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Original Research Article

Comparison of neonatal birthweights and fetomaternal outcomes in gestational diabetes-on diet, metformin and insulin

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ABSTRACT

Background: Review suggested that neonatal birthweight in insulin group was higher than in metformin and diet and metformin had overall better fetomaternal outcomes. We wanted to understand the trend in the patients visiting our hospital.
Methods: This is an observational comparative study conducted in Department of Obstetrics and Gynaecology, AIMS Kochi from 2019-2021. All antenatal patients were screened and total of 153 patients meeting inclusion and exclusion criteria were studied. The data was collected and analysed using SPSS 20 software.
Results: The neonatal birthweight the three groups were comparable, with no significant difference (3.05±0.42 kgs in diet; 2.92±0.37 kgs in metformin; 3.11±0.41 kgs in insulin; p=0.092) and maternal pre-pregnancy weight was associated with birthweight. Insulin group had higher age (31.17±5.54 years versus 27.59±4.62 years in OHA and 29.43±4.56 years in diet; p<0.001). Insulin group delivered at an earlier gestation (37 weeks versus 38 weeks; p<0.001) and most common mode of delivery was cesearean section (74.6% in insulin; 54.2% in diet and 49.8% in OHA). NICU admission (45.8% versus 10.8% in diet and 15.4% in OHA; p<0.001) and need for phototherapy (1.5% in metformin versus 5.4% in diet and 11.8% in insulin; p=0.067) was lesser in metformin group.
Conclusions: Strict glycemic control is important in preventing macrosomia Metformin overall has good fetomaternal outcomes compared to diet or insulin.

Keywords: Macrosomia, GDM, Metformin, Insulin, Diet control

INTRODUCTION

India is considered as diabetes capital of the world and has the largest population in younger reproductive age group. Hence, there is a higher proportion of pregnancies being complicated by diabetes.

Gestational diabetes is defined as has been defined as any degree of glucose intolerance with onset or first recognition during pregnancy irrespective of the gestational age at which it was diagnosed.[1]

Pregnancy in itself is a diabetogenic condition due to increased insulin resistance. Once diagnosed, management can be by pharmacological and non-pharmacological methods. Non pharmacological and first line of treatment includes diet control and exercise with blood sugar monitoring. For patients not responding to the treatment, pharmacologic therapy is added in the form of oral hypoglycemic agents (OHA) like metformin/ glyburide and insulin with insulin being first line therapy.

In comparison to metformin and insulin, insulin has been reported to have higher incidences of LGA fetuses with more episodes of hypoglycemia and hyperbilirubinemia.[2] Among OHAs, glyburide has been shown to have increased rates of pregnancy induced hypertension and increased NICU admissions for newborns than metformin and insulin. Among diet and insulin, insulin was shown to have higher rates of adverse fetomaternal outcomes.[3]

However, there were some studies that found no significant difference in fetomaternal outcomes between metformin and insulin. Maternal obesity has been associated with more adverse fetomaternal outcomes and higher chances of macrosomia.[4]

In view of varied results from different studies, this study was done to see the outcomes among the three groups in our population and compare which mode of treatment has more favourable outcomes among diet, insulin and metformin.

METHODS

It is an observational comparative study conducted in obstetrics and gynaecology department, AIMS, Kochi for delivery from 2019-2021. Out of 3900 deliveries, 153 patients meeting inclusion and exclusion criteria were studied.

Inclusion criteria

Diagnosed as gestational DM at/ after 24 weeks at Amrita or outside hospital and achieving adequate glycemic control on any one out of-diet/ OHA/ insulin as defined by the NHM guidelines of India.[5] Singleton pregnancy, at or after 37 weeks of gestation, age 18-40 years, fetus with correctable defects that are compatible with life like cardiac anomalies (VSD, TGA, TOF), duodenal atresia etc. were included.

Exclusion criteria

Patients with uncontrolled sugars, pregestational diabetic or overt diabetes, multiple pregnancy, less than 37 weeks of gestation, babies with known chromosomal anomalies or gross congenital anomaly not compatible with life, fetus with growth restriction, mothers with existing co-morbidities like chronic hypertension, severe pre-eclampsia, SLE etc. preterm labor and premature rupture of membranes were excluded.

All the patients meeting the inclusion and exclusion criteria were counselled to participate in the study on the day of admission by the respective consultants or the senior obstetrician in labor room. After obtaining informed consent, the sociodemographic data like-parity, age, pre pregnancy weight, gestational age at delivery, current method of glycemic control- diet, metformin or insulin was collected in the proforma.

The mode of delivery was decided as per the treating obstetrician and patient's decision. Primigravidas with favourable pelvis were induced as per hospital's protocol for normal vaginal delivery. Multigravidas with previous cesearean section were given the option for TOLAC and if not willing were taken up for elective cesearean section. Assisted vaginal delivery was done using forceps or "kiwi" vaccum in patients with fully dilated cervix and vertex at +2 to +3 station for indication like fetal distress or failure of maternal power.

Based on the mode of treatment on which the patient's blood sugar were currently well controlled they were divided into 3 groups-diet, metformin and insulin.

After delivery, the condition and weight of newborn was assessed and charted. The babies were followed up during their stay in hospital up to maximum of 4 days of life to assess for any hypoglycemia episodes or hyperbilirubinemia needing phototherapy.

Statistical analysis was carried out using IBM SPSS 20. (SPSS Inc, Chicago, USA).

Descriptive statistics of both groups were expressed as mean±SD and median (Q1-Q3) for continuous variables and frequency and percentage for categorical variables.

To test the statistical significance of the difference in the proportion of categorical variables between the groups, chi square with Fisher's exact test was applied.

To test the statistical significance of the difference in the mean or median difference of numerical variables among groups, one way ANOVA was applied for parametric data and Kruskal Wallis test was applied for non-parametric data.

Multiple comparison tests were done by using Bonferroni test.

To test the statistical significance of the relationship between numerical variables, Pearson correlation coefficient was computed and its statistical significance was tested using linear Reg t test.

All statistical tests were two-sided and conducted in an explorative manner on a significance level of <0.05.

RESULTS

The prevalence of diabetes complicating pregnancy in the study population was 17.9%.

Out of total 153 GDM women studied, glycemic control was achieved by diet in 37 (24.2%), by metformin in 65 (42.5%) and by insulin in 51 (33.3%).

The mean birth weight of the babies in diet group was 3.05±0.42 kgs (n=37), in OHA group was 2.92±0.37 kgs (n=65) and in insulin was 3.11±0.41 kgs (n=51) and was not statistically significant (p=0.092) (Figure 1).

The percentage of neonates with birth weight >4 kg was 4% (n=2/51) in insulin group, 1.5% in metformin group (n=1/65) and 0 in diet group.

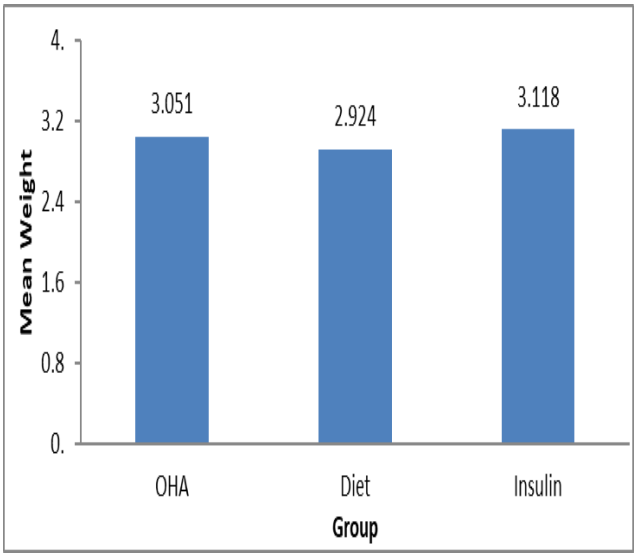

Figure 1: The comparison of baby birth weight among the groups.

The multiple comparison results shows that age was statistically significant differ in Insulin group compared to Diet group (p=0.003). The correlation between age and baby weight was not found to be statistically significant (p=0.184) (Table 1).

Higher pre-pregnancy weight patients needed insulin for attaining better glycemic control (Table 1). The comparison of the mean weight in patients between the 3 groups was found to be statistically significant (p=0.004). Pair wise comparison reflect that Insulin group was statistically significant from OHA (p=0.036) and diet (p=0.006).

On correlating maternal pre-pregnancy weight and birth weight, showed low correlation coefficient (r=0.032) and was found to be statistically significant with p=0.027, which represent that maternal pre-pregnancy weight has relation with birth weight (Figure 2).

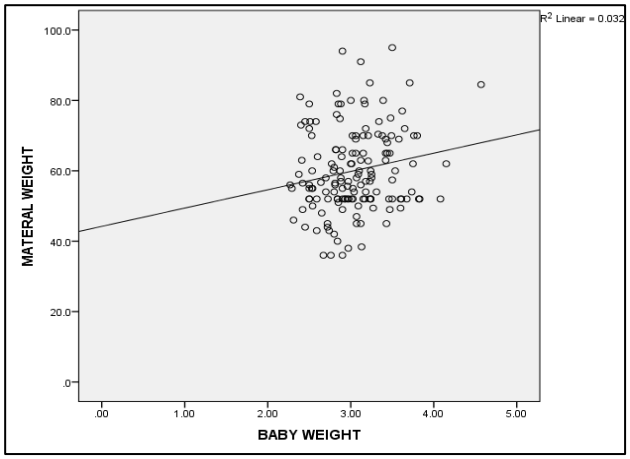

Figure 2: Correlation between maternal weight and birth weight.

The regression equation of Birth weight on maternal weight was birth weight=2.669+0.006* maternal weight.

Patients in insulin group delivered at an earlier gestational age of 37 weeks while on diet and metformin delivered by 38-39 weeks (Table 2). The proportion of pregnancies continuing up to 39 weeks was higher in diet group.

Overall, the cesarean rates were higher in all three groups with slightly higher rates in insulin group (Figure 3). The association of mode of delivery was found to be not statistically significant (p=0.046). The most common indication for cesearean section found was previous cesarean with mobile head.

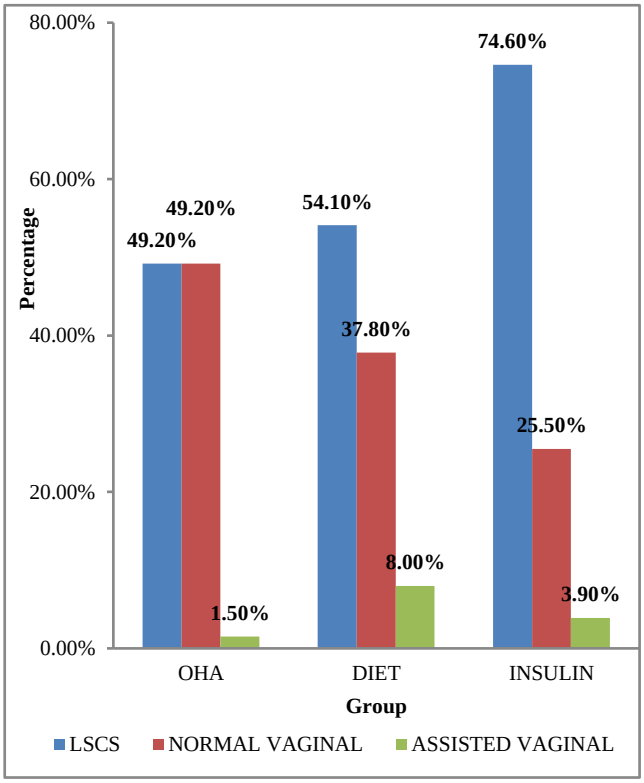

Figure 3: The comparison of mode of delivery among the 3 groups.

There were higher NICU admissions in insulin group 45.1% (n=23/51) as compared to diet 10.8% (n=4/37) and OHA 15.4% (n=10/65). The association of NICU admission with mode of treatment was found to be statistically significant (p<0.001).

The rates of hyperbilirubinemia needing phototherapy were 1.5% (n=1/65 in metformin versus 5.4% (n=2/37) in diet and 11.8% (n=6/51) in insulin; p=0.067, although the results of association of need for phototherapy in 3 groups was found to be not statistically significant (p=0.067). The rates were lower in metformin group as compared to diet and insulin.

Table 1: Comparison of maternal age and pre pregnancy weight between groups.

Variables	OHA, (n=65)	Diet, (n=37)	Insulin, (n=51)	P value
Mean maternal age (years)	27.595±4.62	29.431±4.567	31.176±5.545	0.004
Mean pre-pregnancy weight (kgs)	58.742±11.945	56.327±9.957	64.310±12.386	0.004

Table 2: Comparison of gestational age at delivery.

Groups	37 weeks	38 weeks	39 weeks	P value
OHA, (n=65) (%)	22 (33.8)	30 (46.2)	13 (20)	
Diet, (n=37) (%)	8 (21.6)	18 (48.6)	11 (29.7)	<0.001
Insulin, (n=51) (%)	31 (60.8)	19 (37.3)	1 (2)	

DISCUSSION

A total of 153 patients were included in the study with well controlled blood sugars. The prevalence of diabetes complicating pregnancy in the study population was 17.9% which was similar to previous studies by seshiah et al.[6]

There was a higher prevalence of metformin use in treatment of gestational DM in the population with metformin being used in 42.5% and insulin in 33.3% and diet in 24.2%. Even though metformin is not FDA approved and not first line in management of GDM, better patient compliance and glycemic control is making it an upcoming drug for use.

In our study, the mean age among the three groups was between 27-31 years with higher age groups needing insulin for glycemic control. This finding is confirmed by other studies on maternal age as risk factor for GDM by Li et al and Laine et al which show that Asian women have higher chances of being diagnosed with GDM after 25 years of age.[7,8]

In study by Simeonova-Krstevska et al the mean age group on diet was 31.5±5.2 years, in metformin group was 32.2±4.7 years and in insulin group was 32.7±5.7 years.[9] The use of metformin at relatively younger age in our study could be attributed to more prevalence of PCOD in younger population and difference in the treatment policies.

Among the groups, there was a higher prevalence of multigravidas in our study. No other studies were found comparing the prevalence of parity among the three groups.

HAPO study claimed both obesity and gestational diabetes as independent predictors for macrosomia. In our study, women in insulin group had a higher pre-pregnancy weight. In study by Simeonova-Krstevska et al metformin group had higher BMI that could be due to combined use of drugs as better effect on insulin sensitivity by metformin. However, studies show that almost 30% of GDM on metformin need additional insulin to achieve better glycemic control.[9,10]

Pre pregnancy maternal weight was related to neonatal birth weight as shown in previous studies like by Gaudet et al that showed that maternal obesity was a risk factor for macrosomia.[4] Our study also showed association between maternal pre pregnancy weight and the neonatal birthweight.

Studies by Balani et al and Simeonova-Krstevska et al showed lower gestational age at delivery for diabetics on insulin as compared to other groups (mean gestational age at delivery for GDM on diet and metformin was 38.9±1.4 weeks while for insulin was 37.2±1.2 weeks).[11] In our study also, the mean gestational age for delivery was lower in insulin i.e., at 37 weeks. In meta-analysis by Gui et al the gestational age for metformin group was significantly lower as compared to other groups.[12] Current guidelines by ACOG and as commented by study of Kalra et al delivery is recommended at 39 completed weeks for uncomplicated gestational diabetes which should be a well-informed decision after discussing with the woman and her family taking into account biomedical, environmental and psychosocial factors.[13]

GDM alone is not an indication for cesearean section unless it is complicated by macrosomia or other obstetric indications for cesearean section. Balani et al in their study found no difference in caesarean rates in metformin and insulin group.[10] Study by Slagjana Simeonova-Krstevska et al showed higher cesearean rates among insulin and metformin groups as compared to diet. In our study the rates of cesearean section were slightly higher in insulin group and the results were not statistically significant (Table 3). The higher cesarean rates seen were because majority were multigravidas with most common indication being previous cesearean with mobile head.

Hyperglycemia and hyperinsulinemia stimulate adipogenesis in fetus, increase fat deposition and subsequently increase birth weight. Insulin does not cross the placenta and increases IGF levels thus worsening the hyperglycemia and contributing to macrosomia. Metformin crosses placenta and reduces the hyperglycemia and hence should have lower rates of macrosomia (Table 4). Simeonova-Krstevska et al in their study showed mean birth weight in insulin group to be significantly lower than in metformin and diet.[9] Study by Tertti et al found no statistically significant difference in

birth weight in metformin and insulin.[10] Study by Arshad et al found that in comparison between diet and insulin, the birth weight was significantly higher in insulin group.[18] In our study also, the mean neonatal birth weight in the three groups was comparable in three groups and not statistically significant.

The percentage of neonates with birth weight >4 kg was higher (4%) in insulin group than metformin group (1.5%). This was similar to studies by Gandhi et al and Simeonova-Krstevska et al that suggested lower rates of macrosomia in metformin group.[9,14]

Neonates of GDM on insulin have been found to have higher chances of hypoglycemia after birth and polycythemia due to increase in growth factors. Hence these babies have hyperbilirubinemia and mostly need phototherapy (Table 5) Our study also showed similar results with significantly increased rates of NICU admission and need for phototherapy in insulin group as compared to diet and metformin group. The increased rates of NICU admission were because of increased prevalence of anomalies in the group mainly cardiac anomalies like TGA, VSD which were surgically corrected after birth, with good postoperative result. A very small proportion of babies had hypoglycemia, hypocalcemia and sepsis needing NICU admission.

Table 3: Comparison of mode of delivery with study by Simeonova-Krstevska et al.[9]

Mode of delivery	Diet (%)	OHA (%)	Insulin (%)	P value
Spontaneous	66.1	47.8	34	<0.005
Our study	37.8	49.2	25.5	NS
Assisted vaginal	2.3	0	0	NS
Our study	8.1	1.5	3.9	NS
Cesarean section	31.5	52.2	66	<0.005
Our study	54.1	49.2	74.6	NS

Table 4: Comparison of birth weights in different studies.

Studies	Diet	OHA	Insulin	P value
Thomas et al[16]	-	2.9287 ±418	2.9981± 492.5	0.25
Janet et al[17]	-	3.372± 572	3.413± 569	0.33
Arshad et al[18]	3.09± 0.3	-	3.44± 0.46	0.003
Slagiana Simeonova et al[9]	3.631± 0.65	3.496± 0.48	3.348± 0.74	NS
Our study	2.924± 0.3	3.051± 0.4	3.118± 0.4	0.092

Table 5: Comparison of neonatal outcomes with other studies.

Studies	Diet (%)	OHA (%)	Insulin (%)	P value
NICU admission				
Balani et al[11]	-	6	19	<0.01
Our study	10.8	15.4	45.1	<0.001
Phototherapy				
Balani et al[11]	-	8	30	<0.01
Our study	5.4	1.5	11.8	<0.067

Study by Hellmuth et al showed increased chances of preeclampsia and perinatal mortality in GDM treated by metformin.[15] However in our study overall the maternal and neonatal outcomes were good with metformin and insulin with no mortality or morbidity.

Limitations

The limitation was that it was an observational comparative study with both primi and multigravidas. Prospective targeted studies on association of parity, maternal obesity, maternal comorbidities like preeclampsia and fetal anomalies with birth weight and modalities of treatment are needed. Further study is needed to assess the need for additional insulin or metformin over existing pharmacotherapy for achieving target glycemic control

CONCLUSION

The study was done to compare neonatal birth weights in well controlled gestational diabetics divided into the three groups-metformin, insulin and diet. After assessing the mean weight in the three groups, it was concluded that strict glycemic control is necessary for preventing macrosomia irrespective of mode of treatment. Metformin was found to have overall better neonatal outcomes while insulin was preferred mode of treatment in women with age > 30 years and obesity. Younger age groups attained a better glycemic control with only diet and lifestyle modification with lesser pharmacotherapy. Since metformin overall has good maternal and neonatal outcomes and increases insulin sensitivity with almost similar complication profile, it can be used for patients not able to achieve glycemic control by MNT or insulin.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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