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# Metabolic syndrome in preeclampsia - Analysis of insulin resistance and dyslipidemia.

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**Abstract :** Preeclampsia is multi-factorial in origin, despite extensive research the etiology of preeclampsia remains unfolded. Hence it is referred as disease of the theories. Insulin resistance and dyslipidemia may contribute to the onset of preeclampsia. But available evidences were controversial. Since we belong to high risk ethnicity (south Indian) for insulin resistance, we undertook this study with a aim to analyse lipid profile and insulin resistance (markers of metabolic syndrome) in normotensive and preeclamptic pregnant women. Biochemical analysis was done in 50 normotensive and 50 preeclamptic patients during their third trimester. Preeclamptic women were more insulin resistant ( p value less than 0.05). They had significantly higher triglyceride (p less than 0.0001) and LDL cholesterol levels (p less than 0.012). The HDL cholesterol in preeclamptic group was significantly low. Pre pregnancy BMI more than 25 was significantly associated with insulin resistance. In preeclamptic group 46.2 percent fulfilled the criteria for metabolic syndrome as against only 15.4 percentages in normotensive group. In conclusion preeclamptic women were more insulin resistant and having dyslipidemia to suggest metabolic syndrome.

**Keyword :**preeclampsia, insulin resistance, dyslipidemia, metabolic syndrome

## INTRODUCTION:

Preeclampsia is a multisystem disease and multifactorial in origin. It is a major cause of perinatal and maternal morbidity and mortality, affecting 5% to 8% of all pregnancy[1].The etiology of this disease is still unclear. Insulin resistance has been reported to contribute to the onset of hypertension and coronary artery disease, as a part of metabolic syndrome [2] and it also play a role in hypertensive

disorders of pregnancy [3]. Insulin resistance and resultant hyperinsulinemia are characteristics ofnormal pregnancy and are maximal in the third trimester. This is probably mediated by several hormonal changes, including elevations in the levels of human placental lactogen, progesterone, cortisol and estradiol. There appears to be an exaggeration of insulin resistance and metabolic changes in preeclampsia[4]. Many features of metabolic syndrome including hypertension, obesity and lipid abnormalities have been associated with preeclampsia[5].Although recent research have focused on insulin resistance and its potential role in preeclampsia, the results were controversial. Since we belong to high risk ethnicity having high prevalence of insulin resistance, this study would give a better yield to this controversial area.

The aim of our study was to analyse lipid profile and insulin resistance among normotensive and preeclamptic pregnant women.

## MATERIALS AND METHODS:

The study, designed as case-control study, was carried out in the obstetric department of Coimbatore Medical College Hospital from August to November, 2011. Cases include 50 patients with established preeclampsia and controls were 50 healthy normotensive pregnant women. Preeclampsia was defined as blood pressure 140/90 mmHg, measured at least 2 times 6 hours apart and proteinuria 300 mg in 24 hour urine collection after 20 weeks of gestation.Pre-Pregnancy Body Mass Index (BMI) was obtained from antenatal records. Metabolic syndrome was defined according to the criteria given by joint committee statement from IDF Task Force and American Heart Association [6].Excessive weight gain during pregnancy was based on IOM (Institute of Medicine) criteria[7]**Inclusion criteria:** primiparous women, singleton pregnancy, at third trimester (29-39 weeks). **Exclusion criteria:** presence of any chronic diseases like diabetes mellitus, abnormal OGTT, chronic hypertension, cardiac diseases, lipid abnormality and endocrinological abnormalities. After obtaining consent investigations were taken. Blood sample was collected after eight hours of fasting for blood sugar, plasma insulin and lipid profile measurement. Insulin resistance was calculated using Homeostasis Model Assessment, **HOMA-IR= {fasting insulin (µU/ml) × FBS(mg/dl)}/405**.[8] HOMA-IR value 2.6 was considered as 75$^{th}$ percentile. Continuous variables were expressed as mean ± SD, statistical analysis were done with chi square ($^2$) and unpaired t test.p value less than 0.05 was considered statistically significant.

## RESULTS:

The cases and controls were matched for age, pre pregnancy BMI and for gestational age. Preeclamptic women had significantly higher blood pressure, both systolic and diastolic (table: 1).

### TABLE: 1 CHARACTERISTICS OF THE STUDY POPULATION

Lipid profile analysis of normotensive and preeclamptic women is shown in table:2. Triglycerides and LDL cholesterol were significantly elevated and HDL cholesterol was significantly low in preeclamptic group. Total cholesterol was similar in both groups.

TABLE: 2 LIPID PROFILE Fasting blood sugar, fasting insulin and HOMA-IR were significantly high in preeclamptic group which is depicted in table:3. TABLE: 3 FBS, FASTING INSULIN & HOMA-IR

| Characteristics | Preeclamptic group (n=50) | Normotensive group (n=50) | P value |
|---|---|---|---|
| Age (years) | 24.4 ± 4.2 | 24.8 ± 4.8 | NS |
| Gestation (wks) | 34.2 ± 0.4 | 34.6 ± 0.7 | NS |
| Prepregnancy BMI ($kg/m^2$) | 23.6 ± 0.7 | 22.6 ± 0.5 | NS |
| Systolic BP (mm Hg) | 158 ± 4 | 112 ± 5 | 0.001 |
| Diastolic BP (mm Hg) | 110 ± 7 | 74 ± 7 | 0.001 |

TABLE: 2 LIPID PROFILE

| Parameters | Preeclamptic group (n=50) | Normotensive group (n=50) | t | P value |
|---|---|---|---|---|
| Total cholesterol | 220.80 ± 15.32 | 218.10 ± 16.45 | 1.14 | NS |
| Triglycerides | 276.12 ± 37.96 | 214.95 ± 28.31 | 5.73 | 0.0001 |
| HDL – C | 45.79 ± 8.32 | 59.42 ± 8.49 | 5.14 | 0.001 |
| LDL – C | 137.41 ± 31.92 | 115.55 ± 12.21 | 2.63 | 0.012 |

TABLE: 3 FBS, FASTING INSULIN & HOMA-IR

| Parameters | Preeclamptic group (n=50) | Normotensive group (n=50) | P value |
|---|---|---|---|
| FBS(mg/dl) | 85.92 ± 10.36 | 73.88 ± 6.58 | 0.002 |
| Fasting insulin (μU/ml) | 8.69 ± 3.38 | 5.26 ± 2.75 | 0.025 |
| HOMA – IR ($75^{th}$ percentile) | 24 (48%) | 13 (26%) | 0.05 |

## DISCUSSION:

| BMI ($kg/m^2$) | n=50 | Fasting insulin (µU/ml) | HOMA-IR 75$^{th}$ percentile (%) ( n=24) |
|---|---|---|---|
| <18 | 2 | 5.92 ± 3.60 | NIL |
| 18.0-24.9 | 19 | 6.25 ± 2.75 | 6 (31.57%) |
| 25.0 – 29.9 | 23 | 7.79 ± 4.84 | 14 (60.8%) |
| 30.0 – 39.9 | 6 | 8.07 ± 2.40 | 4 (66.6%) |

| Risk factor | HOMA-IR 75$^{th}$ percentile (%) (n=24) | P value |
|---|---|---|
| BMI >25 (n=29) | 18 (62.06%) | 0.05 |
| Excessive weight gain(n=34) | 20 (58.82%) | 0.05 |
| Age >25 (n=13) | 5 (38.46%) | NS |
| Physical inactivity (n=16) | 7 (43.75%) | NS |

Fasting insulin and HOMA-IR 75$^{th}$ percentile in preeclamptic women were increased significantly with increasing BMI. This is expressed in table: 4.In preeclamptic group 46.2% of the women fulfill the criteria for metabolic syndrome as against only 15.2% in normotensive pregnant women. TABLE: 4 BMI AND INSULIN RESISTANCE IN PREECLAMPTIC GROUP

The univariate analysis of risk factors of relation to the insulin resistance (HOMA - IR) in preeclamptic women is shown in table: 5. When BMI > 25 the HOMA -IR was significantly high ($p < 0.05$). Excessive weight gain was significantly associated with insulin resistance but not age. TABLE: 5 RISK FACTORS FOR INSULIN RESISTANCE IN PREECLAMPSIA GROUP

Hyperinsulinemia may directly predispose to hypertension by increased renal sodium reabsorption and sympathetic nervous stimulation [9]. Increased triglycerides seen in preeclampsia likely to be deposited in uterine spiral arteries and contributes to endothelial dysfunction [10]. LDL has greater capacity to stimulate thromboxane synthesis causing vasoconstriction [11]. Thus insulin resistance and dyslipidemia has been linked to endothelial dysfunction [12]. Changes in endothelial function and vasoactive agents have been proposed as possible pathogenic mechanisms of preeclampsia [13].In our study there was no statistical differance in total cholesterol in the study group consistent with the study by Jayanta., et al 2006[14]. There was a significant elevation in triglycerides ($p <0.0001$) and LDL cholesterol ($p<0.012$) in preeclamptic

group keeping the findings of Sahu., et al 2009[15]. Serum HDL cholesterol was significantly low ($p<0.001$) in preeclamptic group. In our study preeclamptic women were more insulin resistant than normotensive as shown by HOMA -IR 75$^{th}$ percentile (48% vs 26%; p value <0.05).Among patients with BMI >25, 62.06% had HOMA_IR 75$^{th}$ percentile. BMI is the single most important risk factor for increased insulin resistance in our study group [16]. Because obesity is major contributor to insulin resistance and recognized risk factor for preeclampsia, interventions geared to weight reduction before pregnancy and/or avoidance of excessive weight gain during pregnancy may have merit.

**CONCLUSION:**

Preeclamptic women are more insulin resistant and dyslipidemic which implies the association of metabolic syndrome and preeclampsia. Measuring insulin resistance and lipid profile in high risk pregnant women for preeclampsia would result in early detection. Prompt treatment for the same can prevent its complications.

**LIMITATIONS:**

Despite significant association found in our study, it cannot provide cause and effect relationship between insulin resistance syndrome and preeclampsia. This needs prospective evaluation in our population on a large scale.

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