



## A STUDY OF INSULIN RESISTANCE IN NEWBORN IN A TERTIARY CARE CENTRE: A PROSPECTIVE STUDY

### Endocrinology

**Dr Joginder Singh** Assistant Professor Medicine, GMC Doda

**Dr Vinod Kumar\*** Assistant Professor Medicine, GMC Doda \*Corresponding Author

**Dr Ritu Bhagat** Senior Resident, Postgraduate Deptt. of Pathology, GMC Jammu

### ABSTRACT

**Background:** Type-2 diabetes mellitus is fast spreading among young people as the incidence of obesity is increasing with time. This evidence has prompted the American Diabetes Association to include in new classification recommendations of diabetes, a form of type-2 diabetes with pubertal onset, variable insulin secretion, strongly associated with obesity which includes 10-20% of all diabetes in childhood and youth. **AIM:** The objective of the study was to evaluate the insulin resistance by measuring circulating insulin levels of mother and neonate and to determine the relationship between maternal pregravid BMI and neonatal insulin resistance. **Materials and Methods:** This is a prospective study for a period of one year from Dec.2009 to Nov.2010. Forty lean (BMI < 25 kg/m<sup>2</sup>) and forty obese women (BMI > 30kg/m<sup>2</sup>) with singleton term pregnancy were evaluated at elective cesarean section over a period of one year. **Results:** In the present study, the mothers were more insulin resistant than their newborns (p = 0.0001). The obese mothers were more insulin resistant than the lean mothers (p = 0.0001). Similarly, the newborns of the obese mothers were also more insulin resistant (p = 0.0001) than the newborns of lean mothers.

### KEYWORDS

Insulin Resistance, Body Mass Index, Fasting Plasma Glucose, Metabolic Syndrome

### INTRODUCTION:

The association of metabolic dysregulation with type-2 diabetes mellitus has been an intensive focus of research for the last decade<sup>1</sup>. Type-2 diabetes mellitus is fast spreading among young people as the incidence of obesity is increasing with time. This evidence has prompted the American Diabetes Association to include in new classification recommendations of diabetes, a form of type-2 diabetes with pubertal onset, variable insulin secretion, strongly associated with obesity which includes 10-20% of all diabetes in childhood and youth<sup>2</sup>. It is for this purpose that there is a shift of research focus to intrauterine environment which represents a time when changes in metabolism may affect distant metabolic dysfunction in the offspring mediated through physiological and epigenetic mechanism<sup>2,3</sup>. **Neonates of obese mothers with normal glucose tolerance had increased risk of developing the metabolic syndrome later in life<sup>4,5,6</sup>. Maternal pregravid weight\BMI was associated with increased birth weight<sup>7</sup> and insulin resistance in neonates<sup>8,9</sup>.** Intra-uterine exposure to diabetes per se conveyed a high risk for the development of diabetes and obesity in offspring in excess of risk attributable to genetic factors alone<sup>10</sup>. These concepts have led to many studies where long-term follow-up of the off springs of diabetic and/ or obese mothers have convincingly established an association of occurrence of type-2 diabetes mellitus in the off springs of such mothers<sup>1</sup>. Maternal obesity and underlying insulin resistance are significant short and long-term risk factors for both the mother and her fetus<sup>11</sup> which creates the potential of a vicious cycle of obesity & insulin resistance<sup>12</sup>.

From an oasis, India has become an ocean of diabetes mellitus, and this study, which is first of its kind being undertaken in Jammu region, is aimed to evaluate whether the findings regarding insulin resistance in fetuses of obese pregnant women are consistent with recent postulations on the subject.

### MATERIALS and Methods:

This is a prospective study for a period of one year from Dec.2009 to Nov. 2010 performed in Deptt. of Obstetrics and Gynaecology, SMGS hospital GMC, Jammu. All the mothers with singleton pregnancy with obesity (BMI > 30 kg/m<sup>2</sup>), at term, without any clinical evidence of infection and who underwent elective caesarean section and who had remained fasting overnight were the subjects. An equal number of healthy non-obese mothers (BMI < 25 kg/m<sup>2</sup>) with singleton term pregnancy without any clinical evidence of infection and underwent elective caesarean section and who had remained fasting overnight were taken as controls. Maternal blood sample was obtained on admission for delivery and then immediately after birth of the live born baby. Insulin resistance was estimated using Homeostasis Model

Assessment (HOMA-IR). Neonatal assessment was done within 24 hours after delivery. All patients under study were subjected to detail history, clinical examination, systemic examination and laboratory investigations. The OGTT "was performed on the subjects as per the WHO (1998) guidelines. Neonatal serum insulin levels were measured in the Regional Research Laboratory, Jammu by Electrochemiluminescence immunoassay "ECLISA" using Elecsys and Cobas and immunoassay analyzers. Cord Plasma glucose estimation was done by GOD-POD method using Autozyme Stat Glucose Kit provided by Accurex Biomedical Private Limited.

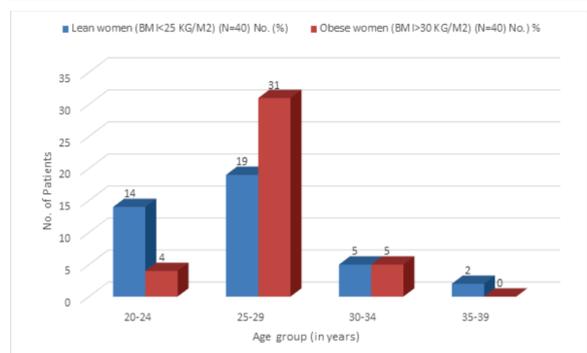
### RESULTS:

Forty lean (BMI < 25 kg/m<sup>2</sup>) and forty obese women (BMI > 30kg/m<sup>2</sup>) with singleton term pregnancy were evaluated at elective cesarean section over a period of one year *w.e.f.* December, 2009 to November, 2010.

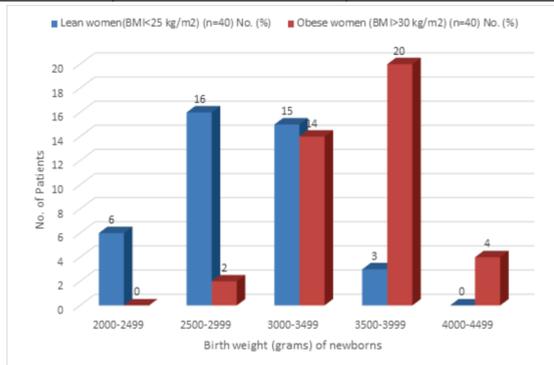
The observations made in the study are as under:

**Table 1: Distribution of lean & Obese women according to pre-pregnancy weight (kg)**

Pre-pregnancy weight (kg)	Lean women (BMI < 25 kg/m <sup>2</sup> ) (n = 40) No. (%)	Pre-pregnancy weight (kg)	Obese women (BMI > 30 kg/m <sup>2</sup> ) (n=40) No. (%)
45 – 49.9	5 (12.50)	65-69.9	1(2.50)
50 – 54.9	17 (42.50)	70-74.9	20(50.00)
55 – 59.9	13 (32.50)	75-79.4	15(37.50)
60 – 64.5	5 (12.50)	80-84.9	4(10.00)
<b>Total</b>	<b>40</b>	<b>Total</b>	<b>40</b>



Birth weight (grams)	Lean women (BMI<25 kg/m <sup>2</sup> ) (n=40) No. (%)	Obese women (BMI>30 kg/m <sup>2</sup> )(n=40) No. (%)
2000-2499	6(15.00)	0
2500-2999	16(40.00)	2(5.00)
3000-3499	15(37.50)	14(35.00)
3500-3999	3(7.50)	20(50.00)
4000-4499	0	4(10.00)
<b>Total</b>	<b>40</b>	<b>40</b>



**Table 3: Distribution of Lean and Obese women according to fasting plasma glucose (mmol/L)**

Maternal fasting plasma glucose (mmol/L)	Lean women (BMI<25 kg/m <sup>2</sup> ) (n=40) No. (%)	Obese women (BMI>30 kg/m <sup>2</sup> ) (n=40) No. (%)
3.3-3.8	1(2.50)	0(0)
3.9-4.3	11(27.50)	2(5.00)
4.4-4.9	18(45.00)	12(30.00)
5-5.5	9(22.50)	14(35.00)
5.6-6.0	1(2.50)	12(30.00)
<b>Mean (mean±SD) (range)</b>	<b>4.58 ± 0.43 (3.8-5.5)</b>	<b>5.09 ± 0.50 (4.3-6.0)</b>
	<b>'t'=-4.85; 'p' = 0.0001</b>	

**Table 4: Distribution of newborns of Lean and Obese mothers according to cord plasma glucose (mmol/L)**

Cord plasma glucose (mmol/L)	Newborns of Lean mothers (n=40) No. (%)	Newborns of Obese mothers (n=40) No. (%)
2.7 – 3.2	6(15.00)	5 (12.50)
3.3 – 3.8	17(42.50)	10 (25.00)
3.9 – 4.3	15 (37.50)	17 (42.50)
4.4 – 4.9	2 (5.00)	7 (17.50)
5.0 – 5.5	0 (0)	1 (2.50)
<b>Mean (mean±SD) (range)</b>	<b>3.76 ± 0.42 (3.3-3.8)</b>	<b>3.95 ± 0.46 (3.9-4.3)</b>
	<b>'t'=-1.90; 'p' = 0.06</b>	

**Table 5: Distribution of Lean and Obese women according to serum insulin level (mU/ml)**

Maternal serum insulin level (mU/ml)	Lean women (BMI < 25 kg/m <sup>2</sup> ) (n=40) No. (%)	Obese women (BMI > 30 kg/m <sup>2</sup> ) (n=40) No. (%)
<2.5	0	0
2.5 – 8.4	17 (42.50)	2 (5.00)
8.5 – 14.4	19 (47.50)	8 (20.00)
14.5 – 20.4	4 (10.00)	15 (37.50)
20.5 – 26.4	0	9 (22.50)
>26.5	0	6 (15.00)
<b>Mean (mean±SD) (range)</b>	<b>9.19 ± 3.65 (3.6-18.2)</b>	<b>19.19 ± 5.89 (7.5-30.4)</b>
	<b>'t'=-9.11; 'p' = 0.0001</b>	

**Table 6: Distribution of newborns of Lean and Obese mothers according to cord serum insulin (mmol/L)**

Cord serum insulin (mU/ml)	Newborns of Lean mothers (n=40) No. (%)	New borns of Obese mothers (n=40) No. (%)
2.5 – 8.4	30 (75.00)	18 (45.00)
8.5 – 14.4	9 (22.50)	20 (50.00)

14.5 – 20.4	1 (2.50)	2 (5.00)
<b>Mean (mean±SD) (range)</b>	<b>6.92 ± 2.88 (2.6-14.7)</b>	<b>9.31 ± 3.04 (3.2-17.2)</b>
	<b>'t'=-3.59; 'p' = 0.0005</b>	

**Table 7: Distribution of Lean and Obese mothers according to insulin resistance index (HOMA-IR)**

Maternal HOMA-IR	Lean mothers (BMI < 25 kg/m <sup>2</sup> ) (n=40) No. (%)	Obese mothers (BMI > 30 kg/m <sup>2</sup> ) (n=40) No. (%)
0 – 1.49	13 (32.50)	0 (0)
1.50 – 2.99	25 (62.50)	5 (12.50)
3.00 – 4.49	2 (5.00)	15 (37.50)
4.50 – 5.99	0 (0)	18 (45.00)
6.00 – 7.49	0 (0)	2 (5.00)
<b>Mean (mean±SD) (range)</b>	<b>1.85 ± 0.06 (0.74-3.07)</b>	<b>4.25 ± 1.11 (1.83-6.17)</b>
	<b>'t'=-11.76; 'p' = 0.0001</b>	

**Table 8 : Distribution of newborns of Lean and Obese mothers according to insulin resistance index (HOMA-IR)**

Neonatal HOMA-IR	Newborns of Lean mothers (n=40) No. (%)	Newborns of Obese mothers (n=40) No. (%)
0 – 0.99	14 (35.000)	3 (7.50)
1.0 – 1.99	25 (62.500)	28 (70.00)
2.0 – 2.99	1 (2.50)	9 (22.50)
<b>Mean (mean±SD) (range)</b>	<b>1.12 ± 0.42 (0.48-2.49)</b>	<b>1.61 ± 0.45 (0.72-2.49)</b>
	<b>'t'=-4.84; 'p' = 0.0001</b>	

**Table 9 : Maternal and umbilical cord biochemical profile in Lean and Obese mothers at birth**

Biochemical profile	Lean mothers (BMI < 25 kg/m <sup>2</sup> )	Obese mothers (BMI > 30 kg/m <sup>2</sup> )	p-value
<b>Maternal</b>			
Mean plasma glucose (mmol/L)	4.58 ± 0.43	5.09 ± 0.50	0.0001
Mean serum insulin (mU/ml)	9.19 ± 3.65	19.19 ± 5.89	0.0001
Mean HOMA-IR	1.85 ± 0.65	4.25 ± 1.11	0.0001
<b>Umbilical cord</b>			
Mean plasma glucose (mmol/L)	3.76 ± 0.42	3.95 ± 0.46	0.06
Mean serum insulin (mU/ml)	4.58 ± 0.43	9.31 ± 3.04	0.0005
Mean HOMA-IR	4.58 ± 0.43	1.61 ± 0.45	0.0001

**DISCUSSION:**

The importance of detecting insulin resistance in newborns of obese mothers and increased fetal adiposity are some of the factors associated with increased risk of development of type-2 diabetes mellitus in later on. Hence, screening of newborns to detect insulin resistance is needful in detecting type-2 diabetes mellitus early in later life especially in newborns of obese mothers.

The present study was undertaken with the objective to establish relationship between maternal obesity and insulin resistance in newborns. In our study, we had 40 lean mothers (BMI < 25 kg/m<sup>2</sup>) and 40 obese mothers (BMI > 30 kg/m<sup>2</sup>).

In our study, the mean prepregnancy BMI of lean mothers was 21.45 ± 1.93 kg/m<sup>2</sup> and of obese mothers was 30.86 ± 0.79 kg/m<sup>2</sup>, whereas in a study by *Catalano et al. (2009)*,<sup>1</sup> the mean prepregnancy BMI of lean mothers was 22.0 ± 1.19 kg/m<sup>2</sup> and of obese mothers was 38.4 ± 6.3 kg/m<sup>2</sup>.

The average birth weight of newborns of lean mothers in our study was 2847 ± 394 grams and that of obese mothers was 3559 ± 332 grams, whereas in a study by *Sewell et al.(2006)*,<sup>6</sup> average birth weight in newborns of lean mothers was 3284 ± 534 grams and of obese mothers was 3438 ± 567 grams (p = 0.05).

In our study, fasting plasma glucose in lean mothers ranged between 3.8 - 5.5 mmol/L with a mean of 4.58 ± 0.43 mmol/L and in obese mothers, fasting plasma glucose levels ranged from 4.3 - 6.0 mmol/L with a mean of 5.095 ± 0.50 (p value = 0.0001). Whereas in a study by *Catalano et al. (2009)*,<sup>1</sup> mean fasting plasma glucose in lean mothers was 4.11 ± 0.38 mmol/L and of obese mothers was 4.38 ± 0.61 mmol/L (p value = 0.009).

In this study, the cord plasma glucose of newborns of lean mothers ranged from 3.0 – 4.8 mmol/L with an overall mean of  $3.76 \pm 0.42$  mmol/L and in newborns of obese mothers, cord plasma glucose ranged from 3.2 – 5.05 mmol/L, with an overall mean of  $3.95 \pm 0.46$  (p value = 0.06). Whereas in a study by **Catalano et al. (2009)**,<sup>1</sup> mean cord plasma glucose of newborns of lean mothers was  $3.33 \pm 0.72$  mmol/L and mean cord plasma glucose of newborns of obese mothers was  $3.66 \pm 0.77$  mmol/L (p value = 0.008).

In our study, the serum insulin levels in lean mothers ranged from 3.6 – 18.2 mU/ml, the overall mean being  $9.19 \pm 3.65$  mU/ml. The serum insulin levels in obese mothers ranged from 7.5 - 30.4, the overall mean being  $19.19 \pm 5.89$  mU/ml. Whereas, in a study by **Catalano et al. (2009)**,<sup>1</sup> mean serum insulin level in lean mothers was  $11.8 \pm 5.6$  mU/ml and mean serum insulin level in obese mothers was  $26.0 \pm 14.6$  mU/ml (p value = 0.0001).

In our study, the cord serum insulin in newborns of lean mothers ranged from 3 - 13.2 mU/ml, with a mean of  $6.92 \pm 2.88$  mU/ml and in newborns of obese mothers, cord serum insulin levels ranged from 4 - 8 mU/ml, with a mean of  $9.31 \pm 3.04$  mU/ml. Whereas in a study by **Catalano et al. (2009)**,<sup>1</sup> mean cord serum insulin in newborns of lean mothers was found to be  $7.0 \pm 3.38$  mU/ml and mean cord insulin in newborns of obese mothers was  $9.2 \pm 4.7$  mU/ml (p = 0.008).

In the present study, the insulin resistance index (HOMA-IR) in lean mothers ranged from 0.74 – 3.07, with an overall mean of  $1.85 \pm 0.64$ . The HOMA-IR indices of obese mothers ranged from 1.83 – 6.17, with an overall mean of  $4.25 \pm 1.11$ . This was found to be statistically highly significant (p = 0.0001).

#### CONCLUSION:

In the present study, the mothers were more insulin resistant than their newborns (p = 0.0001). The obese mothers were more insulin resistant than the lean mothers (p = 0.0001). Similarly, the newborns of the obese mothers were also more insulin resistant (p = 0.0001) than the newborns of lean mothers.

#### REFERENCES

1. Catalano PM, Minium J, Presley L et al. Fetuses of obese mothers develop insulin resistance in utero. *Diabetes Care* 2009; 32: 1076-1080.
2. Mingrone G, Manco M, Mora MEU et al. Influence of maternal obesity on insulin sensitivity and secretion of the offspring. *Diabetes Care* 2008; 31: 1872-1876.
3. Margret JRH, Melisse RM, Linde AB et al. Maternal obesity and fetal metabolic programming: a fertile epigenetic soil. *Am J Physiol Regul Integ Com Physiol* 2010; 299: R711-R722.
4. Boney CM, Verner A, Tucker R et al. Metabolic syndrome in childhood: association with birth weight, maternal obesity and gestational diabetes mellitus. *Pediatrics* 2005; 115: E290-E296.
5. Whitaker RC. Predicting preschooler obesity at birth: the role of maternal obesity in early pregnancy. *Pediatrics* 2004; 114: e29-e36.
6. Sewell MF, Huston-Presley L, Super DM et al. Increased neonatal fat mass and not lean body mass is associated with maternal obesity. *Am J Obstet Gynecol* 2006; 195: 1100-1103.
7. Eastman NJ and Jackson E. Weight relationships in pregnancy. *Obstet Gynecol Surv* 1968; 23: 1003-1025.
8. Abrams B and Laros R. Prepregnancy weight gain and birth weight. *Am J Obstet Gynecol* 1986; 154: 503-509.
9. Ericksson JG, Forgen TJ et al. Pathways of infant and childhood growth that lead to type 2 diabetes. *Diabetes Care* 2003; 26: 3006-3010.
10. Dabelea D, Hanson RL, Lindsay RS et al. Intrauterine exposure to obesity conveys risks for type 2 diabetes and obesity: a study of discordant sib ships. *Diabetes* 2000; 49: 2208-2211.
11. Catalano PM. Obesity insulin resistance and pregnancy outcome. *Reproduction* 2010; 140: 365-371.
12. Catalano PM. Obesity and pregnancy- the propagation of a vicious cycle. *J Clin Endocrinol Metabol* 2003; 88: 3505-3506.