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ORIGINAL ARTICLE

Study of Metformin as first line therapy for control of gestational diabetes in Independent University Hospital.

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ABSTRACT… Objective: To assess the control of gestational diabetes with metformin and to study maternal and fetal outcome in patients using metformin. **Study Design:** Cross Sectional study. **Setting:** Department of Obs & Gynae, Independent University Hospital. **Period:** September 2019 to July 2021. **Material & Methods:** Eighty six patient diagnosed as having gestational diabetes mellitus by oral glucose tolerance test included in study and Metformin used as first line therapy along with diet for control of blood sugar levels. While patients with insulin dependent diabetes and type 2 DM were excluded from study. **Results:** It was observed in study, that with metformin use glycemic control was excellent in 70 (81.3%) of patients. Maternal outcome like risk of maternal weight gain>10kg, preeclampsia, and premature births were low in patient usung metformin in pregnancy and as well as neonatal risk of macrosomia, prematurity, neonatal hypoglycemia and need for hospital admission were low with the use of metformin in patients suffering from gestational diabetes. **Conclusion:** GDM associated adverse outcome for mother like maternal weight gain, pregnancy induced hypertension operative delivery and neonate like macrosomia, birth trauma, neonatal hypoglycemia are well controlled by the use of life style modification and metformin use in almost >80 % of cases only in few cases there is additional need of insulin therapy. Maternal and fetal outcome found to be satisfactory with the use of metformin. Further studies are required to build a more confidence.

Key words: Gestational Diabetes Mellitus, Metformin, Oral Glucose Tolerance Test.

INTRODUCTION

Diabetes is a worldwide challenge and a big health concern. Life style modification, changes in dietry habits and social development has led to massive effect on community. The fact is that not only common population but especially pregnant ladies are at risk of developing gestational diabetes and so complicated by multiple adverse effects on pregnancy.[1] The incidence of gestational diabetes is 3-5% and 1 in 250 pregnant ladies are complicated by pre-existing diabetes.[2] The prevelance of gestational diabetes mellitus among Asian women varies according to maternal age socioeconomic status, race, ethnicity, body composition and genetic factors as well.[3]

Diabetes mellitus increases the risk of certain pregnancy complications like miscarriages, congenital malformation, preeclampsia, increase rate of operative deliveries, intrauterine deaths, fetal hypoglycemia and bad perinatal outcome. Guidelines from several global contexts like UK, New Zealand, and Canada emphasize on the use of metformin for the treatment of metformin as an oral insulin sensitizing and glucose lowering drug.[4] Insulin therapy is considered best because it is very safe and does not cross placenta But there are concern of some problems with the use of insulin that is cost, fear of repeated injections, and risk of hypoglycemia in fetus. That's why interest in the use of oral hypoglycemic agent has generated throughout the world.[5]

Metformin is widely used as oral medication for control of GDM as compare to insulin.Metformin has been shown to result in less maternal weight gain lower postprandial glucose level, less

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pregnancy induced hypertention and less severe neonatal hypoglycemia. However there may be need of insulin therapy in 26.8 -33.8 % of pregnant ladies with GDM.[6] Metformin doses ranging from 500-2500mg/day have been used to treat women with GDM. Metfomin is almost entirely excreted through urine in unchanged form. During pregnancy increase glomerular filtration further help in renal clearance.[7] So it is the hypothesis that we can safely use metformin for the treatment of GDM and may have benefits for patients and neonates.[8] The study aimed to assess control of GDM by metformin in our population amd to study its effects on mother and fetus.[9]

MATERIAL & METHODS

It is a descriptive cross sectional study conducted in tertiary care hospital Independent Medical College Faisalabad from September 2019 to July 2021 after approval from ethical committee (IUH/IRB/000040). Total 86 patient having GDM followed during study period according to predesigned proforma requirement. The main purpose was to collect information regarding risk factors in patient like age, BMI, family history and obstetric history. Diagnosis of GDM by OGTT, control of diabetes with metformin i.e fasting blood sugar <110mg/dl and two hours post prandial blood sugar level <140mg/dl as recommended by WHO and need of insulin adjustment for control of diabetes. Maternal and fetal outcome also observed like maternal weight gain, preeclampsia, gestational age at delivery and mode of delivery. Fetal APGAR score, birth weight, hypoglycemia and need for NICU admission also recorded in proforma.

Inclusion Criteria

All patient who diagnosed as having GDM on outpatient or inpatient evaluation included in study by performing OGTT (Oral Glucose Tolerance Test).

Exclusion Criteria

All those patient having insulin dependent diabetes and pre gestational diabetes controlled on medication excluded from study.

The data analysis was done by SPSS version 16. Frequency and percentages calculated for qualitative data, by applying chi square test.

RESULTS

The total 86 patients were included in this study who were diagnosed as having gestational diabetes mellitus by OGTT. Risk factor evaluation was done by history and examination like age, weight, strong family history of diabetes and previous bad obstetric history as shown in Table-I. OGTT was positive in 68 patients and impaired in 18 patients.

Age	<30 years	>30 years
	40(46.5)%	46(53.4%)
BMI	<30	>30
	25(29%)	61(70.9%)
Parity	primigravida	Multigravida
	35(40.6%)	51(59.3%)
Family history	Positive	Negative
	50(58.1%)	36(41.8%)
Bad obstetric history	Positive	Negative
	46(53.4%)	40(46.5%)
OGTT	Positive	Impaired
	68(79%)	18(20.9%)

Table-I. Demographic features & risk factor

Maternal Outcome

During study it was observed that glycemic control was good in 70 (81.3%) of patients while only 16(18.6%) patient need insulin adjustment for control of glycemic level. Mernal weight gain was <10kg in 60 (69.7%) of patients. Pre eclampsia was positive only in 16 (18.6%) of patients. 78 (90.6%) for patients delivered at term and mode of delivery was LSCS in 66(76.4%) and NVD in 20(23.2%) as shown in Table-II.

Glycemic Control	Good	Impaired
	70(81.3%)	16(18.6%)
Maternal weight gain	<10kg	>10kg
	60(69.7%)	26(30.2%)
Pre eclampsia	Positive	Negative
	16(18.6%)	70(81.3%)
Gestational age at delivery	<37	>37
	8(9.3%)	78(90.6%)
Mode of delivery	NVD	LSCS
	20(23.2%)	66(76.4%)

Table-II. Maternal outcome

Neonatal outcome: macrosomia baby weight >3.5kg was only present in 10 (11.6%) of babies while 76(88%) babies were of weight <3.5kg.

Most babies delivered with good APGAR SCORE 82(95.3%) at term 78(90.6%), only 8(9.3%) babies were premature and need NICU admission in 10 (11.6%). Neonatal hypoglycemia was observed only in 12 (13.9%) as shown in Table-III.

Birth weight	<3.5kg	>3.5kg
	76(88%)	10(11.6%)
prematurity	<37	>37
	8(9.3%)	78(90.6%)
Neonatal hypoglycemia	positive	negative
	12(13.9%)	74(86%)
APGAR SCORE	<7	>7
	4(4.6%)	82(95.3%)
NICU admission	positive	negative
	10 (11.6%)	76(88.3%)

Table-III. Neonatal outcome

DISCUSSION

Gestational diabetes mellitus is a common problem of pregnancy and it is associated with a lot of maternal and fetal complication. Oral agents have been increasingly considered potential alternatives for the control of GDM. Several observational and randomized controlled trials have addressed the use of oral agents in gestational diabetes.[10] In this study 86 patient diagnosed as having GDM on the basis of risk factor evaluation and confirmation by OGTT. Glucose tolerance test was positive in 79 % of cases and impaired in almost 21%. Diet chart and Metformin started in these patients and blood sugar level monitoring done initially on inpatient basis and then on outpatient basis. Metformin dose adjusted accordingly ranging from 750 mg per day to 2000 mg per day. Glycemic control was good in 70(81.3%) and only 16(18.6%) patients need insulin adjustment for glycemic control.

Maternal weight gain was <10kg in 60(75%) of patients, preeclampsia seen in 16(18.6%) cases. Almost 78 (90.6%) delivered after 37 weeks of pregnancy and mode of delivery was mostly by LSCS 66(76.4%) and 20(23.2%) delivered vaginally. In this study fetal outcome also recorded and observed that birthweight of fetuses was <3.5kg in 76 (88%) cases and >3.5 kg in 10 (11.6%) fetuses. Neonatal hypoglycemia was present only in 12 (approx. 4%) of cases, so need for NICU admission was also very low only 10(11.6%). It was also observed that there was need to start insulin in some patient approximately 16(18.6%) of patients for a short period of time during third trimester for better glycemic control achievement.

Like this study, the prospective observational study of hyer et, al assessed the effects of metformin in women with GDM. The metformin group had less maternal weight gain (p=0.04), a reduced incidence of neonatal jaundice, less prone to macrosmia, and had fewer admission to special care baby unit and a lower incidence of neonatal hypoglycemia. Rowen et, al and Moore et, al studies also support our study because they also observed positive maternal and neonatal outcome with metformin use. MIG trial also suggest potential advantage of metformin over insulin in GDM in terms of less maternal weight gain and lower neonatal birth weight.[11] Interestingly, severe hypoglycemic episodes occurred Less frequently in infants of mother taking Metformin. Moreover, study ended with a positive note that Metformin is beneficial for control of GDM.

According to a scoping review that was conducted in southeast Asia, obesity is considered as major risk factor for GDM.[12] As in this study approximately 71% of patient were obese who are suffering from GDM. Therefore reducing obesity in prepregnancy period can reduce the incidence of GDM.

A recent randomized controlled trial of 160 women with GDM reported that monotherapy with metformin resulted in comparable maternal glycemic control as with insulin.[13] In this study 14% of women in the th metformin monotherapy group eventually required insulin for glycemic control. While in the study by rowan, it was noted that there is need for insulin supplementation in 46% of patients.[11] while as compare to these in our study there was need of insulin supplementation in 16(18.6%) of patients. In niromech study pregnancy induced hypertension observed in 5% and cesarean section in 43% with metformin therpy.[13] The study by rowan et al did not find any difference in both groups with metformin and insulin.[11] while in our study pre eclampsia

observed in 18.6% of patients and LSCS done in 76.4 % of cases but premature delivery occurred in only is less than 9.3% of cases.

Neonatal outcome like neonatal hypoglycemia observed in 12(13.9%), NICU admission in 10(11.6%) and birth weight of babies was <3.5 kg in 76(88%) of cases with good APGAR score in patient having GDM controlled by metformin treatment. A small randomized controlled trial by spaulonci et al[14] and a small retrospective by Tertti et al[15] study supports these results because in both stidies ratio of neonatal hypoglycemia and NICU admission was lower as compare to insulin treated group but not a significant difference in birth weight. while randomized controlled trial by Mesdaghina et al fail to support this study because they did not observed any difference of neonatal outcome in both groups treated by metformin and insulin.[16] while a study conducted by Gandhi et al comparing metformin plus lifestyle modification (LSM) to LSM alone showed a great difference in macrosomia 8.2%vs14.3% and lower birth weight 14.8% vs 23.7% in metformin treated group. So it was concluded that Metformin is very effective for control of GDM. It is very practical to use it and gets its benefits related to mother and neonate.

CONCLUSION

GDM associated adverse outcome for mother like maternal weight gain, pregnancy induced hypertension operative delivery and neonate like macrosomia, birth trauma, neonatal hypoglycemia are well controlled by the use of life style modification and metformin use in almost >80 % of cases only in few cases there is additional need of insulin therapy. Maternal and fetal outcome found to be satisfactory with the use of metformin. Further studies are required to build a more confidence.

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