ORIGINAL RESEARCH PAPER
Volume - 11 | Issue - 12 | December - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

TO COMPARE EFFICACY OF METFORMIN VERSUS INSULIN IN IMPROVING GLYCAEMIC CONTROL OF MATERNAL & PERINATAL OUTCOME IN GESTATIONAL DIABETES MELLITUS PATIENTS

Obstetrics & Gynaecology

Dr. Shobha Mukherjee Professor, Department of Obstetrics and Gynaecology, Rohilkhand Medical College and Hospital, Bareilly, U.P, India

Dr. Parru Singh Resident, Department of Obstetrics and Gynaecology, Rohilkhand Medical College and Hospital, Bareilly, U.P, India

Dr. Priyanshi Srivastava* Resident, Department of Obstetrics and Gynaecology, Rohilkhand Medical College and Hospital, Bareilly, U.P, India *Corresponding Author

ABSTRACT

Background: Diabetes Mellitus is a great burden to society. According to ACOG, gestational diabetes mellitus is defined as, any degree of glucose intolerance that either commences, or is first diagnosed in pregnancy Gestational diabetes mellitus pose many risks to the mother and the fetus and its consequences lead to increased maternal and fetal morbidity. Maternal complications includes increased risk of developing pre-eclampsia, preterm labour, chorioamnionitis,etc. The Fetal and Neonatal risks include Growth abnormalities like Macrosomia, Growth Restriction etc. Not enough studies are available to know the efficacy of Metformin. Our aim in this study was to compare efficacy of Metformin with Insulin. **Methods:** An interventional study of all women with GDM whose pregnancy was followed in the Department of Obstetrics and Gynaecology at Rohilkhand Medical College, Bareilly, U.P, India. Our study included 330 women diagnosed as Gestational Diabetes Mellitus who needed medical management for glycaemic control. Group A of 165 women were treated with Tab. Metformin 500 mg. Group B of 165 women were treated with subcutaneous Insulin. **Results:** The baseline characteristics of both the groups were similar with respect to age, enrolment, nulliparity etc. There was no significant statistical difference (p value > 0.05) between the two groups in terms of maternal and perinatal outcomes with respect to indicators like complications, HbA1c, pre eclampsia, side effects, etc. **Conclusion:** In our study we conclude that both metformin and insulin were equally effective in achieving the glycemic control in GDM patients. Both groups were comparable in terms of incidence of maternal and neonatal outcomes and complications with no statistical significant difference.

KEYWORDS

INTRODUCTION

Diabetes Mellitus is a great burden to society. It's the most common medical complication of pregnancy.[1] According to ACOG, gestational diabetes mellitus is defined as, any degree of glucose intolerance that either commences, or is first diagnosed in pregnancy[2]. This definition includes women whose glucose tolerance will return back to normal after pregnancy and also those women who will persist with glucose intolerance and develop Type 2 diabetes mellitus and it also includes those women who had unrecognized Type 2 Diabetes Mellitus prior to pregnancy.

Gestational diabetes mellitus pose many risks and its consequences lead to increased maternal and foetal morbidity. Maternal complications include increased risk of developing pre-eclampsia, which occurs in 10 % of patients with GDM and is its more severe complication. Other complications of diabetes include preterm labour, chorioamnionitis , polyhydramnios, urinary tract infection[2].

The foetal and neonatal risks includes growth abnormalities like macrosomia, growth restriction and congenital malformations, respiratory distress syndrome, etc.

More than 50% of these anomalies affect the central nervous or cardiovascular system. Fetal hypoglycemia due to maternal hypoglycemia can result in sudden intrauterine fetal death. Fetal and neonatal complication also includes chemical imbalances like hypocalcaemia and hypomagnesaemia which occur within 72 hours of birth, risk of neonatal hyperbilirubinemia is increased due to preterm delivery, ineffective erythropoiesis, expanded red cell mass and relative immaturity of the hepatic bilirubin conjugation and excretion.[2]

Long-term sequelae in babies born to diabetic mothers is that they have the risk of developing obesity, type 2 diabetes, cardiovascular disease and impaired cognitive and motor function later in life.

In management of GDM, for 80 % cases diet modification alone is sufficient but for the rest 20% cases medical management is required where we can use Insulin or an oral hypoglycaemic agents. Insulin is a major anabolic hormone, a peptide, administered by subcutaneous route and requires proper storage. Insulin is the classic and still first line agent in pharmacological treatment of GDM with disadvantage being risk of maternal hypoglycaemia with other side effects of insulin being swelling, erythema and stinging, lipodystrophy of subcutaneous fat around the injection site .

Oral hypoglycemic agent,Metformin is safe to use in pregnancy. Its an AMPK activator and acts by suppressing hepatic gluconeogenesis and glucose output from liver.

Not enough studies are available to know the efficacy of Metformin. Our aim in this study was to compare efficacy of Metformin with Insulin.

AIMS AND OBJECTIVE

To compare efficacy of Metformin versus Insulin in improving glycemic control and Maternal & perinatal outcome in gestational diabetes mellitus patients

The study outcome were measured in terms of glycaemic control, maternal complications and neonatal outcomes in terms of incidence of Large for gestational age babies, incidence of prematurity mean birth weight, APGAR score at 5 minutes.

MATERIALS AND METHODS

The present study is an interventional study of all women with GDM whose pregnancy was followed in the Department of Obstetrics and Gynaecology at Rohilkhand Medical College, Bareilly, Uttar Pradesh. All the antenatal care patients underwent the diagnosis of gestational diabetes mellitus with single step OGTT with 75 grams oral glucose (DIPSI).

75 gram glucose was given orally after dissolving in approximately 300 ml water whether the pregnant women came in fasting or non-fasting state, irrespective of the last meal. The intake of the solution was completed within 5-10 minutes .If vomiting occurred within 30 minutes of oral glucose intake, the test was repeated the next day. The screening test was considered positive when 2 hour postprandial blood glucose was more than 140 mg/dl and patient was diagnosed as GDM.

All pregnant women positive for GDM for the first time started on medical nutrition therapy (MNT) and physical exercise for 2 weeks. After 2 weeks again a 2 hour post meal blood sugar test was done. If it was ≥120 mg/dL, medical management (metformin or insulin therapy)

was started. Our study included 330 women diagnosed as Gestational Diabetes Mellitus who needed medical management for gylcemic control and had singleton pregnancy at more than 26 weeks of period of gestation ,who gave informed consent to participate in the study.

Two groups of 165 women each were made after randomization by lottery method. Group A of 165 women were treated with Tab. Metformin 500 mg twice daily orally up to a maximum of 2 gm/day, depending upon the glycaemic control of the patient Group B of 165 women were treated with subcutaneous injection Human premix insulin 30:70 given 30 minutes before breakfast once a day.

Dose of insulin was determined by blood sugar levels, if blood sugar level was 120-160 mg/dl , 4U insulin was given; between 160-200mg/dl , 6 U was given; for more than 200 mg/dl. Insulin vial – 40 IU/mL was used, vial was stored in refrigerator at 4◦C–8◦C.

The desirable target glucose levels were – fasting blood glucose levels <95mg/dl, 2 hr postprandial <120 mg/dl. All women were asked to perform a daily glucose profile (fasting, and 2 hour postprandial measurement) until delivery using a home glucometer and patients were followed till term.

Statistical analysis was performed using SPSS software version 16.0. Chi-square test was used for test of significance with p value <0.05 as significant statistically.

RESULT

Our study included 330 women diagnosed as Gestational Diabetes Mellitus who needed medical management for gylcemic control and had singleton pregnancy at more than 26 weeks of period of gestation ,who gave informed consent to participate in the study.

Table No 1: Demographic Characteristics of Participants

	GROUP A METFORMIN n = 165	GROUP B INSULIN n=165	p value
Age (years)	29 yrs	31yrs	0.072
BMI (Pre pregnancy)	27.7	26.9	0.076
HBA1c	5.3	5.60	0.058
Weight at enrollment (kg)	78kg	79kg	NS

In the table above we can clearly see that the basic characteristics of the two groups randomized for the study is similar with respect to mean age, body mass index, HbA1c levels and weight at time of enrolment with p value more than 0.05 suggesting a non significant difference between the two groups.

Table No 2: Demographic Characteristics of Participants of the study

	GROUP A METFORMIN n = 165	GROUP B INSULIN n=165	p value
GA at enrollment (weeks)	28	27.4	>0.05
Family history of diabetes	50.2%	48.2%	>0.05
Nulliparous	44%	32%	0.099
Past h/o macrosomia	7%	6%	NS

In the above table it is clearly depicted that the two groups are also similar with respect to gestational age, past history and family history suggesting adequate randomization.

Table No 3: Comparison of Maternal Outcome of the study between the two group

	GROUP A METFORMIN n = 165	GROUP B INSULIN n=165	p value
HbA1c at 37 wks POG	5.5	5.7	0.72
Pre-Eclampsia	8.5%	8%	>0.05
Gestational age at delivery	38 $^{+5}$ wk	37^{+6} wk	NS
Mode of delivery a. Spontaneous vaginal delivery b. cesarean section	36 % 64%	32% 68 %	>0.05 >0.05

The above table depicts that there is no statistical significant difference between the two groups treated by oral agent or insulin with respect to indicators of outcome of maternal concern.

Table No 4: Comparison of Maternal Outcome of the study between the two group

	GROUP A METFORMIN n = 165	GROUP B INSULIN n=165	p value
Fasting blood sugar	103	116	0.031
2 hr Postprandial blood sugar	125	143	0.040
Chronic Hypertension	26%	10.2%	0.09
Side effects 1 Nausea 2 Vomiting 3 Loose stool	 1% 2% 3%	 NIL NIL NIL	 >0.05 >0.05 >0.05
Injection site complication	NIL	0.8%	NS

Similarly table above also depicts that there is no statistical significant difference between the two groups treated by oral agent or insulin with respect to indicators of outcome of maternal concern or side effects of insulin injection.

Table No 5: Comparison of Neonatal Outcome of the study between the two group

	GROUP A METFORMIN n = 165	GROUP B INSULIN n=165	
Birth weight (gm)	3368	3402	>0.05
Prematurity	0.6%	0.2%	>0.05
LGA	1.2%	1.3%	NS
SGA	1.1%	0.9%	NS
Neonatal hypoglycemia	2%	3%	>0.05
APGAR at 5	8.6	8.6	NS

The above table depicts that there is no statistical significant difference between the two groups treated by oral agent or insulin with respect to indicators of outcome of neonatal concern.

Table No 6: Comparison of Neonatal Outcome of the study between the two group

	GROUP A METFORMIN n = 165	GROUP B INSULIN n=165	p value
Macrosomia	1.2%	1.3%	>0.05
NICU admission	2.6%	3 %	0.074
Respiratory Distress Syndrome	1.1%	1.4%	>0.05
Hyperbilirubinemia with need of phototherapy	8.7%	8.3%	0.076
IUD	0.7%	0.6%	NS
Perinatal Death	0.8%	0%	NS

The above table depicts that there is no statistical significant difference between the two groups treated by oral agent or insulin with respect to indicators of outcome of neonatal concern.

DISCUSSION

Our study included 330 women diagnosed as Gestational Diabetes Mellitus who needed medical management for gylcemic control and had singleton pregnancy at more than 26 weeks of period of gestation ,who gave informed consent to participate in the study.

In comparison to our study, the study done by Arshad et al[3] had newborns in insulin treated group having significantly more weight (p=0.01) with significant numbers of babies delivered after 38 weeks of pregnancy in Group-B (P=0.021) and significantly higher HbA1C at term in insulin group. (P=0.03) whereas in our study it was all statistically insignificant. There was also more number of cesarean sections due to feto-maternal disproportion in insulin group (28% vs.2%).

Similar to our study, study done by Simeonova et al[4] had groups comparable in age, smoking cigarettes and positive family history of diabetes but Mean glycosylated haemoglobin (HbA1c) at 37 gestation week, mean fasting, postprandial glycaemia, and gestational age at

delivery were lower in diet and metformin than insulin group although no differences in mode of delivery were observed between the metformin and insulin group. Women in metformin group had a significantly lower incidence of LGA newborns than diet and insulin groups. The percent of SGA new-borns was higher in insulin group than diet and metformin groups. The incidence of neonatal hypoglycemia was statistically significantly higher in the insulin group than in the metformin and diet group.

In study done by Rowan et al [5] out of the 363 women assigned to metformin, 92.6% continued to receive metformin until delivery and 46.3% received supplemental insulin. The rate of the primary composite outcome was 32.0% in the group assigned to metformin and 32.2% in the insulin group (relative risk, 0.99; 95% confidence interval, 0.80 to 1.23). More women in the metformin group than in the insulin group stated that they would choose to receive their assigned treatment again (76.6% vs. 27.2%, P<0.001).

Similar to our study the rates of other secondary outcomes did not differ significantly between the groups in the present study. There were no serious adverse events associated with the use of metformin.

In comparison to our study, the study done by Morais Rodrigues et al[6] showed poorer metabolic control with higher rate of pregnant with HbA1c ≥ 6% (42 mmol/mol) (25.6 vs 4.5%, p = 0.001) and more polihydramnios (14.6% vs 3.2%, p = 0.023) with insulin group. There were more newborns weighing < 2500 g in women treated with metformin. No other outcome showed difference with statistical significance, namely maternal weight gain, macrosomia or neonatal comorbidities similar to our study.

CONCLUSION

In our study we conclude that both metformin and insulin were equally effective in achieving the glycaemic control in GDM patients although the drugs had different side effects in mother.

Both groups were comparable in terms of incidence of Large for gestational age babies, incidence of neonatal hypoglycemia, macrosomia, incidence of prematurity, need for NICU admission, mean birth weight, APGAR score at 5 mins.

REFERENCES

1- Dashe JS, Bloom SL, Spong CY, Hoffman BL. Williams obstetrics. McGraw Hill Professional; 2018 Jun 1.
2- Arias F, Bhide AG, Arulkumaran S, Damania K, Daftary SN, editors. Arias' Practical Guide to High-Risk Pregnancy and Delivery: A South Asian Perspective. Elsevier India; 2019 Nov 25.
3- Arshad R, Khanam S, Shaikh F, Karim N. Feto-maternal outcomes and Glycemic control in Metformin versus insulin treated Gestational Diabetics. Pak J Med Sci. 2017;33(5):1182-1187. doi: https://doi.org/10.12669/pjms.335.13286
4 Simeonova-Krstevska S, Bogoev M, Bogoeva K, Zisovska E, Samardziski I, Velkoska-Nakova V, Livrinova V, Todorovska I, Sima A, Blazevska-Siljanoska V. Maternal and neonatal outcomes in pregnant women with gestational diabetes mellitus treated with diet, metformin or insulin. Open Access Maced J Med Sci. 2018 May 20; 6(5):803-807. https://doi.org/10.3889/oamjms.2018.200
5 Rowan, J. A., Hague, W. M., Gao, W., Battin, M. R., & Moore, M. P. (2008). Metformin versus Insulin for the Treatment of Gestational Diabetes. New England Journal of Medicine, 358(19), 2003–2015. doi:10.1056/nejmoa0707193
6 Morais Rodrigues, I., Figueiredo, A., Pereira, N. et al. Metformin as a Safe Option to Insulin in Gestational Diabetes Mellitus: a Retrospective Study. SN Compr. Clin. Med. 2, 272–277 (2020). https://doi.org/10.1007/s42399-020-00229-9