ASSOCIATION OF MATERNAL OBESITY, BIRTH-WEIGHT, INSULIN LEVELS AND HOMA-IR IN NEWBORNS AT TERM IN A TERTIARY CARE CENTRE

Vinod Kumar¹, Shahbaz Khan², Joginder Singh³

¹Assistant Professor, Department of Medicine, GMC, Doda, Jammu, Jammu and Kashmir, India.

²Senior Resident, Department of Medicine, GMC, Doda, Jammu, Jammu and Kashmir, India.

³Assistant Professor, Department of Medicine, GMC, Doda, Jammu, Jammu and Kashmir, India.

ABSTRACT

BACKGROUND

Intrauterine environment represents a time when changes in metabolism may affect distant metabolic dysfunction in the offspring mediated through physiological and epigenetic mechanism. Maternal pregravid weight\BMI is associated with increased birth weight and insulin resistance in neonates. Maternal obesity and underlying insulin resistance are significant short and long-term risk factors for both the mother and her fetus which create the potential of a vicious cycle of obesity & insulin resistance and development of diabetes in later life. We wanted to evaluate the association of maternal pregravid obesity with birth-weight and HOMA-IR in newborns at term.

METHODS

This is a cohort study for a period of one year from Dec. 2010 to Nov. 2011. Neonates of forty lean (BMI < 25 kg/m²) and forty obese women (BMI > 30 kg/m²) with singleton term pregnancy were evaluated at elective cesarean section over a period of one year.

RESULTS

There was a positive relationship between maternal pregravid BMI, birth-weight and newborns insulin resistance ($r = 0.438$, $p = 0.0001$).

CONCLUSIONS

In the present study, Insulin resistance indices (HOMA-IR) were higher in obese mothers (mean value 4.25 ± 1.11) as compared to that of lean mothers (mean value 1.85 ± 0.64). The HOMA-IR index was also higher in newborns of obese mothers (1.61 ± 0.45) as compared to newborns of lean mothers (mean value 1.12 ± 0.42) and this difference was observed to be statistically highly significant ($p = 0.0001$). There was a positive relationship between maternal pregravid BMI, birth-weight and newborns insulin resistance ($r = 0.438$, $p = 0.0001$).

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BACKGROUND

Maternal obesity and underlying insulin resistance are significant short and long-term risk factors for both, the mother and her fetus,¹ which creates the potential of a vicious cycle of obesity & insulin resistance.² For the obese women with subclinical decreased insulin sensitivity, pregnancy represents a metabolic stress test for those disorders in pregnancy, which are the harbinger of the metabolic syndrome in later life.^{3,4,5} The type 2 diabetes is a complex disease characterized by decrease of insulin sensitivity and impaired insulin secretion.⁶ Recent studies have demonstrated that low birth -weight is a risk factor for development of obesity and type 2 diabetes in adulthood,⁷ association that could be explained because during intrauterine growth the fetus does not promote the appropriate growth of beta cells.⁸⁻¹⁰

Furthermore, children with history of high birth-weight also have an elevated risk of developing obesity and type2 diabetes later in life.^{11,12} India is heading towards acquiring the title of the capital of diabetes and cardiovascular diseases in the very near future. 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.^{13,14}

METHODS

This is a cohort study for a period of one year from Dec. 2010 to Nov. 2011 performed in GMC, Jammu. Insulin resistance was estimated using Homeostasis Model Assessment (HOMA-IR).

$$\text{HOMA-IR} = \frac{\text{Fasting plasma insulin (micromol / L)} \times \text{fasting glucose (mil limoles / L)}}{22.5}$$

All patients under study were subjected to detail history, clinical examination, systemic examination and laboratory investigations. BMI, Ponderal index, The OGTT, Neonatal serum insulin levels and Cord Plasma glucose estimation were done.

Sample size was taken based on the convenience of the study.

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Corresponding Author:

Dr. Joginder Singh,

Assistant Professor,

Department of Medicine, GMC, Doda,

Jammu, Jammu and Kashmir,

India.

E-mail: drkatil76@gmail.com

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Sampling Technique

Convenient sampling technique.

Inclusion Criteria

Newborns of healthy pregnant women at term (37th - 40th weeks of gestation) of both obese (BMI > 30 kg/m²) and non-obese group (BMI < 25 kg/m²).

Exclusion Criteria

1. Diabetes mellitus.
2. Impaired Glucose Tolerance Test (IGTT) i. e. 2-hour 75 g glucose challenge test result >140 mg/dL.
3. Clinical evidence of any infection.
4. Major chronic disease like carcinoma and tuberculosis.
5. Diseases leading to accumulation of fluid and appearance of protein in urine like congestive cardiac failure (CCF), renal failure and advanced liver failure.
6. Any women with obstetrical complications viz., PIH, heart disease, APH.
7. Any foetal disorder like AFD, IUHR, polyhydramnios, IUD.

Statistical Methods

Chi square test (χ^2) and Fisher exact test was used to calculate difference between qualitative variables as indicated. Quantitative data were expressed as mean $\pm$ SD (Standard deviation). The significance level for all above mentioned statistical tests was done P-value $\leq$ 0.05.

RESULTS

Forty lean (BMI < 25 kg/m²) and forty obese women (BMI > 30 kg/m²) with singleton term pregnancy were evaluated at elective cesarean section over a period of one-year w.e.f. December, 2010 to November, 2011. The objective of the study was to evaluate to the maternal obesity, birth-weight and HOMA-IR at birth, in newborn at term.

Pre-Pregnancy Weight (kg)	Lean Women (BMI < 25 Kg/m ²) (n=40) No. (%)	Pre-Pregnancy Weight (kg)	Obese Women (BMI > 30 Kg/m ²) (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)
Total	40	Total	40

Table 1. Distribution of Lean & Obese Women According to Pre-Pregnancy Weight (kg)

Birth Weight (Grams)	Lean Women (BMI<25 Kg/m ²) (n=40) No. (%)	Obese Women (BMI>30 Kg/m ²) (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)
Total	40	40

Table 2. Distribution of Newborns of Both, Lean and Obese Mothers According to Their Birth Weight (Grams)

Ponderal Index	Newborns of Lean Women (n=40) No. (%)	Newborns of Obese Women (n=40) No. (%)
1.50-1.99	7 (17.50)	0 (0)
2.00-2.49	23 (57.50)	6 (15.00)
2.50-2.99	10 (25.00)	23 (57.50)
3.00-3.49	0 (0)	10 (25.00)
3.50-3.99	0 (0)	1 (2.50)
Total	40	40

Table 3. Distribution of Newborns of Lean and Obese Mothers According to Their Ponderal Index

Cord Serum Insulin (mU/ml)	Newborns of Lean Mothers (n=40) No. (%)	Newborns 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)
Mean (mean $\pm$ SD) (range)	6.92 $\pm$ 2.88 (2.6-14.7)	9.31 $\pm$ 3.04 (3.2-17.2)
't'=-3.59; 'p' = 0.0005		

Table 4. Distribution of Newborns of Lean and Obese Mothers According to Cord Serum Insulin (mmol/L)

Maternal HOMA-IR	Lean Mothers (BMI < 25 kg/m ²) (n=40) No. (%)	Obese Mothers (BMI > 30 kg/m ²) (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)
Mean (Mean $\pm$ SD) (Range)	1.85 $\pm$ 0.06 (0.74-3.07)	4.25 $\pm$ 1.11 (1.83-6.17)
't'=-11.76; 'p' = 0.0001		

Table 5. Distribution 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 (35.00)	3 (7.50)
1.0 – 1.99	25 (62.50)	28 (70.00)
2.0 – 2.99	1 (2.50)	9 (22.50)
Mean (Mean $\pm$ SD) (Range)	1.12 $\pm$ 0.42 (0.48-2.49)	1.61 $\pm$ 0.45 (0.72-2.49)
't'=-4.84; 'p' = 0.0001		

Table 6. Distribution of Newborns of Lean and Obese Mothers According to Insulin Resistance Index (HOMA-IR)

Biochemical Profile	Lean Mothers (BMI < 25 kg/m ²)	Obese Mothers (BMI > 30 kg/m ²)	p-Value
Maternal			
Mean Plasma Glucose (mmol/L)	4.58 $\pm$ 0.43	5.09 $\pm$ 0.50	0.0001
Mean Serum Insulin (mU/ml)	9.19 $\pm$ 3.65	19.19 $\pm$ 5.89	0.0001
Mean HOMA-IR	1.85 $\pm$ 0.65	4.25 $\pm$ 1.11	0.0001
Umbilical Cord			
Mean Plasma Glucose (mmol/L)	3.76 $\pm$ 0.42	3.95 $\pm$ 0.46	0.06
Mean Serum Insulin (mU/ml)	4.58 $\pm$ 0.43	9.31 $\pm$ 3.04	0.0005
Mean HOMA-IR	4.58 $\pm$ 0.43	1.61 $\pm$ 0.45	0.0001

Table 7. Maternal and Umbilical Cord Biochemical Profile in Lean and Obese Mothers at Birth

DISCUSSION

The present study was undertaken with the objective to establish relationship between maternal obesity, insulin levels and insulin resistance in newborns. In our study, we had 40 lean mothers (BMI < 25 kg/m²) and 40 obese mothers (BMI > 30 kg/m²).

The average age of patients in our study was 25.75 ± 3.99 years in lean mothers and 27.27 ± 3.18 years in obese mothers, whereas in a study by Catalano et al. (2009),¹⁵ mean age of lean mothers was 28 ± 6 years and mean age of obese mothers was 27.8 ± 5.8 years.

In the present study, the average pre-pregnancy weight of lean mothers was 54.48 ± 4.10 kg and that of obese mothers was 74.55 ± 3.35 kg.

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 Catalano et al. (2009),¹⁵ the average birth weight of newborns of lean mothers was 3217 ± 452 grams and of obese mothers was 3320 ± 460 grams (p = 0.22). In a study by Sewell et al. (2006),⁵ 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, the mean Ponderal index of newborns, of lean mothers was 2.30 ± 0.32 and of obese mothers was 2.85 ± 0.25 (p value = 0.0001), whereas in a study by Catalano et al. (2009),¹⁵ the mean Ponderal index of newborns of lean mothers was 2.7 ± 0.2 and newborns of obese mothers was 2.8 ± 0.2 (p value = 0.004).

In our study, the mean prepregnancy BMI of lean mothers was 21.45 ± 1.93 kg/m² and of obese mothers was 30.86 ± 0.79 kg/m², whereas in a study by Catalano et al. (2009),¹⁵ the mean prepregnancy BMI of lean mothers was 22.0 ± 1.19 kg/m² and of obese mothers was 38.4 ± 6.3 kg/m².

In our study, the serum insulin levels in lean mothers ranged from 3.6 – 18.2 mU/ml, the overall mean being 9.19 ± 3.65 mU/ml. the serum insulin levels in obese mothers ranged from 7.5 - 30.4, the overall mean being 19.19 ± 5.89 mU/ml. Whereas, in a study by Catalano et al. (2009),¹⁵ mean serum insulin level in lean mothers was 11.8 ± 5.6 mU/ml and mean serum insulin level in obese mothers was 26.0 ± 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 ± 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 ± 3.04 mU/ml. Whereas in a study by Catalano et al. (2009),¹⁵ mean cord serum insulin in newborns of lean mothers was found to be 7.0 ± 3.38 mU/ml and mean cord insulin in newborns of obese mothers was 9.2 ± 4.7 mU/ml (p = 0.008).

CONCLUSION

In the present study, Insulin resistance indices (HOMA-IR) was higher in obese mothers (mean value 4.25 ± 1.11) as compared to that of lean mothers (mean value 1.85 ± 0.64). The HOMA-IR index was also higher in newborns of obese mothers (1.61 ± 0.45) as compared to newborns of lean mothers (mean value 1.12 ± 0.42) and this difference was

observed to be statistically highly significant (p = 0.0001). There was a positive relationship between maternal pregravid BMI, birth-weight and newborns insulin resistance (r = 0.438, p = 0.0001).

REFERENCES

- [1] Catalano PM. Obesity insulin resistance and pregnancy outcome. *Reproduction* 2010;140(3):365-71.
- [2] Catalano PM. Obesity and pregnancy - the propagation of a viscous cycle? *J Clin Endocrinol Metabol* 2003;88(8):3505-6.
- [3] Boney CM, Verma A, Tucker R, et al. Metabolic syndrome in childhood: association with birth weight, maternal obesity and gestational diabetes mellitus. *Pediatrics* 2005;115(3):e290-e6.
- [4] Whitaker RC. Predicting preschooler obesity at birth: the role of maternal obesity in early pregnancy. *Pediatrics* 2004;114(1):e29-e36.
- [5] 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(4):1100-3.
- [6] Helmrigh SP, Ragland DR, Leung RW, et al. Physical activity and reduced occurrence of non-insulin dependent diabetes mellitus. *N Engl J Med* 1991;325(3):147-52.
- [7] Jovanoic L. Type2 diabetes trends in offspring of type 2 diabetic mothers. *Diabetes Care* 2000;23:1219-20.
- [8] Leon DA, Koupilova I, Lithell O, et al. Failure to realize growth potential in utero and adult obesity in relation to blood pressure in 50 year old Swedish men. *BMJ* 1996;312(7028):401-6.
- [9] Silverman BL, Metzger BE, Cho NH, et al. Impaired glucose tolerance in adolescent offspring of diabetic mothers: Relationship to fetal hyperinsulinism. *Diabetes Care* 1995;18(5):611-7.
- [10] Pettitt DJ, Aleck KA, Baird HR, et al. Congenital susceptibility to NIDDM. Role or intrauterine environment. *Diabetes* 1988;37(5):622-8.
- [11] Pettitt DJ, Baird HR, Aleck KA, et al. Excessive obesity in offspring of Pima Indian women with diabetes during pregnancy. *N Eng J Med* 1983;308(5):242-5.
- [12] McCance DR, Pettitt DJ, Hanson RL, et al. Birth weight and non-insulin dependent diabetes: thrifty genotype, thrifty phenotype or surviving small baby genotype? *BMJ* 1994;308(6934):942-5.
- [13] Mingrone G, Manco M, Mora ME, et al. Influence of maternal obesity on insulin sensitivity and secretion offspring. *Diabetes Care* 2008;31(9):1872-6.
- [14] Heerwagen MJ, Miller MR, Barbour LA, et al. Maternal obesity and fetal metabolic programming: a fertile epigenetic soil. *Am J Physiol Regul Integr Comp Physiol* 2010;299(3): R711-R22.
- [15] Catalano PM, Presley L, Minium J, et al. Fetuses of obese mothers develop insulin resistance in utero. *Diabetes Care* 2009;32(6):1076-80.