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Original research article

Insulin versus glibenclamide for the treatment of gestational diabetes

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Abstract

Background: Gestational diabetes mellitus is glucose intolerance with onset or first detection during pregnancy, regardless of insulin administration. Hyperglycemia is linked to pregnancy complications in GDM.

Methods: The Kakatiya Medical College, Warangal, Telangana conducted the study "Comparison of Insulin and Glibenclamide in Gestational Diabetes Mellitus" between April 2021 and March 2022 with approval from the hospital's ethics board. We screened for Gestational Diabetes Mellitus in around 150 individuals who visited our antenatal clinic.

Results: The AN clinic examined around 50 female patients at random for GDM using a 75 gm OGTT. If their fasting plasma glucose was greater than or equal to 95 mg/dl, and their 2-hour post meal glucose was greater than or equal to 140 mg/dl, then they were classified as having GDM. Insulin was administered to 25 patients and glibenclamide was given to another 25. Unfortunately, we were unable to complete the study due to the loss of 2 patients in the glibenclamide group.

Conclusion: In the trial, glycemic control and perinatal outcomes were practically the same for those treated with glibenclamide and insulin, save for one adverse result in the glibenclamide group who had a second trimester abortion due to late discovery and one macrosomic infant in the Insulin group.

Keywords: Insulin, glibenclamide, treatment, gestational diabetes

Introduction

Diabetes Mellitus causes complications in two to twenty percent of all pregnancies. The majority, or 90%, of these cases are due to gestational diabetes mellitus [1]. Carbohydrate intolerance of variable severity with onset or first recognition during pregnancy is the definition of gestational diabetes mellitus. This definition applies regardless of whether or not insulin is used as a treatment for the condition. Women who have gestational diabetes mellitus are more likely to have unfavorable birth outcomes if they have hyperglycemia during pregnancy [2-4]. Dietary therapy is the primary method that is used to achieve glycemic control in pregnant women who have diabetes and the administration of insulin has been the standard therapy for dietary failures up until the recent years. About 30-40% of patients have conditions that require treatment with pharmaceuticals [5]. Antihyperglycemic medications were not taken by the mother while she was carrying a child out of concern that doing so might result in low blood sugar in the newborn or foetal abnormalities. This is primarily based on studies that were conducted before the release of drugs such as glibenclamide and glipizide, both of which are in widespread use today [6]. In contrast to older sulfonylurea drugs and metformin, research has shown that glibenclamide does not cross the placenta of humans in significant quantities. Insulin therapy's drawbacks include patient discomfort, the inconvenience of injections and the expense, all of which have the potential to compromise compliance with the treatment [7-9]. On the basis of these findings and the relatively mild hyperglycemia that is present in the majority of pregnant women who have gestational diabetes mellitus, glibenclamide may be an alternative therapy for patients who have gestational diabetes mellitus [10]. Because of the negligible amount of glibenclamide that was transferred across the placenta in humans when *in vitro* models like placental perfusion models were used, it was determined that the use of glibenclamide during pregnancy is safe. This was the result of the successful clinical trial of glibenclamide [11]. Comparing Glibenclamide to Insulin as a Treatment for Gestational Diabetes Mellitus in the Indian Population The purpose of this study was to evaluate the safety and efficacy of Glibenclamide in comparison to Insulin in the treatment of Gestational Diabetes Mellitus in the Indian population. The primary goal here is to achieve a level of glycemic control that is satisfactory [12, 13]. The outcome of the mother and the newborn baby is a secondary end point.

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Materials and Methods

With approval from the hospital's ethics board Kakatiya Medical College, Warangal, Telangana conducted a study between April 2021 and March 2022, titled "Comparison of Insulin and Glibenclamide in Gestational Diabetes Mellitus". The antenatal clinic screened about 50 individuals for Gestational Diabetes Mellitus. The patients' gestational ages ranged from 11 to 33 weeks, and they were chosen at random. Patients were instructed to fast for three days before returning for a 75 gm oral glucose tolerance test, which was performed at the initial visit.

Two blood samples, each about 2cc in size, were collected from each patient: the first while they were fasting, and the second two hours after they had consumed 75 g of glucose in 200 ml of water. In the lab, these samples were run through a semi-automatic analyzer. Gestational diabetes mellitus was diagnosed if the patient had a fasting plasma glucose level greater than or equal to 95 mg/dl and/or a 2-hour postprandial glucose level greater than or equal to 140 mg/dl. Thirty-five of the 150 patients met the diagnostic criteria for GDM.

Five of these patients declined to participate in the trial due to lack of consent. After informing the remaining 30 patients about the study's purpose, 15 of them received Insulin treatment and 15 received pill Glibenclamide. According to the treatment protocol, these women were given either Insulin or Glibenclamide. A complete obstetric, family history and clinical examination are performed at the treatment facility. Results showed that 14% of participants had GDM.

The pregnant women in the research were all given typical dietary advice, which included eating three meals and three snacks per day. At each clinic visit, patients were asked about their progress on the diet and given encouragement to stay on track. The diet was designed to provide 25 kcal/kg of body weight for the obese women (BMI>27) and 35 kcal/kg (BMI<27) for the non-obese women with 40-45 % of the calories from carbohydrate. In the women assigned to receive Insulin, it is started at a lower dose of 6units and a maximum of 55 units was used in the study. The dose was adjusted according to the glycaemic status. In the glibenclamide group the starting was 0.625 mg orally, gradually increasing the dose and a maximum of 2.5 mg was used in the study to achieve adequate glycaemic control. The patients were instructed to come every 15 days for glycaemic profile. Mean plasma glucose was to be maintained at 105 mg/dl measured at any time of day, with fasting plasma glucose kept below 90 mg/dl and postprandial plasma glucose kept below 120 mg/dl. The patient's HbA1c level was checked before therapy began and again after the baby was born. Each visit includes a thorough evaluation of the patient's general and obstetric health. Menstrual history and, if possible, early ultrasound were used to estimate the expected delivery date. To rule out macrosomia, ultrasounds were performed at 22, 28, 32, and 36 weeks. All newborns were checked out by the neonatal team right after birth. To be born at a weight of more than 3.5 kilograms is considered macrosomia. Checking insulin levels in newborns' cord blood and analyzing their blood sugar levels. When a newborn's plasma glucose level falls below 35 mg/dl, this condition is known as hypoglycemia. Insulin levels in cord blood that are higher than 20 mIu/ml are considered abnormal. If a baby showed signs of jaundice, their serum bilirubin level was checked, and they were given phototherapy if necessary.

Inclusion criteria

- Women who wanted to have their babies between 11 and 33 weeks pregnant and were open to having them at Kakatiya Medical College, Warangal.

Exclusion criteria

- Pregnant women between 11 and 33 weeks of pregnancy.
- Women who do not wish to give birth at Kakatiya Medical College, Warangal.

Results

There were approximately 50 AN women who went through a random screening for GDM using a 75 gm OGTT while they were at the AN clinic. Those who had fasting plasma glucose levels greater than or equal to 95 mg/dl and/or 2-hour post glucose levels greater than or equal to 140 mg/dl were classified as having GDM. Protocol dictated that 25 patients receive insulin and the same number receive glibenclamide. 2 patients were lost in follow-up in the glibenclamide group. The demographic details were summarized in the table 1.

Table 1: Statistics of the population were compiled

	Group-I (Insulin) (N=25)	Group-II (Glibenclamide) (N=25)
Age	26.21 ± 4.0	23.6 ± 4.1
Pre-pregnancy wt	58.5 ± 10.4	48.8 ± 12.2
BMI	26.3 ± 5.1	22.7 ± 2.23
GA at entry into study	25.6 ± 6.11	22.4 ± 7.23

Both the insulin and glibenclamide groups shared similar demographics.

The largest proportion of patients on either insulin or glibenclamide are young adults (ages 20-30). Most

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people with diabetes on both insulin and glibenclamide have a high body mass index.

Table 2: Distribution of gravity

Gravidity	Group-I (Insulin) (N=25)	Group-II(Glibenclamide) (N=25)
Primi	9(52.1%)	10(54.4%)
Multi	8(45.9%)	9(48.9%)

Both the insulin and glibenclamide groups had a similar number of first-time and repeat mothers.
Patients who have a strong diabetic family history and a negative obstetrical history are distributed as shown in Table 3.

Table 3: Overview of the prevalence of patients with a diabetes-positive family history

	Group-I(Insulin)(N=25)	Group-II(Glibenclamide)(N=25)
BOH	6(32.5%)	7(39.1%)
Positive family history	7(39.1%)	5(33.3%)

Women who were pregnant and had a positive family history of diabetes or a poor obstetric history were about equally likely to be assigned to the insulin or glibenclamide group. The following table-IV summarizes the results of the screenings performed on plasma sugar levels.

Table 4: plasma sugar values are summarized

	Group-I (Insulin) (N=25)	Group-II (Glibenclamide) (N=25)	'P' Value
Fasting Plasma Glucose	91.06 ± 19.5	74.50 ± 19	0.061
2hr Post Glucose Plasma Glucose	161.9 ± 25.3	180.4 ± 26.46	0.75

There were 6 individuals with fasting plasma glucose greater than or equal to 95 mg/dl in the insulin group and 2 patients in the glibenclamide group. Screened patients were assigned at random to receive either insulin or glibenclamide. Table 5 summarizes the women's glycemic control levels as they progressed through treatment.

Table 5: During therapy, women's glycemia

	Group-I (Insulin) (N=25)	Group-II (Glibenclamide) (N=25)	'P' Value
Fasting Plasma Glucose	69.56 ± 22.6	62.27 ± 71	0.89
2hr Post	96.8 ± 11.2	97.7 ± 9.1	0.54

The target of treatment was to maintain blood sugar levels below 90 mg/dl in the fasting state, 120 mg/dl in the postprandial state, and 105 mg/dl in the 24-hour mean. Both the insulin and glibenclamide groups managed to get their blood sugar levels down to a healthy range. The highest glibenclamide dose that worked to lower blood sugar in the trial was 2.5 mg.
Examining HbA1c levels before and after therapy (Table-6).

Table 6: Pre-and post-treatment HbA1c

	Group-I (Insulin) (N=25)	Group-II (Glibenclamide) (N=25)	'P' Value
Pre-Treatment HbA1c	6.1 ± 0.79	6.2± 0.54	0.62
Post Treatment HbA1c	6.1±0.47	6.00±0.25	0.62

HbA1c readings were similar between the two groups both before and after treatment. The lack of statistical significance suggests that HbA1c may not be particularly helpful in GDM, where hypoglycemia is less common.
Pregnancy outcomes were documented by following the patients until they gave birth. Table 7 shows the results of the pregnancies.

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Table 7: Neonatal out come

	Group-I (Insulin) (N=25)	Group-II (Glibenclamide) (N=25)	'P' Value
Birth weight	3.78 ± 0.38	3.1 ± 0.72	0.42
New born Plasma Glucose	81.21 ± 27.6	68.3 ± 15.25	0.85
Cord Blood Insulin	6.14 ± 3.1	3.56 ± 3.9	0.92
NICU Admission for phototherapy	4(28%)	2(8.1%)	-

Table 8: Maternal out Come

	Group-I (Insulin) (N=25)	Group-II (Glibenclamide) (N =25)
PIH	3(15.4%)	2(8.1%)
Poly hydramnios	Nil	Nil
Retinopathy	Nil	Nil
Caesarean Deliveries	11(62.8%)	10(70.3%)

Results of the pregnancies were comparable between the two groups. One patient in the insulin group delivered a macrosomic baby, while one patient in the glibenclamide group experienced a late-term abortion (3.5 kg). No infants in either group showed signs of hypoglycemia. Clinical jaundice affected three infants in the insulin group and one infant in the glibenclamide group for 1–2 days, requiring phototherapy. Both groups' cord blood insulin levels were within the normal range, showing that hyperinsulinemia was not present. In the research, no one was born with a serious birth defect. Both groups had normal postpartum HbA1c levels, indicating successful management of blood sugar levels. Both the insulin and glibenclamide groups had comparable rates of PIH and cesarean section.
Before any patient was allowed to leave the hospital, their fasting and post prandial plasma glucose levels were checked. You can see a breakdown of this in table 9.

Table 9: All patients had fasting and postprandial plasma glucose tests

	Group-I (Insulin)	Group-II (Glibenclamide)	'P' Value
Fasting Plasma Glucose	70.08 ± 17.8	60.28 ± 6.8	0.68
2 hr. Post-Prandial Plasma Glucose	89.84 ± 11.81	88.7 ± 5.8	0.79

After delivery, both fasting plasma glucose and post-prandial plasma glucose were within normal ranges for all of the patients. According to the results of the student's t-test, there were no significant differences between the two groups in any of the features that were portrayed in any of the tables. This indicates that both medications are equally effective.

Discussion

A total of 50 patients with GDM participated in the current trial, with 25 receiving insulin and 25 receiving glibenclamide. There was a loss of contact with 2 patients in the glibenclamide group. This study's age distribution is significantly younger than Langer *et al*., but otherwise similar. Younger ages at marriage may explain the slightly more even distribution of ages seen in the present study. Compared to Langer *et al*., [16] who included more obese patients in both the insulin (65%) and glibenclamide (70%) groups, the current study included more non-obese patients with BMI 27. Both the present study and the study by Langer *et al*. [16] had similar and equivalent entrance gestational ages.

Table 10: Glucose levels when being treated

	Insulin Group		Glibenclamide Group	
	Fasting Plasma Glucose	Postprandial Plasma Glucose	Fasting Plasma Glucose	Postprandial Plasma Glucose
Present Study	59.89±15.6	91.9±11.2	59.23±6.2	90.8±5.9
Langer *et al*., Study	88.1±12.0	99.90±32	91.2±17.1	114.0±17.1

Both the insulin group and the glibenclamide group achieved adequate glycaemic control in the present trial and no patients were transferred to insulin due to inadequate glycaemic control. In the trial by Langer *et al*., patients in both groups achieved good glycaemic control, with the exception of 8 patients (4%), who were moved to insulin due to poor glycaemic control with the highest dose of glibenclamide (20 mg) [14, 15]. The table shows the patients' self-assessed blood sugar levels from the Langer *et al*. study, which correlates strongly with their blood sugar levels measured at clinic visits. At clinic visits, the average plasma glucose concentration was 102 + 24 mg/dl for those on glibenclamide and 99 +22 mg /dl for those taking insulin. HbA1c levels prior to pregnancy in the current study compared to the study of

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Langer *et al.* [16].

Table 11: Pre-Pregnant HbA1

	Insulin Group	Glibenclamide Group	'P' Value
Present Study	6.2±0.45	6.2±0.87	0.57
Langer *et al*. Study	6.9±2.1	7.9±2.1	0.51

Both the pre-pregnancy HbA1c levels in the present study and the Langer *et al*. study were within the normal range. This study's neonatal outcome was compared to that of a previous study by Langer *et al*. In contrast to the study by Langer *et al*., where one stillbirth and one infant death occurred in each of the insulin and glibenclamide groups, neither event occurred in the current investigation. One participant in the insulin group (6.6%) and none in the glibenclamide group experienced macrosomia during this trial. The incidence of macrosomia was higher in the glibenclamide group (8%) than in the insulin group (6%) in the study by Langer *et al*. Both studies found normal levels of insulin in cord blood, ruling out the possibility of hyperinsulinemia. Compared to the study by Langer *et al*., where preeclampsia occurred at a rate of 6% across both groups, the current study found an incidence of preeclampsia of 13.3% in the insulin group and 7.7% in the glibenclamide group. In the present study, the rate of cesarean section was 66.7% in the insulin group and 69.2% in the glibenclamide group, whereas the corresponding figures for Langer *et al.* [16].

Another research employing glyburide to treat pregnancy-related diabetes was conducted by Kremer *et al*. Eighty-two percent (59) of glyburide-treated patients reported feeling better after treatment. All patients in the present research had excellent glycemic control. The current investigation found no cases of macrosomia in the glibenclamide group, but the kremer *et al*. study found 19% to have macrosomic infants. Comparable newborn and maternal outcomes were observed across the insulin and glibenclamide groups in a previous study by Hellmuth *et al*., [17] which included 118 individuals treated with OHA.

33 patients were given glibenclamide and 21 were given insulin in a separate trial by Lim J M, Tayob Y, O'Brien PM and Shaw RW [18]. There was no statistically significant difference in mother and fetal outcome between the two therapy groups. Since glibenclamide was only tested in a small number of people with GDM, we know very little about its effectiveness. The field needs more research before it can be used in clinical settings.

Conclusion

In the trial, glycemic control and perinatal outcomes were practically the same for those treated with glibenclamide and insulin, save for one adverse result in the glibenclamide group who had a second trimester abortion due to late discovery and one macrosomic infant in the Insulin group. The lack of disparities between the two treatment groups' newborns verified the mother's results. Maternal hyperglycemia in GDM is transferred to the foetus, causing foetal hyperglycemia, which is more harmful than the medicine used to treat GDM.

Conflict of Interest: None.

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