VOLUME-9, ISSUE-4, APRIL -2020 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Obstetrics & Gynaecology

COMPARISON BETWEEN TABLET METFORMIN AND INJECTION INSULIN IN THE TREATMENT OF GESTATIONAL DIABETES MELLITUS: PROSPECTIVE STUDY

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ABSTRACT

INTRODUCTION: Gestational diabetes mellitus is defined as glucose intolerance of different severity recognsied first time during pregnancy.

GDM is diagnosed in 3-7% of pregnancies.

The main purpose of treatment of GDM is to prevent hyperinsulinemia and fetal macrosomia by improving maternal glycemic control.

AIM: To compare metformin and injection insulin in the treatment of GDM and its maternal and fetal outcome

METHOD: In this prospective study conducted during (march 2018-september 2019) 100 Women include who visited in antenatal clinic and/or admitted in ward between 20-36 yr of age at gestational age between 20 to 36 weeks who were diagnosed by had done OGCT by DIPSI method and value more than >140 mg/dl diagnosed as GDM and 50 women were given Metformin and 50 were given Insulin. Results were compared.

RESULTS: Both groups were comparable with respect to age, parity, family history of DM and weight gain during pregnancy. Glycemic control was slightly better in Insulin treated group than Metformin treated group throughout gestation (p value =0.38).

CONCLUSION: In this study we found that slightly better glycaemic control was found in Insulin group than Metformin group but there was no significant difference between two groups.

KEYWORDS : Gestational diabetes mellitus, Metformin, Insulin

INTRODUCTION

Gestational diabetes mellitus is defined as glucose intolerance of different severity with onset or first recognition during pregnancy[1]. It implies whether or not insulin is used for treatment and undoubtedly includes women with unrecognized overt diabetes.

GDM is diagnosed in approximately 3-7% of pregnancies.[2,3] The incidence of GDM increases in older and more obese pregnant women. Within 20years more than half of the women with gestational diabetes develop overt diabetes. Increasing prevalence in developing countries due to increased urbanization, decreased physical activity, changes in dietary patterns and increasing prevalence of obesity.

In first trimester due to insulin sensitivity there is hypoglycaemia. In second and third trimester increase in insulin resistance as it starts providing nutrition to the growin fetus.

Patients with history of GDM are at increased risk of adverse perinatal outcome and also increase risk of Type 2 DM in patient itself and their children were also at risk of Type 2 DM.

Adverse maternal complication include hypertension, preeclampsia, hydramnios, increased operative intervention and Type 2 DM. Fetal outcome include macrosomia, RDS, hypoglycaemia etc.

The main purpose of treatment of GDM is to prevent hyperinsulinemia and fetal macrosomia by improving maternal glycemic control. Initially start on diet and exercise counselling, but there was addition of insulin be done on some patients.

The percentage of GDM patients need in pharmacological treatment varies from 20-60%.

As Metformin found to be alternative to insulin in the treatment of diabetes in pregnancy. Decreased hepatic gluconeogenesis and improves peripheral glucose uptake.[4] It does not cause Hypoglycemia and it is not associated with increased weight gain. There is no evidence of adverse fetal effects or increased risk of major malformations when metformin is used in pregnant women, although it cross placenta. Insulin causes weight gain, hypoglycaemia and compliance is poor due to subcutaneous injection.

METHODS:

It is a prospective comparative study to be conducted at department of Obstetrics and Gynaecology of Tertiary Health Care Centre for the period of 18 month (March 2018 –September 2019). By convenient sampling 100 women were recruited for study and 50 in each arm that included 50 women in the Metformin group and 50 women in the Insulin group.

SOURCE OF DATA

Patients diagnosed at Tertiary Health Care Centre as GDM from 20 week to 36 weeks who got admitted and /or visited outdoor patient department in Obstetrics and Gynaecology department over period of 18 month.

INCLUSION CRITERIA:

A) All the cases diagnosed as GDM who got admitted and visited to outdoor patient department women age between 20-36-year age, between 20 weeks to 36-week gestation.
B) Patient who was willing to participate in the study.

EXCLUSION CRITERIA:

The following women were excluded

A) Pre pregnancy diagnosis of diabetes, (a contraindication to Metformin)
B) Fetal anomaly.
C) Rupture membrane
D) Multiple pregnancy.
E) Patient not willing for study.

METHODS

All cases of GDM who get admitted to and/or visit outdoor patient department Obstetrics and Gynaecology in Tertiary

Health Care Centre between 20-36 week of age 20-36 year were informed about the study.

Demographic and clinical data were recorded at enrolment. Blood samples were obtained to asses baseline blood glucose and to ensure the renal and liver function test did not preclude the use of Metformin.

100 women diagnosed with gestational diabetes mellitus according to DIPSI criteria and/or WHO criteria of glucose tolerance test and/or HbA1c these women alternatively divided into two groups, 50 patients in Metformin group and 50 patients in Insulin group.

DIPSI criteria: 2 hours post prandial >140mg/dl following a 75gm glucose load by venous sample or by glucometer irrespective of their fasting status or previous meal

An informed written consent were taken from patient.

In group1.The patient was given diabetic diet and started on Tablet Metformin 500mg once daily. If blood glucose not controlled in 1week, dosage was increased to 500mg twice daily after food. Maximum dosage of 1700mg/day (850mg twice daily) were given. During this period self-blood glucose monitoring were done by capillary blood glucose test with glucometer meter. Good glycemic control is considered when fasting <90mg/dl and 2 hr post prandial <140mg/dl done 6 times a day (fasting, post breakfast, pre-lunch, post lunch, pre-dinner, post dinner). If there were poor control after maximum Metformin dosage, these patients were added Insulin along with Metformin as treatment.

In group 2: The patient was given diabetic diet and started on human Insulin in 2/3rd and 1/3rd regimen. The dose of Insulin titrated accordingly, to achieve glycemic target.

Optimum glycemic control and maternal and neonatal outcome were compared between two groups.

DATA ANALYSIS:

Data entry had done in MS Excel 2010 and analysed using professional statistics package EPI Info 7.0 version for windows. Descriptive data represented as mean ± SD for numeric variables, percentages and proportions for categorical variables.

Appropriate tests of significance to be used depending on nature & distribution of variables like Chi square test, Fisher exact test for categorical variables. Value of p <0.05 considered as statistically significant.

RESULTS

TABLE NO. 1 SHOWING DISTRIBUTION OF STUDY SUBJECT BETWEEN METFORMIN AND INSULIN GROUP ACCORDING TO SOCIODEMOGRAPHIC FACTOR

	METFORMIN N=50	INSULIN N=50	p value
Age (mean±SD) yrs	26.88± 4.30	25.86±3.64	0.67
Primipara (n, %)	28 (56%)	29(58%)	0.83
Multipara (n, %)	22 (44%)	21(42%)	
Family history DM (n, %)	17 (34%)	11(22%)	
Weight gain >12.5kg(n, %) during pregnancy	22 (44%)	14(28%)	0.10
H/o GDM in previous pregnancy n (%)	10 (45.5%)	6 (28.6%)	0.28
OGCT 140- 200(mg/dl) >200 (mg/dl)	40(80%) 10 (20%)	38(56%) 12 (24%)	0.63
Gestational age at the time of diagnosis			
20-28 weeks 28/1- 36 weeks	16 24	17 23	
METFORMIN+ Insulin	**12**	0	

TABLE NO. 2 SHOWING MATERNAL OUTCOMES OF PREGNANCY IN METFORMIN AND INSULIN GROUP.

		Metformin N=50 (%)	Insulin N=50 (%)	p value
Blood glucose controlled		29 (58%)	30 (60%)	0.83
Dose increases		9 (18%)	20 (40%)	
Delivery at ≥37 weeks		36 (72%)	32 (64%)	
Mode of delivery LSCS ASSISTED VAGINAL VAGINAL		 35 (70%) 0 15 (30%)	 36 (72%) 0 14 (28%)	
Weight of baby 2.6 – 2.999 3.0- 3.499kg 3.5- 3.999kg ≥4kg		 8 (16%) 14 (28%) 8(18%) 5 (10%)	 18 (36%) 11(22%) 4 (8%) 4(%)	0.65
Apgar score at 5 min (7-10)		50	50	
NICU stay		21 (42%)	22 (44%)	0.84
	HYPOGLYCEMIA	4 (8%)	3 (6%)	0.71
	HYPERBILIRUBINEMIA	6 (12%)	11 (22%)	0.19
	RESPIRATORY DISTRESS	4 (8%)	0	<0.001
	LOW BIRTH WEIGHT AND OTHER CAUSE LIKE PRETERM, HYPOCALCEMIA, SEPSIS	7(14%)	9(18%)	0.66

TABLE NO. 3 SHOWING COMORBIDITIES IN PATIENTS DEVELOPED DURING PREGNANCY

	Comorbidities	Metformin (n=50)	Insulin (n=50)	p Value
Not Related With Pregnancy	PCOS	3(6%)	4(8%)	0.66
	Chronic Hypertension	1(2%)	0	0.50
Related With Pregnancy	Preeclampsia	2 (4%)	4 (8%)	0.44
	Polyhydramnios	7 (14%)	3 (6%)	0.20
	Oligo Hydramnios	1(2%)	0	0.50

7 Patients had PCOS before pregnancy and they were already taking Metformin in which 3 (6%) patients continued with Metformin and 4 (8%) patient were started on Insulin. Dose of Insulin increases to achieve targeted blood glucose level.

DISCUSSION

Munshi et al (2014)[5] reported that in Metformin group 84% continued to receive Metformin until delivery and 16% received supplemental Insulin while in our study 76% continued with Metformin and 18 % required added Insulin along with Metformin.

In the study conducted by Rowan et al (2008)[6] 45 (12.4%) women delivered at less than 37 weeks in Metformin group while 45 (12.2%) women delivered at less than 37 weeks in Insulin group while in our study delivery before 37 week was slightly more in Insulin group.

In our study 2 % patient in metformin group had chronic hypertension which did not matched with study conducted by Goh et al (2011)[7] they had 5.4% of patient had chronic hypertension in Metformin group. Compared with non –

diabetic chronic hypertension was more common in diabetic group women. In 3-5% of pregnancies chronic hypertension is estimated to be present.

Najafian et al (2016)[8] in their study showed that 6 (8.8%) women developed Preeclampsia in Metformin group and 10 (14.2%) women developed preeclampsia in Insulin group while in current study patient preeclampsia developed more in Insulin group 4 (8%) than Metformin group 2 (4%). And there was ethnicity difference as Najafian done their study in Persian ethnic while our study was done in Asian women.

In our study of the 2 patients in Metformin group who developed preeclampsia one of them had low birth weight baby. In both the babies Apgar score was <7 at 5 minutes while of 4 patients in Insulin group who developed preeclampsia of 2 of the participants had low birth weight babies and 3 babies had Apgar score <7 at 5 minutes.

Ghomian et al (2018)[9] reported in their study that new born having Apgar score at 5minute less than 7 in Metformin group were19 (13.2%) and Insulin were16 (11.1%) and it is not comparable with current study.

Hassan et al (2012)[10] reported in their study that there was statistically significant difference in birth weight in both groups (p value = 0.05) while in our study (p value 0.65) which is statistically not significant. Mean birth weight was found in Hassan et al in their study in Metformin group were 3.4±0.4 kg and in Insulin group were 3.6±0.46kg while in our study Mean birth weight in Metformin group were 2.4±.4kg and in Insulin group 2.3±.4 kg.

CONCLUSION:

This study adds stronger evidence that Metformin is a convenient alternative and equally effective as Insulin. Though slightly better glycaemic control was found in Insulin group than Metformin group but there was no significant difference between two groups. Metformin therapy is practical and cheap compared to Insulin especially relevant in the low resource settings.

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