Original Article

# Metformin versus Insulin in the Management of Gestational Diabetes Mellitus

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## Abstract

**Background:** Gestational diabetes mellitus (GDM) is one of the most common medical conditions complicating pregnancy and its prevalence increasing nowadays due to the increasing obesity in our society. The whole story is due to insulin resistance which is best managed by metformin rather than insulin. **Objective:** The main objective of the study is to compare the efficacy of metformin in controlling hyperglycemia in GDM or their effect on the pregnancy outcome versus insulin therapy. **Materials and Methods:** This study was carried out at the Obstetrics and Gynecology Department of Al-Zahraa Teaching Hospital in Al-Najaf from February 2015 to November 2015, as 100 pregnant ladies from (20 to 32) weeks of gestational age were already diagnosed to have GDM or we diagnosed them by formal 75 g oral glucose tolerance test. **Results:** Metformin was better in controlling blood sugar (111 mg/dl versus 145 mg/dl in insulin). Neonatal complication and cesarean section rates were higher in insulin limb. **Conclusion:** Metformin was better in controlling blood sugar in GDM than insulin, with better neonatal outcome.

**Keywords:** Diabetes mellitus, gestational diabetes mellitus, metformin, pregnancy

## Introduction

Gestational diabetes mellitus (GDM) is defined as impaired carbohydrate tolerance diagnosed during pregnancy with a return to normal glucose tolerance after delivery.[1] The incidence is about 3%–7% of pregnancies, and it increases as the pregnancy population is becoming older and fatter.[2] Studies investigating risk factors for development of GDM vary with the definition of the disorder, however, these factors are: obesity, advanced maternal age, family history of diabetes, high weight gain in early adulthood, current smoking, previous baby >4.5 kg, glucosuria, current suspected macrosomia, and polyhydramnios.[3] Other traditional risk factors for which less evidence include twin pregnancy, polycystic ovarian disease, parity related to maternal age, previous congenital abnormality, and previous stillbirth. The risk for developing GDM in subsequent pregnancies is high with recurrence rates about 30%, women who have required insulin treatment for GDM in previous pregnancy have recurrent risk of 75%.[4]

Basal and postprandial glucose metabolism is altered in pregnancy; during pregnancy, there is increased pancreatic B-cell response and hyperinsulinemia; this facilitates the supply of glucose to the fetus by altering maternal energy metabolism from carbohydrate to lipids. On the other hand, there is increased insulin resistant secondary to secretion of placental hormones as progesterone, cortisol, placental lactogen, growth hormone, and prolactin. This resistance is evident by the second trimester and forward and resolved with delivery of the placenta.[5]

Women with GDM have exaggeration of this insulin resistance, possibly due to the decreased ability of pancreatic B-cell to increase insulin secretion, and this may be due to: In turn, the insulin resistance results in increased blood glucose level in response to glucose load which can exert adverse fetal outcome by fetal hyperglycemia and hyperinsulinemia.[6] GDM is an asymptomatic condition, so it can only be detected by

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**Submission:** 22-02-2019 **Accepted:** 01-10-2019 **Published Online:** 23-12-2019



**How to cite this article:** Mahmood OA. Metformin versus insulin in the management of gestational diabetes mellitus. Med J Babylon 2019;16:346-50.

Access this article online

Quick Response Code:

Website: www.medjbabylon.org

DOI: 10.4103/MJBL.MJBL_11_19

screening. However, there is controversy over the optimum screening test and to whom we apply the screening test.[7,8]

## Materials and Methods

The aim of our study was to compare the efficacy of metformin in controlling hyperglycemia in GDM or their effect on the pregnancy outcome versus insulin therapy. This study was conducted at the Obstetrics and Gynecology Department of Alzahraa Teaching Hospital, Najaf, from February 2017 to November 2017. Hundred pregnant ladies from (20 to 32) weeks of gestational age were already diagnosed to have GDM or we have diagnosed these women by formal 75 g oral glucose tolerance test.

Exclusion criteria included preeclampsia, renal disease, liver disease, hypothyroidism, twin pregnancy, and diagnosed congenital anomaly.

Then, we randomly divided those 100 women into 50 women as control whom their diabetes with metformin and the other 50 women were managed with insulin. The dose of metformin500 mg three times daily maximum dose 2000 mg per day. The type of insulin used is mixture, the dose was titrated according to the reading.

We followed our patient by 1 h postprandial blood sugar and the target is <8 mmol/l. We also followed the pregnancy by fetal surveillance by 2 weekly ultrasound to measure (amniotic fluid index, abdominal circumference, and head circumference).

Patients were followed either as inpatient till control their sugar profile and then followed as outpatient by continua's attachment by phone or management as outpatient and followed by phone.

The pregnant outcome was analyzed for gestational age at delivery, mode of delivery, and the neonatal outcome regarding (birth weight, Apgar score, neonatal care unit admission, and complication).

### Ethical consideration

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out the patients verbal and analytical approval before sample managed. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee.

## Results

This study consists of 100 women with GDM, half of them were on insulin while the other half were on metformin. The demographic comparison between the two groups are shown in Table 1.

The number of cesarean section in the insulin treatment group (60%) was higher than in the metformin treatment group (46%) Table 2.

The number of neonate admitted to the NCU higher in the insulin-treated group (58%) than in metformin-treated group (6%) Table 3.

**Table 1: Comparison between metformin and insulin groups in different parameters**

| Variable | Metformin ($n=50$) | Insulin ($n=50$) | *P* |
|---|---|---|---|
| Age/years | 34.20±6.44 | 31.24±6.76 | 0.027 |
| Weight/kg | 91.7±10.61 | 92.76±10.28 | 0.613 |
| Gravida | 3.78±2.36 | 3.18±1.89 | 0.165 |
| Parity | 2.46±2.10 | 1.72±1.59 | 0.050 |
| Birth date/weeks | 38.16±1.29 | 38.44±1.12 | 0.253 |
| RBS | 111.38±5.03 | 145.9±44.018 | <0.001 |
| Weight of baby/kg | 3.68±0.404 | 3.96±0.623 | 0.008 |
| Apgar score | 7.62±0.53 | 6.84±0.81 | <0.001 |

RBS: Rundum blood sugar

**Table 2: Relation between the type of treatment and mode of delivery**

| Mode | Insulin (%) | Metformin (%) | *P* |
|---|---|---|---|
| NVD | 20 (40) | 27 (54) | 0.161 |
| C/S | 30 (60) | 23 (46) | |
| Total | 50 (100) | 50 (100) | |

NVD: Normal vaginal delivery, C/S: Cesarean section

**Table 3: Comparison between the two groups regarding admission to the NCU**

| NCU | Group (%) | | *P* |
|---|---|---|---|
| | Metformin | Insulin | |
| Yes | 3 (6) | 29 (58) | <0.001 |
| No | 47 (94) | 21 (42) | |
| Total | 50 (100) | 50 (100) | 100 |

NCU: Neonatal care unite

**Table 4: Comparison between two groups regarding complication among those admitted to NCU**

| Complication | Insulin group (29) (%) | Metformin group (3) (%) |
|---|---|---|
| RDS | 19 (65.5) | 1 (33.3) |
| Hypoglycemia | 10 (34.4) | 1 (33.3) |
| Seizure | 8 (27.5) | 0 (0) |
| Jaundice | 7 (24.1) | 0 (0) |
| Hypocalcemia | 6 (20.6) | 0 (0) |
| Preterm | 0 (0) | 2 (66.7) |

RDS: Respiratory distress syndrome, NCU: Neonatal care unite

There were high percentage of complications among insulin group which lead to admission to NCU. The total number of complication differs from total number of patients in each group because some patients had more than one complication Table 4.

## Discussion

In our study, we found that metformin is safe and effective alternative to insulin in GDM.[9]

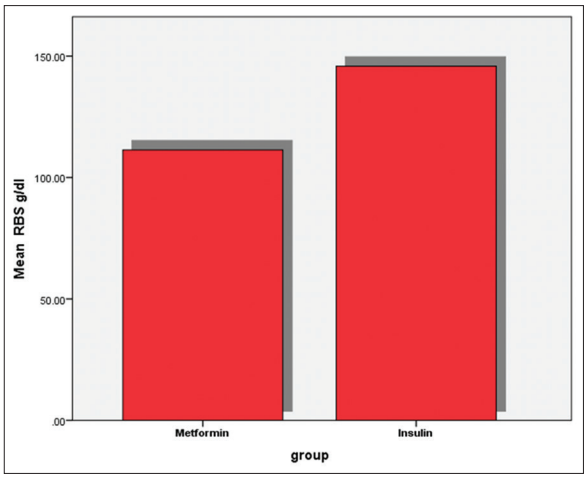


**Figure 1:** Comparison of blood sugar level between the metformin and insulin groups

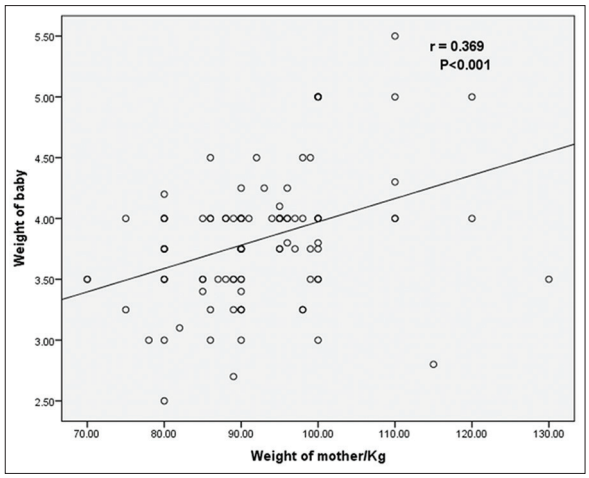


**Figure 2:** Correlation between the weight of baby and weight of mother

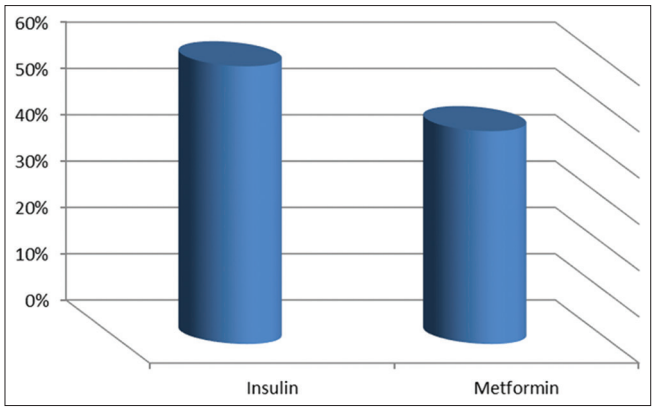


**Figure 3:** Cesarean section rate among the studied groups

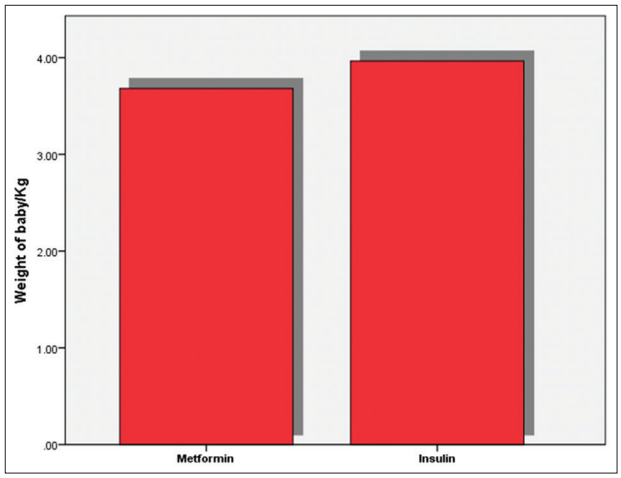


**Figure 4:** Comparison between the two groups regarding the weight of baby

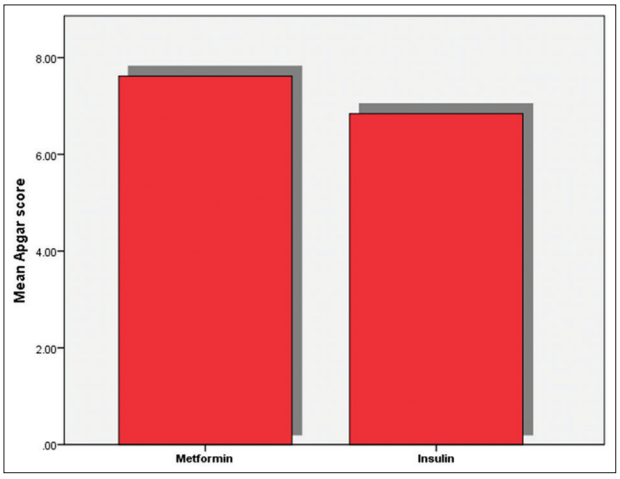


**Figure 5:** Comparison between the two groups regarding Apgar score

Insulin improves glycemic profile but not for insulin resistance which is an important feature of pregnant GDM which can be overcome by metformin.[10]

Metformin is an insulin sensitizer which targets insulin resistance without enhancing insulin production in addition it reduce plasma insulin levels and hence reduces fetal macrosomia.[11-13]

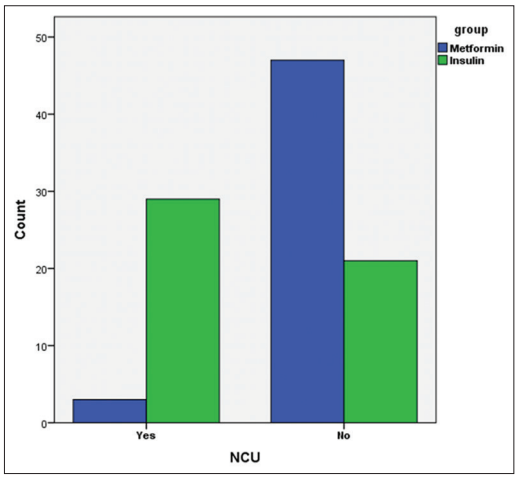


**Figure 6:** Comparison between the two groups regarding admission to the NCU

Metformin is an insulin sensitizer which targets insulin resistance without enhancing insulin production in addition it reduce plasma insulin levels and hence reduces fetal macrosomia.[11-12-13]

In our society, most of the patient are not complaint to follow-up, moniterhng of blood glucose and for parental injection of insulin, so metformin meet our expectation, as it offer better glycemic control and so avoiding neonatal complication.[14-16] We found in [Figure 1] that blood sugar control was better in metformin group than in insulin-treated woman mean blood sugar (111 mg/dl) in metformin group versus (145 mg/ dl) in insulin group, which reflected the fact that gestational diabetes is a state of insulin resistant which can be difficult to be controlled with insulin alone.[17,18] These results were in agreement with the Indian study by Lavanya[19] and the Pakistan study by Hassan.[20] In our study [Figure 2] There is weak significant posetive correlation between weight of mother and weight of baby. So that the macrosomia is related to the poor diabetis control in insulin treated group not to the obesity of mother. In our study, [Figure 3] the number of cesarean section in the insulin group was higher (60%) versus (46%) in the metformin group. But statistically, it was not significant result was compatible with several authors However, cesarean section rate was found to be higher in insulin-treated women in Jahan Hassan study, so our result did not agree with this study.[21] Neonatal complications were more in the insulin-treated group [Figure 4]. Neonatal birth weight were more in the insulin-treated group (3.9 kg) versus (3.6 kg) in metformin-treated group, and this can be explained again[22] by poorer glycemic control in insulin-treated group than in metformin acts as insulin sensitizer so less endogenous insulin production and less macrosomia; this result was compatible with study conducted by Tertti *et al*. and Ijäs *et al*.[23]

Low Apgar score <6 [Figure 5] at 5 min was more in the insulin-treated group. The fact can be explained by the possibility of respiratory distress syndrome due to poor antenatal glycemic control and hence by collapse. Our results were not in agreement with the results of Jahan Ara Hassan, who found no difference in Apgar score between two groups.[24]

Table 4 show NICU admission was more in the insulin-treated group Figure 6 (58%) due to respiratory distress syndrome (65.5%), hypoglycemia at birth (34.4%) or jaundice (27.5%), seizure (20.6%) while in metformin-treated group (6%) due to respiratory distress syndrome (33.3%), hypoglycemia (33.3%), preterm (66.7%) again the explanation is attributed to prenatal maternal hyperglycemia which cause neonatal hypoglycemia at birth result agreed by Mig TRIALS.[25]

Limitation of this study was small number of the collected sample due to short study period.

## Conclusion

Metformin is safe, effective, and cheap with better and quicker glucose control than insulin. As metformin can better control glucose than insulin without attacks of hypoglycemia, so it adds no burden on the patient from hospitalization and frequent blood glucose monitoring. Oral therapy for GDM seems to be more convenient to patient from any parenteral injection an advantage which is more optimal in patient not complaint to any medical supervision.


### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.


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