139.1±12.5 mg/dl in Glibenclamide treated group versus 138.9±11.9 mg/dl in insulin treated group (p=0.650) and 2-hours postprandial glucose levels were 194.8±31.1 in Glibenclamide treated group versus 192.1±28.4 mg/dl in insulin treated group (p=0.625). Regarding postprandial blood glucose after introduction of the drugs, there was no significant differences between the studied groups after one week, at follow-up levels and till delivery time. The uncontrolled cases of Glibenclamide treated group mostly shift to insulin in weeks 4 and 5 after introduction of the drug. Regarding mode of delivery, Cesarean delivery was non-significantly less frequent in Glibenclamide group. 53.3% of patients in Glibenclamide group underwent cesarean delivery versus 61.7% in insulin group (p value=0.356). maternal complications of hypoglycemia

were significantly less frequent in Glibenclamide group (p value =0.027) and GIT upset was significantly more frequent in Glibenclamide group (p value =0.032) while Polyhydramnios was non-significantly more frequent in Glibenclamide group (p value=0.491). Regarding neonatal outcome, neonatal birth weight was significantly lower in Glibenclamide group (Glibenclamide 3.3±0.3 kg versus 3.5±0.4 kg in insulin group, p value=0.006). In terms of newborn problems, fetal macrosomia, newborn hypoglycemia, RDS, NICU hospitalization, and congenital anomalies did not significantly differ between the two groups.

Conclusion: Glibenclamide appears to be an effective medicine in the treatment of pregnant women with GDM, maintaining appropriate glycemic control with decreased risk of hypoglycemia and with maternal and newborn morbidities equivalent to insulin. The therapy is significantly less expensive; nonetheless, further appropriately powered and randomized clinical trials, including long-term child follow-up, are needed to establish the relevance of glibenclamide as an alternative to insulin in the management of GDM in women.

Keywords: Glibenclamide in pregnancy, gestational diabetes mellitus.

Introduction

GDM is one of the most frequent and hazardous postpartum outcomes (1). The number of Egyptian women with GDM who would require insulin each year, assuming a 50% rate of GDM women requiring it and a minimum 5% incidence of GDM, would represent a substantial financial and medical burden (2). Every year, more than two million people are born in Egypt.

The fetal and neonatal complications associated with gestational diabetes mellitus include intrauterine fetal death, congenital abnormality, fetal macrosomia, birth traumas, hypoglycemia, hyperbilirubinemia, respiratory distress, cardiomyopathy, hypocalcemia, preterm, and pulmonary hyaline membrane disease. Later-life GDM problems in children might include metabolic syndrome and diseases including obesity, hypertension, dyslipidemia, and glucose intolerance (3).

Preeclampsia, urinary tract infections, hyperglycemia crises, and an increased risk of cesarean delivery are among the maternal short-term consequences of GDM. Long-term effects also include a higher risk of type 2 diabetes and cardiovascular diseases such hypertension and hyperlipidemia(4).

A common oral hypoglycemic medication is glibenclamide, which takes one hour to absorb and peaks in roughly four hours. Its half-life is ten hours, and once a single dose is administered, its antiglycemic effects last for up to twenty-four hours before being eliminated from plasma (5). The placental barriers are not considerably breached by glibenclamide(6).

While glibenclamide has not been approved for use in pregnancy, many recommendations recommend it as a therapeutic aid for gestational diabetes. Glibenclamide, for instance, was recognized at the Fifth International Workshop-Conference in Gestational Diabetes Mellitus(7), and the National Institute for Health and Care Excellence (NICE) guidelines and the American College of Obstetricians and Gynecologists (ACOG) practice bulletin both consider glibenclamide and metformin (8).

Aim of the work

This study objective was compare the effectiveness of insulin and glibenclamide in establishing sufficient glycemic control.

Patients and methods

This randomized controlled experiment was carried out at Ain Shams University hospitals from July 2018 to June 2019 on a total of 120 patients diagnosed with gestational diabetes mellitus during the second trimester of pregnancy, after authorization by the ethics committee (FMASU MS126/2021).

Study population: Pregnant women attending antenatal care diabetic clinic in Ain Shams Maternity Hospital and diagnosed with gestational DM and divided into 2 groups; the glibenclamide as the study group (A) and the insulin group as the control group(B) by Simple randomization by using a random number generator.

Inclusion criteria: Maternal age between 18 and 35 years old, Singleton pregnancy, previously normal HbA1c indicating euglycemia in the previous three months, the patient is diagnosed with GDM when performing the OGTT in the morning after an overnight fast of at least 8 hours. When two or more of the following criteria are satisfied or exceeded, GDM is diagnosed:

- Fasting: 92 mg/dL (5.1 mmol/L)
- 1 hour: 180 mg/dL (10.0 mmol/L)
- 2-hour: 153 mg/dL (8.5 mmol/L)
- 3-hour: 140 mg/dL (9).

Exclusion criteria: Diabetes mellitus before pregnancy, Cases of premature membrane rupture, known renal, hepatic, haematological, or cardiovascular illness. Patient is unable to follow-up till birth. Contraindications to glibenclamide include fetal anomalies and gestational hypertension.

Study Procedures: All patients enrolled in the trial were counselled and signed a written consent explaining the details of the trial and subjected to:

History: including

Personal history, date of LMP, detailed obstetric history of diabetes (history of IUFD, Macrosomic baby, CFMF), history of any medical illness.

Particular attention was paid to the BMI, blood pressure, estimated fetal weight, and fundal height throughout the examination.

- Following a thorough history taking and obstetric examination, all participants received dietary advice for women diagnosed with GDM. These recommendations included three meals and four snacks per day, with 40–45% of the calories coming from carbs. It was also suggested to exercise, preferably for 20 minutes a day, walking. Following a two-week food regimen, capillary glucose monitoring was acquired (6).
- Failure of dietary treatment was defined as FBS > 126 mg/dl and 2-hour PPBS > 140 mg/dl for two weeks. These patients were subjected into two arms (6):

Insulin and glibenclamide doses:

- Glibenclamide (trade name: (Daonil) is supplied in New Zealand by: Sanofi-Aventis New Zealand Limited, Level 8, 56 Cawley Street, Ellerslie, Auckland, New Zealand) was started on a dose of 2.5 mg per day and then was increased at 3-day increments of 2.5 mg up to a maximum of 20mg per day. As the patients were monitored firstly after two weeks then every two days by taking blood sample of 2-3 ml and measuring blood glucose level till gaining the required plasma glucose level, an increase of glibenclamide dosage was recommended when the capillary blood glucose levels are above the desired levels (FBS>126 mg/dl and 2hrPPBS >120 mg/dl) with follow up weekly (6).
- If blood sugar did not return to normal after two weeks of taking the maximum dosage of glibenclamide, insulin treatment was initiated.
- To achieve glycemic control, the insulin group was given a total insulin dosage ranging from 0.7 to 2 units per kg (present pregnant weight). The insulin was distributed in accordance with the schedule listed below: 50% as three preprandial rapid-acting

Table 1. Demographic characteristics among the studied groups.

Items	Measure	Glibenclamide (N=60)	Insulin (N=60)	P-value
Age (years)	Mean±SD	27.9±3.6	28.1±3.7	^0.804
	Range	22.0–35.0	21.0–35.0	
BMI (kg/m2)	Mean±SD	29.6±2.6	29.9±2.4	^0.504
	Range	24.0–35.3	25.4–36.7	
Parity	Nulli	16 (26.7%)	13 (21.7%)	#0.522
	Multi	44 (73.3%)	47 (78.3%)	
GA (weeks)	Mean±SD	25.2±1.4	25.4±1.2	^0.528
	Range	24.0–28.0	24.0–28.0	

BMI: Body mass index. GA: Gestational age. ^Independent t-test. #Chi square test

insulin injections and 50% as intermediate-acting insulin, such as NPH (given in two equal doses before breakfast and before bedtime). (9)

• Generally speaking, fasting and premeal glucose levels of 95 mg/dl or less, as well as 1- or 2-hour postprandial levels of 140 mg/dl or fewer, were the glucose objectives. Blood glucose levels shouldn't drop below 60 mg/dl over the course of the night.

• Ultrasonography was used to test all patients for growth and HbA1c levels at 30 to 32 weeks of gestation, then again at 36 to 38 weeks to detect macrosomia and polyhydramnios.

• HbA1c and blood sugar tests were correlated to maternal outcome.

• Mode of delivery was determined according to maternal and fetal condition.

Glibenclamide side effects:

Diarrhea nausea, vomiting or abdominal pain.

Antidiarrheal drug like clopramide for nausea the drug was taken after meals and cyclizine was given to improve the nauseating effect.

Low blood glucose level (hypoglycaemia):

The patient was educated to monitor her blood glucose 5 times per day (Fasting, 2-hour after each meal and at mid-night) and at clinic every month and the patient was educated about hypoglycemia symptoms like drowsiness, thirst, sweating, heart racing, and to take any sugary drink at once and seek medical advice.

Temporary visual disturbances at start of treatment:

Stop the drug and seek advice immediately.

Table 2. HbA1c (%).

Time	Measure	Glibenclamide (N=60)	Insulin (N=60)	^P-value	Effect size Mean±SE 95% CI
Pre diabetess	Mean±SD	5.1±0.3	5.2±0.3	0.349	-0.1±0.1
	Range	4.6-5.6	4.5-5.7		-0.1–0.1
Baseline	Mean±SD	6.5±0.1	6.5±0.1	0.762	0.0±0.0
	Range	6.2–6.7	6.1–6.8		-0.1–0.1
Delivery	Mean±SD	5.3±0.1	5.2±0.1	0.162	0.1±0.1
	Range	5.0–5.5	4.9–5.6		-0.1–0.1
Change at Delivery	Mean±SD	-1.2±0.1	-1.2±0.1	0.163	0.0±0.0
	Range	-1.5–-1.1	-1.5–-1.2		-0.1–0.1

^Independent t-test. Effect size: Value of Glibenclamide relative to insulin. SE: Standard error. CI: Confidence interval. Change=follow up - baseline, negative values indicate reduction.

Table 3. Fasting blood glucose (mg/dL).

Time	Measure	Glibenclamide (N=60)	Insulin (N=60)	^P-value	Effect size Mean±SE 95% CI
Baseline	Mean±SD	139.9±12.5	138.9±11.9	0.650	1.0±2.2
	Range	113.0–160.0	111.0–159.0		-3.4–5.4
Week 30-32	Mean±SD	123.4±11.1	120.3±14.2	0.187	3.1±2.3
	Range	98.0–150.0	95.0–155.0		-1.5–7.7
Week 36-38	Mean±SD	119.5±15.0	115.8±12.1	0.143	3.7±2.5
	Range	91.0–151.0	89.0–140.0		-1.3–8.6
Change at week 30-32	Mean±SD	-16.5±8.3	-18.6±11.3	0.255	2.1±1.8
	Range	-34.0–2.0	-44.0–5.0		-1.5–5.6
Change at week 36-38	Mean±SD	-20.5±8.4	-23.1±6.7	0.058	2.7±1.4
	Range	-39.0–-6.0	-40.0–-7.0		-0.1–5.4

^Independent t-test. Effect size: Value of Glibenclamide relative to insulin. SE: Standard error. CI: Confidence interval. Change=follow up - baseline, negative values indicate reduction.

Insulin side effects:

Low blood sugar:

Good monitoring and educate the patient how to use the glucometer and the dose was adjusted according to the case blood sugar measurements.

Rash over your entire body:

Change insulin type to human source and we monitored the patient after injecting new type to ensure their safety.

Sample Size: Using PASS version 15 setting the alpha error 5% and power at 90%. Results from previous study *Pavithra et al.,* (6) showed that the mean HbA1c among glibenclamide were 5.3±0.34 compared 5.5±0.62 for insulin group based on hypothesis of non-inferiority between the two groups with a margin of non-inferiority equal to 0.1 powered sample size of 60 cases per group taking in account 20% drop out.

Sample size of 120 cases divided into two groups taking in account 20% drop out.

Outcome measures:

Primary Outcome Measures: Glycaemic control using glucose values downloaded from home blood glucose monitoring, which include the number and percentage of blood glucose excursions below 60 mg/dl (hypoglycemia in this study), as well as the number and percentage of blood glucose excursions

Table 4. Postprandial blood glucose (mg/dL).

Time	Measure	Glibenclamide (N=60)	Insulin (N=60)	^P-value	Effect size Mean±SE 95% CI
Baseline	Mean±SD	194.8±31.1	192.1±28.4	0.625	2.7±5.4
	Range	135.0–259.0	134.0–254.0		-8.1–13.4
Week 30-32	Mean±SD	148.6±17.9	143.3±21.1	0.145	5.3±3.6
	Range	116.0–182.0	112.0–183.0		-1.8–12.3
Week 36-38	Mean±SD	136.3±14.2	132.4±9.7	0.079	3.9±2.2
	Range	112.0–177.0	106.0–154.0		-0.5–8.3
Change at week 30-32	Mean±SD	-46.2±20.8	-48.8±22.3	0.513	2.6±3.9
	Range	-105.0–-12.0	-108.0–-8.0		-5.2–10.4
Change at week 36-38	Mean±SD	-58.5±20.3	-59.8±20.8	0.736	1.3±3.7
	Range	-103.0–-19.0	-110.0–-17.0		-6.2–8.7

^Independent t-test. Effect size: Value of Glibenclamide relative to insulin. SE: Standard error. CI: Confidence interval. Change=follow up - baseline, negative values indicate reduction.

Table 5. Glycemic control.

Glycemic control	Glibenclamide	Insulin (N=60)	#P-value (N=60)	Effect size Relative rate 95% CI
Controlled	49 (81.7%)	53 (88.3%)	0.306	0.92
Not controlled	11 (18.3%)	7 (11.7%)		(0.79–1.08)

#Chi square test. Effect size: Value of Glibenclamide relative to insulin. CI: Confidence interval.

equal to or exceeding 120 mg/dL at the 2-hour postprandial test and 95 mg/dL at the fasting test.

Secondary Outcome Measures:

- Clinical outcomes including mode and gestational age of delivery, birthweight (adjusted for sex and gestation at birth) (10).

- Apgar scores, NICU admission, IUFD, hypoglycemia (blood glucose <40 mg/dl), respiratory distress, fetal abnormalities, Macrosomia (birth weight >4000 g), and hospitalization in a neonatal unit were among the neonatal outcomes that were documented. (11)

Ethical Considerations: The patient information was private. Patient confidentiality was maintained and data were presented according to diagnosis rather than by name. Every participant signed an informed consent form, which was verified with a date and time in Arabic. By giving each patient's initials a number, confidentiality was maintained and only the investigator was aware of it.

Conflict of interest: The candidate stated that they had no conflicts of interest and that they had covered the study's expenses.

Statistical analysis: SPSS for Windows v20.0 will be used to conduct the analysis. The data should be presented as range, mean, and standard deviation for numerical parametric variables, range, median, and inter-quartile range for numerical non-parametric variables, or as number and percentage for categorical variables. The independent student's t-test, the mean difference, and its 95% confidence interval (CI) should be used to analyze the difference between two independent groups for numerical parametric variables; for categorical variables, the chi-squared test, the risk ratio, and its 95% confidence interval (CI) should be utilized. Binary logistic regression analysis is required to ascertain the correlation between a good or bad response and the variables under investigation. To estimate the validity of measured variables as predictors of a good or poor response, ROC curves must be developed. The presentation of validity should include the associated 95% confidence intervals for sensitivity, specificity, positive, and negative predictive values. The 0.05 chi-square significance level is used.

Results

During this trial, 159 individuals were evaluated for eligibility, and 120 were enrolled. Of all eligible patients, 32 were eliminated from the trial due to inclusion requirements, while 7 declined to participate.

Ultimately, the analysis was based on the data of 120 patients were diagnosed with GDM and accepted to participate in the study.

Table (1) shows that no significant difference between the studied groups regarding age, BMI, parity and gestational age at presentation.

Table (2) reveals that there is no significant differ-

Table 6. Shift to insulin time among uncontrolled cases in glibenclamide group

Time after treatment	N	%
Week-3	2	18.1
Week-4	5	45.5
Week-5	4	36.4

Table 7. Gestational age at delivery (week).

Variables	Measure	Glibenclamide (N=60)	Insulin (N=60)	^P-value	Effect size Mean±SE 95% CI
GA at delivery	Mean±SD	38.5±0.7	38.2±0.9	0.060	0.3±0.1
	Range	36.0–39.0	36.0–39.0		0.0–0.6
Prolongation of pregnancy	Mean±SD	13.3±1.6	12.8±1.3	0.107	0.4±0.3
	Range	9.0–15.0	10.0–15.0		-0.1–1.0

GA: Gestational age. ^Independent t-test. Effect size: Value of Glibenclamide relative to insulin. SE: Standard error.

ence between the examined groups in terms of HbA1c baseline, delivery levels, and changes from baseline at delivery.

Table (3) shows that that no significant difference between the studied groups regarding Fasting blood glucose; baseline, follow-up levels and changes from baseline at follow-ups.

Table (4) shows that no significant difference between the studied groups regarding postprandial blood glucose; baseline, follow-up levels and changes from baseline at follow-ups.

Table (5) demonstrates that the Glibenclamide group had non-significantly fewer instances of glucose control (81.7 versus 88.3%, respectively). In the Glibenclamide group, all uncontrolled patients were switched to insulin and eventually brought under control.

Table (6) shows that Shift to insulin mostly occurred in weeks 4 and 5 after treatment beginning (81.9%).

Table (7) shows that Gestational age at delivery and prolongation of pregnancy were non-significantly higher in glibenclamide group.

Table 8. Mode of delivery.

Mode of delivery	Glibenclamide	Insulin (N=60)	#P-value (N=60)	Effect size Relative rate 95% CI
Cesarean	32 (53.3%)	37 (61.7%)	0.356	0.86 (0.63–1.18)
Vaginal	28 (46.7%)	23 (38.3%)		

#Chi square test. Effect size: Value of Glibenclamide relative to insulin.

Table (8) shows that Cesarean delivery was non-significantly less frequent in Glibenclamide group.

Table (9) shows that Maternal hypoglycemia was significantly less frequent in Glibenclamide group. Maternal GIT upset was significantly more frequent in Glibenclamide group. Polyhydroamnios was non-significantly more frequent in Glibenclamide group.

Table 9. Maternal side effects.

Side effects	Glibenclamide	Insulin (N=60)	#P-value (N=60)	Effect size Relative rate 95% CI
Hypoglycemia (0.05–0.99)	2 (3.3%)	9 (15.0%)	#0.027*	0.22
GIT upset (1.03–8.78)	12 (20.0%)	4 (6.7%)	#0.032*	3.00
Polyhydroamnios (0.52–7.63)	6 (10.0%)	3 (5.0%)	§0.491	2.00
Allergic condition	0 (0.0%)	0 (0.0%)	Not applicable	
Visual disturbances	0 (0.0%)	0 (0.0%)	Not applicable	
Rash	0 (0.0%)	0 (0.0%)	Not applicable	

GIT: Gastrointestinal tract. #Chi square test. §Fisher's Exact test. Effect size: Value of Glibenclamide relative to insulin.

Table 10. Neonatal condtion and complications.

Side effects		Glibenclamide (N=60)	Insulin (N=60)	P-value	Effect size Mean±SE 95% CI
Weight (kg)	Mean±SD	3.3±0.3	3.5±0.4	^0.006*	-0.2±0.1
	Range	2.7–4.1	2.8–4.3		-0.3–-0.1
APGAR 1	Mean±SD	6.9±1.1	6.6±1.2	^0.106	0.4±0.2
	Range	4.0–9.0	4.0–9.0		-0.1–0.8
APGAR 5	Mean±SD	7.7±1.1	7.3±1.3	^0.063	0.4±0.2
	Range	5.0–9.0	5.0–9.0		0.0–0.9
					Relative rate 95% CI
Macrosomia		3 (5.0%)	6 (10.0%)	§0.491	0.50 (0.13–1.91)
Hypoglycemia		6 (10.0%)	11 (18.3%)	#0.191	0.55 (0.22–1.38)
Congenital malformations		0 (0.0%)	0 (0.0%)	Not applicable	
Respiratory distress syndrome		2 (3.3%)	6 (10.0%)	§0.272	0.33 (0.07–1.59)
NICU admission		4 (6.7%)	10 (16.7%)	#0.088	0.40 (0.13–1.21)

NICU: Neonatal intensive care unit. #Chi square test. Effect size: Value of Glibenclamide relative to insulin. CI: Confidence interval.

Table (10) shows neonatal weight was significantly lower in Glibenclamide group. APGAR scores were non-significantly higher in Glibenclamide group. In the Glibenclamide group, the incidence of macrosomia, hypoglycemia, respiratory distress syndrome, and NICU hospitalization was not statistically lower.

Discussion

Comparison of Glibenclamide and insulin for the treatment of gestational diabetes mellitus as a predictor of controlled GDM and healthy newborn outcome was highlighted as the main topic of interest (6-12), since control of gestational diabetes and neonatal outcome represent considerable conflict.

Thus, the purpose of this study was to compare the effectiveness of insulin and glibenclamide in establishing appropriate glycemic control.

A total of 120 patients with GDM were included in this prospective trial, which ran from October 2020 to July 2021 at the tertiary care hospital at Ain Shams University hospitals.

During this trial, 159 subject were evaluated for eligibility, and 120 were enrolled. Of all eligible patients, 32 were eliminated from the trial due to inclusion requirements, while 7 declined to participate.

Finally, the analysis was based on data from 120 individuals who were diagnosed with GDM and agreed to participate in the study.

There were no significant variations in patient characteristics between the two groups in terms of maternal age, parity, BMI, gestational age at enrollment, and HbA1c at baseline and follow-up levels, with no changes from baseline to delivery.

These findings are consistent with prior research by *Reda Ahmed et al*. (12), who conducted a prospective comparison study including 100 women under the age of 35 to assess the efficacy of glibenclamide against insulin in the management of GDM in the second half of pregnancy.

In terms of gestational age at birth and delivery duration, GA was not significantly greater in the glibenclamide group (p = 0.060, 0.107, respectively).

These results are in line with earlier studies by *Reda Ahmed et al*. (12), who found that the gestational age at delivery was similar in both groups, and by *Mohamed et al*. (13) at Sohag University in Egypt, who found no difference in the two groups' gestational ages at delivery (38.05 in the hypoglycemic

group versus 38.26 in the insulin group).

At the time of enrollment, before treatment, there was no discernible difference in the mean glucose levels between the two groups in terms of glycemic control. The fasting glucose levels were 139.1±12.5 mg/dl in the group treated with Glibenclamide, while the 2-hour postprandial glucose levels were 194.8±31.1 in the group treated with Glibenclamide, and 192.1±28.4 mg/dl in the group treated with Insulin (p=0.650).

After the medications were introduced, though, there was no discernible difference in the groups under study when it came to follow-up levels, delivery, or fasting blood glucose after a week.

Following the administration of the drugs, there were no statistically significant differences in postprandial blood glucose levels between the study groups after one week, at follow-up levels, and until delivery time.

The uncontrolled cases of Glibenclamide treated group mostly shift to insulin in weeks 4 and 5 after introduction of the drug.

These outcomes were consistent with the data provided by *Reda Ahmed et al.* (12), which showed that both groups' fasting and postprandial blood sugar levels were similar after achieving the right dosage of medication.

These results supported those of *Behrashi et al*. (14) who conducted a randomized controlled clinical trial between weeks 11 and 33 of gestation, enrolling 249 pregnant women with gestational diabetes, ages 18 to 45, to compare the effects of insulin and glibenclamide on maternal blood glucose. At the time of delivery, the trial did not find any statistically significant differences in GA between the two groups.

Additionally, *Coustan et al*. (15) carried out a prospective randomized observational clinical study over a 22-month period, enrolling 100 patients with GDM. Glyburide-treated women had better control over their fasting glucose levels than insulin-treated women (71.7% in the glyburide group vs. 63.2% in the insulin group; P = 0.003), and postprandial levels were better, though the difference did not reach statistical significance (57.8% in the glyburide group vs. 49.3% in the insulin group; P =.051). The study compared the use of glibenclamide and insulin in the treatment of gestational diabetes mellitus and its outcomes.

Also, *Pavithra et al*., (6) who conducted a prospective observational study including 100 women, revealed that the success rate for achieving established levels of glycaemic control is similar in insulin and glibenclamide treated patients.

In terms of delivery method, the Glibenclamide group had a non-significantly less frequency of cesarean deliveries. 53.3% of patients in Glibenclamide group underwent cesarean delivery versus 61.7% in insulin group (p value=0.356).

According to the findings of *Reda Ahmed et al*. (12) and the current study, the mode of delivery was similar in both groups: 28% of women in the glibenclamide group and 22% of women in the insulin group gave birth vaginally, while 72% and 78% of women in the glibenclamide and insulin groups, respectively, had a cesarean section.

These findings corroborated those of *Mirzamoradi et al*. (16), who discovered that, in the glibenclamide group, 24.3% of women gave birth vaginally, while in the insulin group, 28.8% of women did the same. Those who received insulin had a cesarean birth rate of 75.7%, whereas those who received glibenclamide had a rate of 71.2%.

Also, *Pavithra et al.*, (6) had reported similar LSCS rates among the patients of both groups as 42% in the insulin arm and 32% in the glibenclamide arm had LSCS done.

The current research study results revealed that maternal complications of hypoglycemia were significantly less frequent in Glibenclamide group (p value =0.027) and GIT upset was significantly more fre-

quent in Glibenclamide group (p value =0.032) while Polyhydramnios was non-significantly more frequent in Glibenclamide group (p value=0.491).

These results aligned with data from *Reda Ahmed et al*. (12), which showed that the proportion of polyhydramnios formation was non-significantly greater in the glibenclamide group (4 instances on glibenclamide group compared to 2 cases on insulin group).

These outcomes were consistent with the information provided by *Reda Ahmed et al*.(12), which demonstrated that the glibenclamide group had a non-significantly higher percentage of polyhydramnios development (4 cases on glibenclamide group developed polyhydramnios compared to 2 cases on insulin group).

Also, *Rao et al*., (17) had reported that hypoglycemia was significantly less frequent in Glibenclamide group (4%) while 12% in insulin group.

However, the current study has strong point of observation and follow-up of other maternal complications of maternal hypoglycemia and GIT upset than other previous studies of *Reda Ahmed et al*, (12), Rao et al., (17) and *Pavithra et al*., (6).

Regarding neonatal outcome, neonatal birth weight was significantly lower in Glibenclamide group (Glibenclamide 3.3±0.3 kg versus 3.5±0.4 kg in insulin group, p value=0.006).

There was no statistically significant difference between the two groups for the 1-minute Apgar score (p=0.106), and the same was true for the 5-minute Apgar score (p=0.063).

In terms of infant concerns, there were no significant differences between the two groups in fetal macrosomia, RDS, NICU hospitalization, congenital abnormalities, or neonatal hypoglycemia.

These results are consistent with earlier research. According to *Reda Ahmed et al*. (12), there was a difference in the birth weight between the two groups, with the glibenclamide group having a significantly lower birth weight (3250 ±500 gms versus 3600 ±750 gms in the insulin group) (p value >0.001). Additionally, although the differences were not statistically significant, the oral hypoglycemic group saw a decreased incidence of newborn hypoglycemia (occurring in 2% of the group and 4% in the insulin group).

Additionally, *Reda Ahmed et al*. (12) found that the percentage of newborns admitted to the Neonatal ICU was similar for both groups: almost 6% of those hospitalized in the oral hypoglycemic group and 10% in the insulin group. Hypoglycemia and respiratory distress were the most prevalent signs in both groups.

Pavithra et al., (6) revealed that fetal macrosomia and neonatal hypoglycemia were more common in insulin group but, the differences were not statistically significant (P = 0.37, 0.74) respectively. This could be attributed to the characteristics of the study population which was high BMI and positive family history.

In contrast to the current study, *Sénat et al*.(18) reported that the incidence of infant hypoglycemia was higher in the oral hypoglycemic group (12.2%) and comparable to the insulin group (7.2%).

Additionally, neither group's maternal nor newborn morbidities showed a statistically significant difference. According to the 2013 ACOG practice advisory on gestational diabetes mellitus, there are currently no negative short-term consequences of oral hypoglycemic medication therapy on the health of mothers and newborns, but long-term results need to be investigated (17).

Sénat et al. (18), in contrast to the current investigation, discovered that the incidence of newborn hypoglycemia was greater in the oral hypoglycemic group (12.2%), and was equivalent to the insulin group's 7.2%.

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difference. According to the 2013 ACOG practice advisory on gestational diabetes mellitus, there are currently no negative short-term consequences of oral hypoglycemic medication therapy on the health of mothers and newborns, but long-term results need to be investigated (17).

Glibenclamide appears to be a potential medication for neonates, according to this study; nevertheless, larger investigations are advised to determine the long-term effects on exposed children.

The main strength point of this current study is that firstly its prospective design and relatively larger sample size related to the previous studies by *Reda Ahmed et al*, (12), *Rao et al.*, (17) and *Pavithra et al*., (6). Secondly, the diagnosis and follow-up of all patients in a single hospital.

This study limitations are, lack of observation of complications of delivery as shoulder dystocia, perinatal mortality and patient compliance of oral hypoglycemics.

Balsells et al. (19) conducted a thorough analysis of the short-term results of randomized controlled trials comparing metformin and glibenclamide to insulin or each other in women who required pharmaceutical therapy due to gestational diabetes. The results showed that the glibenclamide and metformin groups had similar baseline characteristics, with the exception of a higher maternal age (pooled mean difference 1.36 years, 95% confidence interval 0.07 to 2.64) and a higher number of prior pregnancies/patient (0.20 to 0.72) in the metformin group (19).

Metformin was associated to less macrosomia (pooled risk ratio 0.33), less large for gestational age (pooled risk ratio 0.44), reduced maternal weight gain (pooled mean difference −2.06 kg), and lower birth weight (pooled mean difference −209 g) when compared to glibenclamide. In the metformin group, the average treatment failure rate was 26.8% (48/179), whereas in the glibenclamide group, it was 23.5% (40/170) (19).

Metformin was associated to increased fasting blood glucose levels throughout treatment (pooled mean difference of 0.15 mmol/L) for secondary outcomes (19).

Conclusion

Glibenclamide seems to be a helpful drug for treating pregnant women with gestational diabetes mellitus. It has comparable side effects as insulin for mothers and fetuses and aids in achieving proper glycemic control with a lower risk of hypoglycemia. The medication is incredibly cheap, but more suitably powered, randomized clinical trials are still required to address a number of issues, including long-term child follow-up, before it can be determined whether glibenclamide can replace insulin in the treatment of women with gestational diabetes mellitus.

Glibenclamide is recommended as a replacement for insulin therapy in the control of blood glucose in individuals with GDM when diet therapy and exercise are not enough to reduce blood glucose levels.

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