Original article:

Association of Maternal obesity, birth-weight, insulin levels and HOMA-IR in newborns at term in a tertiary care centre

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ABSTRACT

Introduction: Intrauterine environment which 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 was 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 creates the potential of a vicious cycle of obesity & insulin resistance and development of diabetes in later life.

Aim: The objective of the study was to evaluate the association of maternal pregravid obesity with birth-weight and HOMA-IR in newborns at term**.**

Materials and Methods: This is a prospective study for a period of one year from Dec.2010 to Nov.2011. Neonates of Forty lean (BMI < 25 kg/m^2) and forty obese women (BMI > 30kg/m^2) 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).

Keywords: diabetes mellitus, body mass index , insulin resistance

INTRODUCTION:

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].

MATERIALS AND METHODS:

This is a prospective 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).

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

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.

INCLUSION CRITERIA: Newborns of healthy pregnant women at term (37^{th} - 40^{th} weeks of gestation) of both obese (BMI > 30 kg/m^2) and non-obese group (BMI < 25 kg/m^2).

EXCLUSION CRITERIA

1. Diabetes mellitus.
2. Impaired Glucose Tolerance Test (IGGT) *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.

RESULTS:

Forty lean (BMI < 25 kg/m^2) and forty obese women (BMI > 30kg/m^2) 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.

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^2) (n = 40) No. (%)**	**Pre-pregnancy weight (kg)**	**Obese women (BMI > 30 kg/m^2) (n=40) No. (%)**
45 – 49.9	5 912.50)	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	5 912.50)	80-84.9	4(10.00)
Total	**40**	**Total**	**40**

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Table 2: Distribution of newborns of both, Lean and Obese mothers according to their birth weight (grams)

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 3: Distribution of newborns of Lean and Obese mothers according to their Ponderal index

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

Cord serum insulin (mU/ml)	**Neborns 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)
Mean (mean±SD) (range)	**6.92 ± 2.88 (2.6-14.7)**	**9.31 ± 3.04 (3.2-17.2)**
	't'=-3.59; 'p' = 0.0005	

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Table 5: Distribution of Lean and Obese mothers according to insulin resistance index (HOMA-IR)

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±SD) (range)	**1.85 ± 0.06 (0.74-3.07)**	**4.25 ± 1.11 (1.83-6.17)**
	't'=-11.76; 'p' = 0.0001	

Table 6 : 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)
Mean (mean±SD) (range)	**1.12 ± 0.42 (0.48-2.49)**	**1.61 ± 0.45 (0.72-2.49)**
	't'=-4.84; 'p' = 0.0001	

Table 7 : Maternal and umbilical cord biochemical profile in Lean and Obese mothers at birth

Biochemical profile	**Lean mothers (BMI < 25 kg/m^2)**	**Obese mothers (BMI > 30 kg/m^2)**	**p-palue**
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

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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/m^2) and 40 obese mothers (BMI > 30 kg/m^2). 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 prepregnancy 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 kgm^2 and of obese mothers was 30.86 ± 0.79 kg/m^2, whereas in a study by **Catalano *et al.* (2009)[15],** the mean prepregnancy BMI of lean mothers was 22.0 ± 1.19 kg/m^2 and of obese mothers was 38.4 ± 6.3 kg/m^2.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).

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