



Assessment of insulin resistance in cord blood of infants born to diabetic mothers and it's correlation with anthropometry

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ABSTRACT

Background: Intrauterine exposure to maternal diabetes and large size at birth are known risk factors for the development of insulin resistance and metabolic syndrome. **Objective:** To assess insulin resistance at birth in babies born to diabetic mothers (GDM/ TYPE2DM). To compare Insulin resistance between babies born to diabetic mother and non-diabetic mother with risk factors and also with non diabetic mothers without risk factors. To compare anthropometry of infants of diabetic mothers with severity of insulin resistance. **Participants:** The Observational study from Tertiary care hospital in Bangalore, Karnataka Total 159 newborns including 57 newborns of GDM/type2 diabetic mothers, 52 of non-diabetic mothers with risk factors and 50 of control mothers. **Intervention:** Umbilical cord blood was collected immediately after delivery and glucose and insulin levels were measured, insulin resistance was calculated. Neonatal anthropometry was measured within 24hrs after delivery. Maternal height, pre pregnancy weight, gestational age and investigations were taken from maternal records. These parameters were compared across the three groups. **Results:** In this study hyperinsulinemia was found in 9(15.8%) of infants born to diabetic mothers (Mean insulin $7.83 \pm 3.53 \mu\text{U/ml}$), in comparison to 1(1.9%) infants born to non-diabetic mothers with risk factors (Mean insulin $4.14 \pm 2.71 \mu\text{U/ml}$) and 1(2%) control group (Mean insulin $3.68 \pm 1.95 \mu\text{U/ml}$) ($P < 0.001$, CI 2.38; 5.01). Insulin resistance was found in 7(12.3%) infants born to diabetic mothers (Mean IR= 1.32 ± 0.7), which was high in comparison to 1(1.9%) in infants born to non-diabetic mothers with risk factors (Mean IR= 0.62 ± 0.5) and control mothers (Mean IR 0.50 ± 0.27) ($P < 0.001$, CI 0.04;0.96). **Conclusion:** Infants born to diabetic mothers had higher birth weight, hyperinsulinemia and increased insulin resistance in comparison to controls

INTRODUCTION

Diabetes Mellitus refers to a group of common metabolic disorder that share the phenotype of hyperglycemia. Gestational Diabetes is defined as carbohydrate intolerance of variable

severity with onset or first recognition during pregnancy. There is significant rise in recent years in adult obesity and type2 diabetes, becoming a major public health problem both in developed and developing countries resulting in huge



economic burden in developing countries because of enormous population. There is lot of interest in events that precede diabetes, including the intrauterine environment, where early imprinting is believed to have effects later in life. During in utero development fetus relies primarily on glucose as an energy substrate. There is a steady supply of glucose even during maternal fasting state, because of 30% increase in hepatic glucose production in late gestation. Maternal insulin resistance during gestation results in lipolysis with increase in the availability of FFA to be used as adipogenic substrate in fetus. Therefore understanding mechanisms through which a fetus growing in nutrient rich environment becomes insulin resistant is a major challenge. Assessment of insulin at birth may be particularly a useful way of assessing whether fetus was exposed to abnormally high levels of glucose in utero, resulting in increased insulin resistance and metabolic sequelae. There is an urgent need to identify insulin resistance in babies as early as possible so that lifestyle measures such as healthy dietary habits and exercise could be introduced at the earliest in order to prevent the potential long term implications of altered fetal growth in already genetically predisposed south-east Asian population.

METHODS

It was a single centre, observational study conducted from June 2021 to May 2022 at tertiary care teaching hospital in Bangalore, Karnataka. Approval was obtained from the institutional ethics committee. Informed and written consent was obtained from the parents of the babies. Purposive sampling method was employed and a total of 939 pregnant women aged between 19-36 years who

delivered between June 2021 and May 2022 who had been screened for GDM at or before 24 weeks were screened for the study. Screening for GDM was done as early as possible by DIPSI criteria using 75 gm oral glucose load and GDM was diagnosed if 2-hour post prandial glucose is ≥ 140 mg/dl (7.8 mmol/l) and confirmed by Carpenter and Coustan criteria using 100gm oral glucose and diagnosed as GDM if fasting glucose was >92 mg/dl and/or a 1-h value 180 mg/dl, 2-h value 155 mg/dl. Three groups were made amongst the babies included in the study. Babies born to diabetic mothers (GDM/TYPE2DM) were included in group 1. Babies born to non diabetic mothers with risk factors (obesity, family history of diabetes, in first degree relatives, previous large for date baby, diabetes in previous pregnancy, gestational hypertension, CVD, etc.) were included in group 2 and babies born to non diabetic mothers without risk factors were included in group 3. Those mothers who gave multiple births and delivered before the gestational period of 34 weeks, those who had been given steroids within 24 hrs. before birth, those for whom there was a delay of >20 mins. before cord blood was collected and those for whom there was a delay of >60 mins. before freezing of the plasma were excluded from the study. A total of 79 women with diabetes were included in the cases (group 1) for the study of which 22 women were excluded due to 1 miscarriage, 3 twin pregnancies, 2 antenatal glucocorticoids had been administered in 24hrs. before birth, 7 delivered before 34 weeks gestation, 3 intrauterine death. 6 samples were not collected due to delay between sample collection and freezing. Finally 57 women were eligible for the study in group 1. 52 women who were categorised as risk group (group 2) included those who were



obese or had family H/O diabetes in first degree relatives, previous large for date baby, diabetes in previous pregnancy, gestational hypertension, CVD etc. and routine screening for diabetes being negative in current pregnancy. After obtaining consent, mothers were subjected to detailed history taking (including GDM/type 2 DM, HTN, family history of diabetes in first degree relatives, previous large for date baby, diabetes in previous pregnancy, gestational hypertension, CVD and other obstetric complications), physical examination mother's age, weight, height were recorded, pre-gestational BMI was calculated and maternal investigations (RBS, OGCT, GTT, HbA1C) were collected from the case records. Gestational age at birth was calculated from LMP, USG and New Ballard scoring was done. Neonates' anthropometry was performed by a paediatrician within 24 hours of birth. Birth weight was measured using a digital electronic weighing scale (to the nearest 0.1 kg) after uncovering (removing all clothes) the baby and before the first feeding. Length was measured by infantometer. The infant was placed supine on infantometer and vertex of head touching the fixed vertical plank, legs fully extended by pressing over the knees and feet are kept vertical at 90 degree, the movable pedal plank of infantometer is snugly apposed against the soles and length is read from scale. The Occipito-frontal head circumference (after 24 Hrs.) was measured by using a non stretchable fibre-glass measuring tape, encircle over the most prominent part of occiput and supraorbital frontal area. Mid arm circumference was measured by using a non stretchable fibre-glass measuring tape at the midpoint between acromion and olecranon. Abdominal circumference was measured

by using a non stretchable fibre-glass measuring tape just above the level of umbilicus.

CORD BLOOD MEASUREMENTS

Umbilical venous blood was drawn via syringe from the double-clamped cord immediately after delivery of the baby and before delivery of the placenta. Cord blood was collected in EDTA tubes and centrifuged within 30 min and stored at (-80°C) till assessment of insulin levels. Plasma insulin was measured by using a Fully automated chemiluminescent immune assay (Roche, Germany). Plasma glucose was assessed by the glucose oxidase method and Insulin resistance was estimated by homeostasis model assessment (HOMAIR).¹

HOMA- IR index = $\frac{\text{fasting insulin (micro U/ml)} \times \text{fasting glucose (mmol/l)}}{22.5}$

22.5

HOMAIR index = $\frac{\text{fasting insulin (micro U/ml)} \times \text{fasting glucose (mg/dl)}}{405}$

405

Hyperinsulinemia was defined by serum insulin levels $\geq 13.0 \mu\text{U/ml}$ and IR by HOMA-IR ≥ 2.60 . In the absence of standard cut-off points for insulin levels and HOMA-IR index in the newborn, these values were considered as the cut-off points.²

STATISTICAL ANALYSIS

The data collected in this study was analysed statistically by computing descriptive statistics like number and percentages for categorical data, mean standard deviation and 95% confidence interval for continuous data. The one way analysis of variants between the 3 groups was applied to find the differences in means of insulin resistance and insulin levels. The relation between insulin



resistance and insulin levels with anthropometric measures of baby, for mother's insulin levels and insulin resistance were correlated with BMI, RBS, HbA1C using Pearson's correlation coefficient. The results were considered statistically significant whenever $P \leq 0.05$. The Statistical software namely SPSS V21.0 was used.

RESULTS

In this study, most of the patients 71.9% (41) with GDM/Type2 diabetes were in the agegroup of 21-30yrs.19.3% (11)GDM/Type2 mothers were between age group of 31- 40yrs which was slightly high compared to the non diabetic mothers with risk factors 7.7%(4) and the controls mothers 10%(5). Coming to the gestational score details, amongst the cases group i.e. GDM/Type2 diabetic mothers, 40.4% (23)were primi and59.6%(34) were multiparous, and in the non diabetic mothers with risk factors 26.9% (14)were primi and 73.1%(38) were multiparous,and in the control group 56%(28) were primi and 44%(22) were multiparous. Also the BMI of the mothers

was found to be higher in GDM/Type 2 diabetic motherscompared to non diabetic mothers with risk factors and control mothers. 19.3% (11) GDM/Type 2 diabetic mothers were overweight withBMI between (23-24.9) and 52.6 %(30) were obese with BMI above 25 kg/m2. Also in non diabetic mothers with risk factors, 25% (13) were overweight and42.3 %(22) were obese, in control group 20%(10) were overweight and 24%(12) were obese. Amongst the cases group (group1) 20 mothers (35.1%) had a serum HbA1c level of <6 %, 19 (33.3%) had between 6-6.5% and 18 mothers (31.6%) had HbA1c levels of >6.5%. Coming to the mode of delivery, 48(84.2%) of GDM/Type-2diabetic mothers delivered bycaesarean section, 8 (13.5%) were emergency LSCS and remaining were elective LSCS. Moving on to the gestational age of the babies included in the study, out of 57 babies born to GDM/Type2 diabetic mothers, 44(77.2%) were term babies and 13 (22.8%) were preterm babies.

Insulin levels	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
Group I (Diabetic mothers with or without risk factors)	57	7.83	3.530	.468	6.90	8.77
Group II (Non-diabetic mothers with risk factors)	52	4.14	2.713	.376	3.38	4.89
Group III (Non-diabetic mothers without risk factors)	50	3.68	1.950	.276	3.13	4.24
Total	159	5.32	3.399	.270	4.79	5.85

P<0.001



Table 1 Comparison of the cord insulin levels in the three study groups

Insulin Resistance	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
Group I (Diabetic mothers with or without risk factors)	57	1.3222	.70386	.09323	1.1354	1.5090
Group II (Non-diabetic mothers with risk factors)	52	.6158	.51933	.07202	.4712	.7604
Group III (Non-diabetic mothers without risk factors)	50	.5024	.27267	.03856	.4249	.5799
Total	159	.8334	.64973	.05153	.7316	.9352

P= <0.001

Table 2 Comparison of insulin resistance in the three study groups

Anthropometry of baby	r	P value
Birth weight	0.61	<0.001
Length	0.55	<0.001
Head circumference	0.38	=0.003
Abdominal circumference	0.58	<0.001
Chest circumference	0.66	<0.001
Mid arm circumference	0.46	<0.001
PI	-0.09	=0.499

Table 3. Correlation of cord blood insulin levels with anthropometric measurements



Anthropometry of baby	r	P value
Birth weight	0.58	<0.001
Length	0.54	<0.001
Head circumference	0.37	=0.005
Abdominal circumference	0.57	<0.001
Chest circumference	0.57	<0.001
Mid arm circumference	0.46	<0.001
PI	-0.13	=0.32

Table 4. Correlation of insulin resistance with anthropometric measurements

Mother's values	r	P value
BMI	0.20	0.12
HbA1C	0.37	0.004
RBS	0.15	0.60

Table 5. Correlation of insulin levels with BMI, HbA1C and RBS values

Mother values	r	P value
BMI	0.22	0.105
HbA1C	0.49	<0.001
RBS	0.14	0.674



Table 6. Correlation of insulin resistance with BMI, HbA1C and RBS values

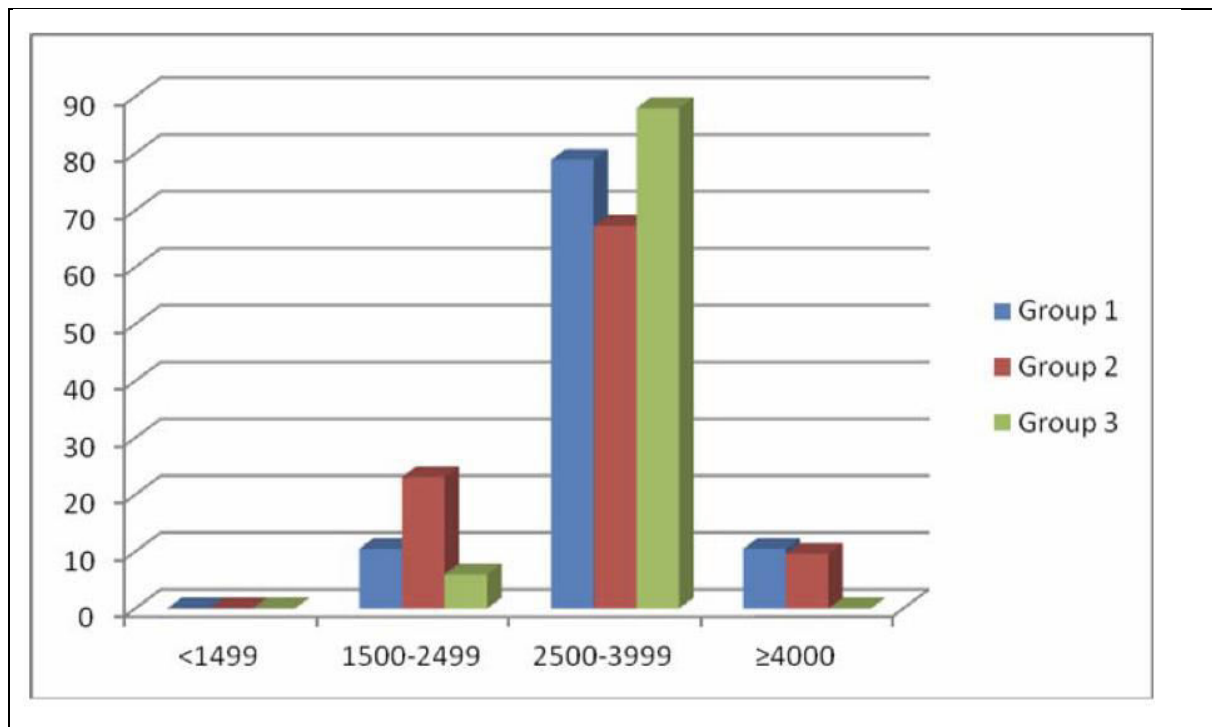


Figure 1. Comparison of the birth weights of the babies from the three study groups

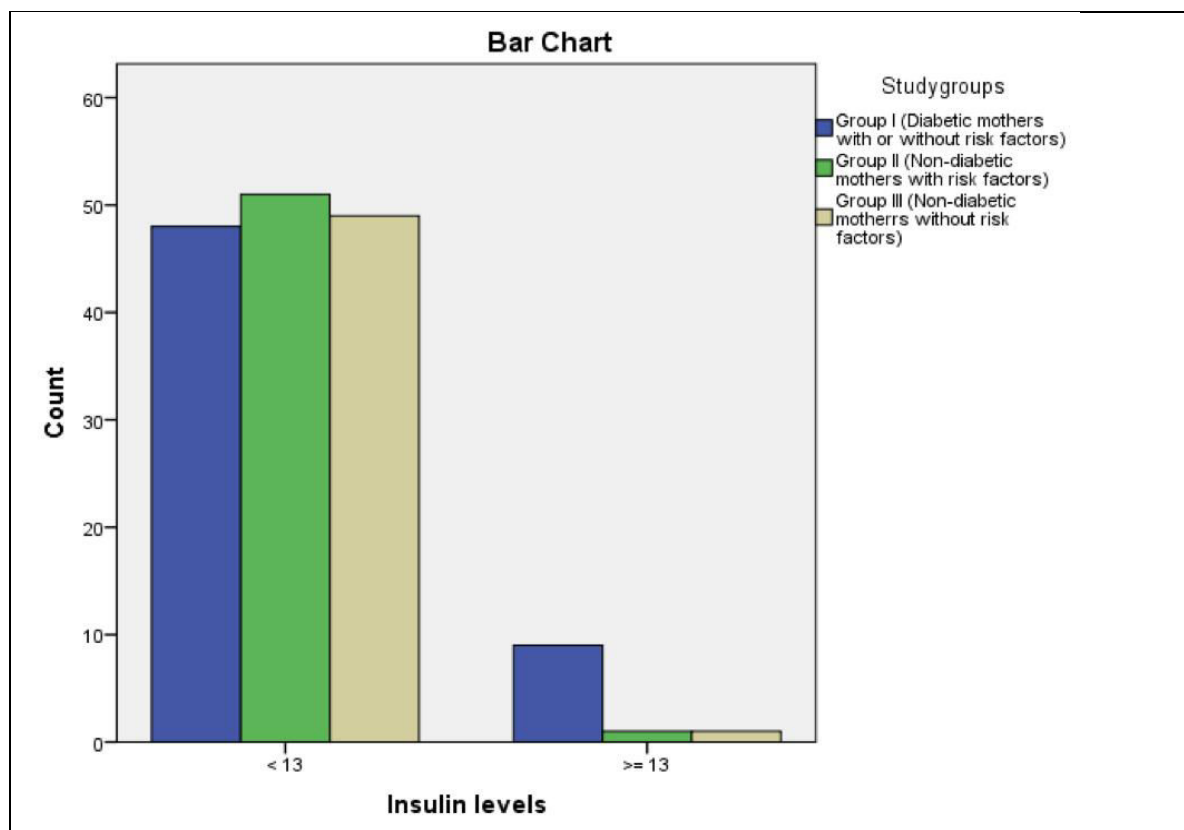


Figure 2. Comparison of the cord blood insulin levels of the three study groups



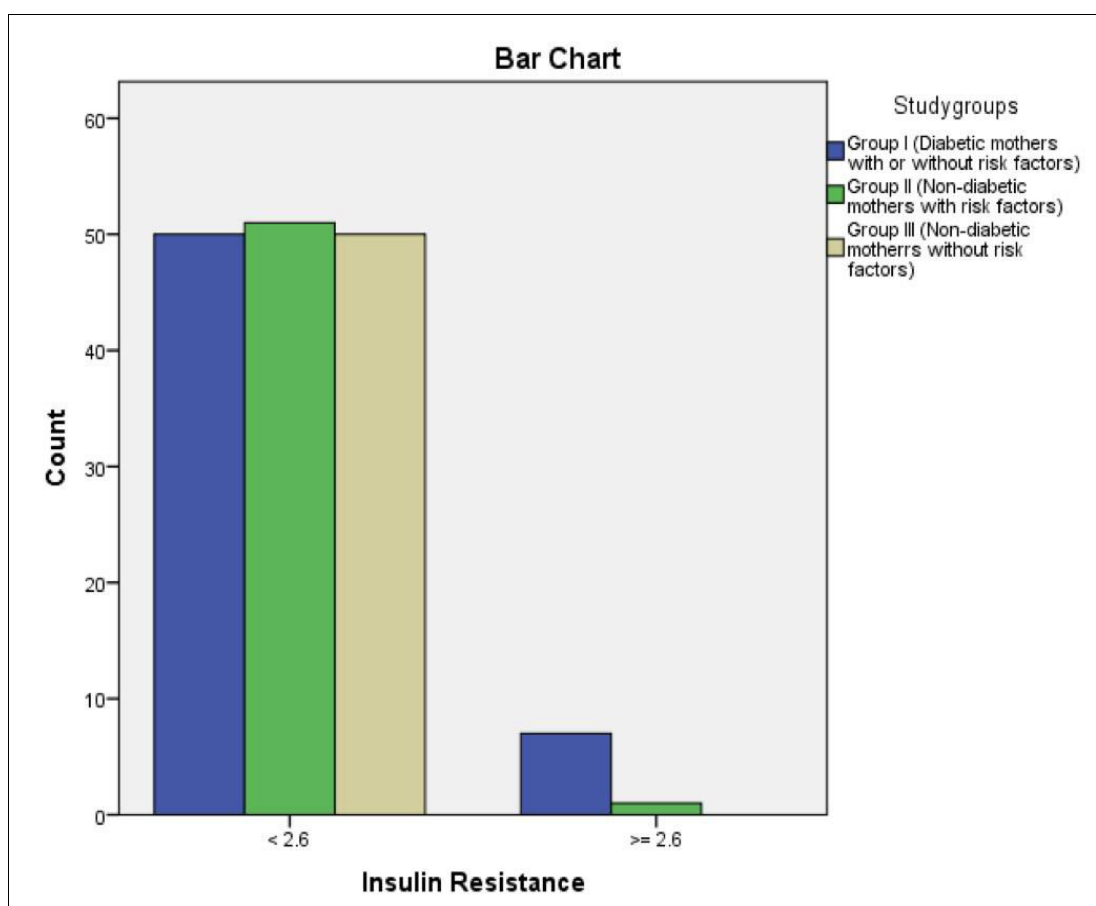


Figure 3. Comparison of the insulin resistance calculated in the three study groups

Moving on to the birth weight of the babies included in the study, significant difference of birth weight was found between three groups as seen in **figure 1**. Infants born to GDM/Type-2 diabetic mothers were having more birth weight compared to infants born to non diabetic mothers with risk factors and the control mothers. 10.5% (6) of GDM/Type-2 diabetic mothers had babies with birth weight between 1.5-2.49kg 10.5% (6) of GDM /Type-2 diabetic mothers had babies with birth weight above 4kg. On assessing the ponderal index of the babies, a PI of between 2 to 2.5 was found in 19.3%(11) infants born to GDM/Type-2 and 48.1% (25) infants born to non diabetic mothers with risk factors, compared to 16%(8) in the infants born to control mothers. PI <2 was found in 3.8% (2) in infants born to

non diabetic mothers with risk factors, and 2% (1) in the infants born to control mothers. Coming to the cord plasma insulin concentration, it was significantly higher in infants born to GDM/Type-2 diabetic mothers compared to infants born to non-diabetic mothers with risk factors, and control mothers as depicted in **figure 2**. 15.8%(9) infants born to diabetic mothers/Type-2 diabetes had hyperinsulinemia compared to 1.9%(1) in infants born to non diabetic mothers with risk factors, and 2% (1) in infants born to control mothers. As seen in **table 1**, a comparison of the cord insulin levels between the three groups, the Mean±SD insulin levels in infants born to GDM/Type2 diabetic mothers was 7.83 ±3.53, infants born to non-diabetic mothers with risk factors was 4.14 ±2.71, and control mothers was 3.68± 1.95. The



difference in all the 3 means are found to be statistically significant.($F=35.07$, $P<0.001$),however in the Post Hoc analysis there was a significant difference between the means of infants born to GDM/Type 2 diabetic mothers was and infants born to non-diabetic mothers with risk factors ($P<0.001$) with 95% confidence interval (2.38;5.01). Also the Insulin resistance HOMA-IR was found in babies born to GDM/Type2diabetic mothers as seen in **figure 3**. Insulin resistance was found in 12.3% (7) babies born to GDM/Type2 diabeticmothers and 1.9%(1) in babies born to non diabetic mother with risk factors and compared to babies born to control group. As seen in **table 2** , a comparison of insulin resistance between the three groups, the Mean \pm SD IR of infants born to GDM/Type 2diabetic mothers was 1.32 ± 0.70 , infants born to non-diabetic mothers with risk factors was 0.62 ± 0.52 , and control mothers was 0.50 ± 0.27 .The difference in all the 3 means are found to be statistically significant.($F=37.249$, $P<0.001$),however in the post hoc analysis there was a significant difference between the means of infants born to GDM/Type 2 diabetic mothers was and infants born to non-diabetic mothers with risk factors ($P<0.001$) with 95% confidence interval (0.46;0.96).It was observed that correlation between Insulin levels of all the 57 cases with anthropometric measurements of infants of GDM/Type 2 diabetic mothers ,were positively moderately correlated which were statistically highly significant as seen in **table 3**, showing the relation between Insulin levels and anthropometric measurements .However there was weak negative correlation between Insulin levels and PI which was not statistically significant. It was also observed that correlation between IR of all the 57 cases

with anthropometric measurements of infants of GDM/Type 2 diabetic mothers,were positively moderately correlated which were statistically highly significant as seen in **table 4**, showing the relation between IR and anthropometric measurements .However there was weak negative correlation between IR and PI which was not statistically significant. The correlation between Insulin levels and mother's BMI, and investigations is shown in **table 5**. It was observed that correlation between Insulin levels of all the 57 cases with HbA1C of diabetic mothers was positively moderately correlated which were statistically highly significant, showing the relation between insulin levels and HbA1C .However there was weak correlation between Insulin levels and BMI,RBS which were not statistically significant. The correlation between Insulin resistance and mother BMI, and investigations is shown in **table 6**. It was observed that correlation between IR of all the 57 cases with HbA1C of diabetic mothers was positively moderately correlated which were statistically highly significant, showing the relation between IR and HbA1C .However there was weak correlation between IR and BMI,RBS which were not statistically significant.

DISCUSSION

Diabetes during pregnancy is a common and increasing complication of pregnancy. The "fetal origin of disease" hypothesis proposes that gestational programming may critically influence adult health and disease. Infant of diabetic mothers are exposed to hyperglycemic and hyperinsulinemic intrauterine environment which results in permanent" malprogramming" of metabolic and /or neuroendocrine systems leading to functional teratogenesis. Exposure to



maternal diabetes in pregnancy is associated with high birth weight, increased childhood and adult obesity and increased risk of type 2 diabetes. We recruited 57 GDM/Type 2 diabetic mothers, 52 non diabetic mothers with risk factors and 50 control mothers and their newborns. Most of the mothers were in the age group of 21-30yrs and multiparous. Mothers between age group of 31-40yrs were slightly higher 11 (19.3%) in GDM/Type 2 diabetic mothers compared to the 4 (7.7%) non diabetic mothers with risk factors and the 5 (10%) control mothers. BMI was found to be higher both in GDM/Type 2 diabetic mothers and non diabetic mothers with risk factors when compared to control mothers. 11 (19.3%) GDM/Type 2 diabetic mothers were overweight with BMI between (23-24.9) and 30 (52.6%) were obese with BMI above 25kg/m² and in non diabetic mothers with risk factors 13 (25%) were overweight and 22 (42.3%) were obese which was similar to other studies. Prevalence of GDM increased, as the age and BMI increased (Sesiah et al.). Obesity is independent risk for developing GDM with a risk of about 20%, found two fold increase in rate of GDM. Kunasi et al found 29.5% GDM in the obese. Late preterms (34-36 weeks, 6 days) were 13 (22.8%), 6 (11.5%) and 6 (12%) respectively in diabetic, non-diabetic mothers with risk factors and controls. Preterm deliveries were higher in GDM/Type -2 DM mothers in comparison to other 2 groups. Similar pattern was seen by Eidem and associates (2011) who analyzed births in women with diabetes from the Norwegian Medical Birth Registry and found > 26 % were delivered preterm compared with 6.8% in the general obstetrical population. In the Canadian study, the incidence of preterm birth was 28%, a fivefold increase compared with that of their normal

population. In this study, rate of caesarean section was 84.2% (48) in GDM/Type-2. Birth weight in infants born to GDM/Type-2 Diabetic mother's and 67.3% (35) in non diabetic mothers with risk factors compared to 62% (31) in controls. Similar rates of caesarean section were seen in various studies and ranged between 50-80% among diabetic mothers (Hawathorne G Robson et al, Gabbe et al). Caesarean section rate was high in GDM'S because of associated complications like macrosomia, shoulder dystocia etc. In the present study the incidence of macrosomia in GDM was 10.5%. Birth weight in infants born to GDM/Type-2 Diabetic mother's and Non diabetic mothers with risk factors was higher compared to controls. Of infants born to GDM/Type-2 diabetic mothers 10.5% were LGA, 10.5% were SGA, 79% were AGA. Mean HbA1C is 8.8% in diabetic mothers of LGA babies, showing moderate metabolic control of their diabetes. Infants born to GDM/Type-2 Diabetic mother's had greater length, HC, CC, MAC, AC compared to other two groups. Studies had shown that large birth weight may reflect the influence of maternal diabetes in promoting both larger birth size and conferring offspring diabetic risk.³ An association between birth measurements and adult onset of diabetes showed that higher PI at birth was a predictor of later onset diabetes.⁴ In the absence of standard cut-off points for insulin levels and IR in the newborns, these values were taken from other studies.² In this study cord plasma insulin concentrations were significantly higher in infants born to diabetic mothers/Type 2 diabetic mothers with mean insulin levels (7.83 ± 3.53 µU/ml) compared to infants born to non diabetic mothers with risk factors (4.14 ± .71 µU/ml) and control mothers (3.68 ± 1.95 µU/ml).



Hyperinsulinemia was found in 9(15.8%) infants born to GDM / Type 2 diabetic mothers, in comparison to 1(1.9%) infants born to non diabetic mothers with risk factors, 1(2%) and control group. ($P < 0.001$). Out of 9 babies who had hyperinsulinemia, 6(67%) were LGA, 1 (11.5%) were SGA, 1(11.5%) were AGA. Insulin levels in infants born to diabetic mothers/Type 2 diabetic mothers were correlated to birth weight, PI, length, HC, CC, MAC, and abdominal circumference, which were higher compared to other two groups. Insulin levels were positively correlated with birth weight, length, AC, HC, CC, MAC ($P < 0.001$) and negatively correlated with PI. Insulin levels were correlated with maternal BMI, HbA1C, RBS and insulin levels were positively correlated with HbA1C ($p = 0.004$). The results of the present study were comparable to other studies. Jenny A Westgate, Franzcog et al in New Zealand, in their study on newborns of 138 mothers with GDM, 39 mothers with Type 2 DM and 95 control mothers, found hyperinsulinemia in 29% infants born to diabetic mothers and 31% in Type 2 diabetic mothers compared to controls (3%) and also birth weight was higher in offspring of mothers with both GDM/Type 2 diabetes and insulin correlates with cord glucose and maternal HbA1C.⁵ R.S.Lindsay, J.D.Walker et al conducted study on insulin like molecules in cord blood in relation to birth weight, maternal glycemia and cord glucose in 140 offspring of diabetic mothers and 49 offspring of control mothers and found that maternal diabetes was associated with increase in insulin levels 63.5% compared to 50.3% in controls and insulin was more strongly related to birth weight, cord glucose concentration and maternal HbA1C.⁶ In a similar study conducted by Luis E Simental, Argelia et al, Mexico on

107 newborns and showed that hyperinsulinemia in 12.1% and more in LGA. Weiss et al reported that a more pronounced and prolonged maternal hyperglycemia in IDM could be presumed to be the main reason of higher fetal and neonatal insulin levels in IDM.⁷ Beverly et al conducted study on insulin, IR, insulin related peptides and found insulin concentrations were significantly correlated with all measures, birth weight, length, HC and also found maternal glucose to be significantly associated with insulin concentration, reflecting that maternal glycemia is a major determinant of fetal insulin secretion.⁸ In the present study HOMA-IR was significantly higher in infants born to GDM/Type 2 diabetic mothers (Mean IR = 1.32 ± 0.7), compared to infants born to non-diabetic mothers with risk factors (Mean IR = 0.62 ± 0.5), and control mothers (Mean IR = 0.50 ± 0.27). Out of 57 infants born to GDM/Type 2 diabetic mothers, 7(12.3%) had IR in comparison to 1(1.9%) in infants born to non-diabetic mothers with risk factors ($P < 0.001$). Out of 7 cases with IR, 5(72%) were LGA, 1(14%) were AGA, 1(14%) were SGA. Severity of insulin resistance ($IR \geq 2.6$) in infants born to GDM/Type 2 diabetic mothers was correlated to birth weight, CC, HC, MAC and abdominal circumference, but correlation was not found due to small sample size (only 7 newborns showed $IR \geq 2.6$). But when overall IR (of all 57 babies) was correlated to birth weight, PI, CC, HC, MAC, and abdominal circumference, correlation was found and statistically significant and higher when compared to other two groups. However IR was negatively correlated with PI. IR was correlated with maternal BMI, HbA1C, RBS and found to be higher compared to other two groups. IR was positively correlated with HbA1C, however there was weak correlation



between IR and BMI, RBS which were not statistically significant. This study was comparable to other studies. Martha vela et al conducted study on insulin and leptin levels in AGA of diabetic mothers on 182 AGA infants (86 IDM; 96NIDM) in Mexico and showed insulin and IR were significantly higher in IDM(Mean insulin 10.9 μ U/ml; Mean IR- 1.7) than in NIDM(Mean insulin 3.723 μ U/ml; Mean IR-0.56). Study conducted by Jennifer at al showed reduced insulin sensitivity in LGA babies⁹. Soto et al observed greater insulin sensitivity at birth in SGA neonates.¹⁰ Patrick m. Catalano etal conducted study on 53 lean and 68 obese women, and found the fetuses of obese mothers had greater percent of insulin resistance (1.51 ± 0.86 vs. 1.06 ± 0.70 , $P = 0.003$) than fetuses of lean women and also there was a strong positive correlation between maternal Pregestational BMI and fetal insulin resistance ($r = 0.31$, $P = 0.007$).They also reported that there was a positive correlation between fetal insulin resistance and fetal adiposity¹¹ Bavdekar et al studied glucose and insulin levels in 8 yr old children at Pune, and found high insulin resistance in those with low birth weight and high current weight, i.e. children with abnormal weight gain.¹²

LIMITATIONS OF STUDY

This was a cross sectional study and sample size was smaller. Further studies with larger sample size and long term follow up is required to establish the effect of insulin resistance detected at birth with metabolic effects occurring in later childhood and adolescents.

CONCLUSION

In the present study, infants born to diabetic mothers had higher birth weight, hyperinsulinemia and increased insulin resistance in comparison to controls.

Fetal insulin is potentially an important indicator of the metabolic effect of maternal diabetes on the fetus and later health of the child. The population health impact of GDM is not only limited to offspring but also affects maternal health. It is imperative to understand the trans-generational epidemiology and etiology of diabetes. So glucose intolerance screening during pregnancy and consequently, health care for all pregnant diabetic women are recommended in order to avoid or atleast reduce the increased morbidity in their newborns and children by developing simple economical and effective prevention strategies, and also it is necessary to pay attention to later development of children.



What is already known?

- Exposure to maternal diabetes in pregnancy is associated with high birthweight , increased childhood and adult obesity and increased risk of type 2 diabetes

What this study adds?

- Insulin resistance and hyperinsulinemia is present from as early as the in utero period in infants of diabetic mothers and this can be screened for and will help in initiating early effective preventive strategies in reducing morbidity and mortality to this non communicable disease with massive global burden

REFERENCES

1. Matthews DR, Hosker JP, Rudenski AS, et al; Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985, 28:412–419.
2. Luis E Simental-Mendía, Argelia , Birth-weight, insulin levels, and HOMA-IR in newborns at term, *BMC Pediatrics* 2012, 12:94.
3. Fall CHD, Stein CE, Kumaran K, Cox V, Osmond C, Barker DJP, Hales CN. Size at birth, maternal weight , and type 2 diabetes in South India. *Diabetic Med* 1998 ; 15:220–227.
4. Dabelea D, Hanson RL, Lindsay RS, Pettitt DJ, Imperatore G, Gabir MM, Roumain J, Bennett PH & Knowler WC. Intrauterine exposure to diabetes conveys risks for type 2 diabetes and obesity: a study of discordant sibships. *Diabetes* 2000 49:2208–2211.
5. Jenny A. Westgate, *franzcog, MD* Hyperinsulinemia in Cord Blood in Mothers With Type 2 Diabetes and Gestational Diabetes Mellitus in New Zealand. *Diabetic care* June 2006 Vol 29 .no.6:1345-1350.
6. R. S. Lindsay, J. D. Walker Insulin and Insulin Pro-peptides at Birth in Offspring of Diabetic Mothers *The Journal of Clinical Endocrinology & Metabolism* 88(4):1664–1671. doi: 10.1210/jc.2002-021018.
7. Weiss PAM , Hofmann et al, Fetal insulin balance ; gestational diabetes and postpartal screening. *Obstet gynecol* 64;65-68.
8. Beverly M. Shields, Bridget et al; Measurement of Cord Insulin and Insulin-related peptides suggests that girls are more insulin resistant than boys at birth; *Diabetic Care*; October 2007 vol 30 no.10 2661-2666.
9. Jennifer Shine Dyer, Charles R. Rosenfelde et al; Insulin Resistance in Hispanic Large-for-Gestational-Age Neonates at Birth; *The Journal of Clinical Endocrinology & Metabolism*. Volume 92, Issue 10.
10. Soto N, Bazaes RA, Peña V, Salazar T, Avila A, Iniguez G, Ong KK, Dunger DB, Mericq MV 2003 Insulin sensitivity and secretion are related to catch-up growth in small-for-gestational-age infants at age 1 year: results from a prospective cohort. *J Clin Endocrinol Metab* 88: 3645–3650.
11. Patrick M. Catalano et al; Fetuses of Obese Mothers Develop Insulin Resistance in Utero; *diabetes care*, volume 32, number 6, June 2009.



12. Bavdekar A, Yajnik CS, Fall CH, Bapat S, et al. Insulin resistance syndrome in 8-year-old Indian children: small at birth, big at 8 years, or both? Diabetes 1999; 48:2422-9.

