ORIGINAL ARTICLE

# Insulin Resistance Estimated by HOMA IR for Diagnosis of Gestational Diabetes in Squatter Settlement of Karachi

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**ABSTRACT**

**Background:** Gestational diabetes mellitus (GDM), one of the most common metabolic disorders of pregnancy, is estimated to raise 16-27% worldwide every 10 years. Researchers, using Homeostasis model assessment test (HOMA IR), a tool for assessing insulin resistance, have found a number of causes. This study was designed to investigate the correlation between insulin resistance and GDM in the second trimester.

**Methods:** This study recruited 84 pregnant women (24 to 28 weeks of gestation) from OPD of Gynaecology/Obstetrics and Family Medicine Department, Dr. Ziauddin Hospital Karachi Pakistan from May 2018 to January 2019. A thorough anthropometric measurements and antenatal history was recorded through structured questionnaire after informed consent. After 10 hours fast, venous blood (5ml) was drawn for fasting blood glucose (FBS), insulin levels and Glucose challenge test (GCT) for screening gestational diabetes.

**Results:** Out of 84 subjects, 37 had higher GCT values while 47 had normal level. FBS was found significantly associated ($p < 0.05$). With GCT among GDM subjects 16(19%) had normal Body Mass Index (BMI) and 18(21.4%) had normal body fat percentage however, 2(2.4%) had high insulin levels and 13(15.5%) high FBS levels. The value HOMA IR, ≤1.29 was found in 38(45.2) healthy mothers and 25(29.8) GDM. Patients' GCT had positive association with parity, FBS, insulin, HOMA IR and BMI.

**Conclusion:** Linear strong positive correlation was found between insulin resistance and GCT in the second trimester. Patients with significantly higher GCT values and index value of HOMA IR greater than >1.29 are at risk for developing GDM.

**Keywords:** Insulin Resistance; Diabetes, Gestational; Pregnancy Trimester, Second; Economic Status.

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## INTRODUCTION

Gestational diabetes mellitus (GDM) is one of the most common metabolic disorders of pregnancy[1]. Worldwide the rise in its prevalence is estimated to be 16-27% every 10 years[2]. In Pakistan, its prevalence is estimated to be 8%[3]. It's devastating complications affects not only neonate but also the mother increasing the probabilities of developing type 2 diabetes mellitus (T2DM) later in life[4,5]. According to American Diabetic Association (ADA) recommended two steps approach; first to perform glucose challenge test (GCT) in random state, measuring 1hr postprandial plasma glucose levels. In case of abnormal results, second step is glucose tolerance test to diagnose GDM[6].

Pakistan, being a developing country, has approximately 24.3% of low socioeconomic (SES) population, living below the poverty line[7]. Individuals living in low SES are exposed to negative physical, mental, and behavioral conditions. These insults, especially during pregnancy, deprives women of healthy and thriving outcome mainly because of nutritional deficiencies resulting in compromised biological processes including homeostasis of glucose[8]. To ensure health care during pregnancy,

GDM needs to be screened during second trimester but the endorsed approaches are troublesome for mothers and healthcare professionals in developing countries. First step approach is commonly used as a screening tool knowing the limitations in relation to its diagnostic value[9]. Homeostasis model assessment test for insulin reistance (HOMA IR),designed by Mathews in 1985, is a tool used for understanding the feedback loop between the liver and pancreatic beta cells. This model helps in explaining the insulin resistance (IR) and pancretic beta cell functions at different concentration of glucose and insulin in a fasting state[10].

Therefore, we need to implement tools that would help in predicting women prone to diabetes after postpartum, insulin resistance can be prevented by simple life style measures such as diet and exercise. Hence, GDM screening using GCT during 2nd trimester, finding its association with fasting blood sugar (FBS) and insulin with homeostasis assessment model of insulin resistance (HOMA IR) was aimed. This study was designed to investigate the correlation between insulin resistance (IR) and GCT in the second trimester, which may lead to GDM.

## METHODS

This comparative, cross sectional study was designed to recruit 84 pregnant women between 24 to 28 weeks of gestation, normal and GDM, were included, from the outpatient Department of Gynaecology and Obstetrics and Family Medicine at Dr. Ziauddin Hospital Karachi Pakistan. The study was conducted from May 2018 to January 2019. The sample size was calculated using Open-Epi calculator taking 8% as prevalence at confidence level 95%.

All recruited pregnant women signed written informed consent. A thorough antenatal history was recorded comprising all the information regarding socioeconomic status, education, lifestyle, previous obstetric history including gestational diabetes, family history of diabetes, etc. Women having co-morbids with pregnancy like type 2 diabetes, kidney impairment, cardiovascular disease, asthma, stillbirths, twin pregnancy or preterm delivery were excluded from the study.

Anthropometric measurements were taken, including height, weight, and waist/hip ratio. Weight on first visit was recorded and using bioelectrical impedance method, BMI and body fat percentage (WHO criteria 2015) through Omron analyser (HBF-306C) were measured. Venous blood (5ml) was drawn after 10 hours fasting for FBS and insulin levels. Fasting insulin level was calculated by chemiluminescence (Siemens IMMULITE® 1000 Chemiluminescent) at a certified laboratory whereas; FBS was calculated according to ADA guidelines 2018 by Rximola automated photometer. GCT was done as screening test for gestational diabetes. According to the ADA criteria, if blood glucose levels at one hour after 50g glucose ingestion are equal to or greater than 140mg/dl then women is considered GDM. HOMA IR was taken normal according to Sokup et al[11]. SPSS 20 software was used for statistical analysis. Association was analysed using fisher exact test and spearman correlation. p value less than 0.05 was used as statistically significant.

## RESULTS

Out of 84 pregnant candidates, 37 were found at risk of gestational diabetes while 47 had normal GCT levels. Out of 37 gestational diabetic women, 2 (2.4%) had high insulin levels and 13(15.5%) high FBS levels. HOMA IR above 1.29 was considered high according to study by Sokup et al[11]. Among GDM pregnant, 12(14.3%) had HOMA IR above 1.29, 16(19%) had normal BMI and 18(21.4%) had normal body fat percentage as shown in Table 1. The association of FBS with GCT was found statistically significant (0.015) whereas, all other parameters had p value greater than 0.05.

**Table 1: Comparison of GDM and Healthy Group with metabolic Parameters.**

| Parameters | N (%) | | p-value |
|---|---|---|---|
| | Healthy = 47(56) | GDM = 37(44) | |
| **Insulin (μU/ml)** | | | |
| | 21(25) | 14(16.7) | 0.827 |
| Normal | 23(27.4) | 21(25) | |
| High | 3(3.6) | 2(2.4) | |
| **FBS (mg/dl)** | | | |
| Normal | 41(48.8) | 24(28.6) | 0.015* |
| High | 6(7.1) | 13(15.5) | |
| | | | |
| **1.29** | 38(45.2) | 25(29.8) | 0.127 |
| >1.29 | 9(10.7) | 12(14.3) | |
| **BMI** | | | |
| Low | 2(2.4) | 1(1.2) | 0.531 |
| Normal | 26(31) | 16(19) | |
| Overweight | 13(15.5) | 11(13.1) | |
| Obese | 6(7.1) | 9(10.7) | |
| **Body Fat (%)** | | | |
| Low | 14(16.7) | 7(8.3) | 0.488 |
| Normal | 23(27.4) | 18(21.4) | |
| High | 8(9.5) | 8(9.5) | |
| Very high | 2(2.4) | 4(4.8) | |

*Fisher Exact Test*
**p- value < 0.05 statistically significant*

HOMA IR in 8(9.5%) normal and obese pregnant

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women was above 1.29 whereas, 10(11.9%) had normal body fat with HOMA IR above 1.29 as shown in Table 2. An association of GCT with other numeric parameters showed GCT had a positive correlation with parity, FBS, insulin, HOMA-IR and BMI whereas, association with body fat percentage was found none. The correlation of GCT with FBS was statistically significant (0.002) as shown in Table 3.

**Table 2: Association of HOMA IR with BMI and Body fat.**

| Parameters | HOMA IR= N (%) | | p-value |
|---|---|---|---|
| | Less than 1.29 =63(75) | Greater than 1.29 = 21(25) | |
| **BMI** | | | |
| **Low** | 2(2.4) | 1(1.2) | 0.045* |
| **Normal** | 34(40.5) | 8(9.5) | |
| **Over weight** | 20(23.8) | 4(4.8) | |
| **Obese** | 7(8.3) | 8(9.5) | |
| **BODY FAT** | | | |
| **Low** | 18(21.4) | 3(3.6) | 0.297 |
| **Normal** | 31(36.9) | 10(11.9) | |
| **High** | 11(13.1) | 5(6) | |
| **Very high** | 3(3.6) | 3(3.6) | |

*Fisher Exact Test*
** p value <0.05 significant*

**Table 3: Association of GCT with metabolic parameters.**

| Parameters | Correlation | p-value |
|---|---|---|
| **PARITY** | 0.178 | 0.053 |
| **FBS(mg/dl)** | 0.311** | 0.002 |
| **INSULIN( μu/ml)** | 0.120 | 0.139 |
| **HOMAIR** | 0.235* | 0.016 |
| **BMI** | 0.156 | 0.076 |
| **BODY FAT (%)** | 0.086 | 0.218 |

*Spearman Correlation*
***Correlation is significant at the 0.01 level, *Correlation is significant at the 0.05 level*

## DISCUSSION

Despite abundant research on GDM and its improved methods of detection and recognition of poor outcome for baby and mother, there is still controversy regarding the result, diagnosis and treatment of GDM and largely remains debatable[12]. Gestational Diabetes Mellitus is assessed by the HOMA index, which shows association of IR with the severity and pathophysiological heterogeneity of the disease[11]. In this study, GDM women showed a positive association with HOMA IR and FBS. Women had insulin resistance at normal plasma concentration of insulin, this maybe, is due to defects at the level of molecular structure, receptor or signaling pathway and insulin is unable to produce the desired effects in the body tissues[13]. Our study is in accordance with study conducted by Wang et al. who observed that women developing GDM in late pregnancy displayed high value of HOMA IR compared to control group[14]. Also in a prospective cohort study, HOMA IR values were high among diagnosed GDM women compared to healthy control subjects[15]. In another study, researchers compared IR in three different trimester of pregnancy. They observed that insulin resistance using HOMA IR tool was high in second and third trimester compared to first trimester[16].

During pregnancy compensation to initial hyper-insulinemia occurs but if the condition becomes chronic then insulin levels declines as its secretion by pancreas decreases and causes diabetes mellitus (DM)[13]. Therefore, as the pregnancy advances the IR tends to increase. However, rise in the pregnancy hormones such as human placental lactogen (hPL), estrogen and progesterone[17] drop off insulin sensitivity to 50% especially during last trimesters[18]. To evaluate IR, HOMA IR is a secondary tool used for assessing insulin resistance among diabetic patients[19]. According to study by Sokup et al. the index value of HOMA-IR greater than >1.29 was found linked with severity of GDM. If we take >1.29 of HOMAIR as cutoff value for our population then HOMA IR was high in 1.2% underweight, 4.8% overweight 9.5% obese pregnant women. Researchers showed that values above >1.29 show less secretion of insulin and advocate towards the need for treatment11. This clearly demonstrates reduction in β cell function. Thus, overall change in diet and lifestyle towards a healthier living is required to be adapted by the females during pregnancy according to weight and calorie need and also counseling through regular verbal and printed brochures during weekly antenatal follow ups is required[20].

In this study out of 37(44%) GDM women, 8(9.5%) had high levels of body fat, 2(2.4%) had high insulin levels, compared to 47(56%) healthy women, only 2(2.4%) had very high body fat, 3(3.6%) high insulin. Obesity and excessive gestational weight gain can lead to numerous complications in the mother as well as the fetus. These complications are mainly summarized as pre-GDM or GDM in which uterine programming of insulin resistance is disrupted resulting in obesity and Type 2 diabetes mellitus (T2DM) in the mother. Children born during this time, due to disruption in intrauterine programming, have also been found at risk for developing cardiovascular complications[21].

Obesity during pregnancy results primarily due to overeating because of disturbed signals of the hypothalamus regarding satiety and hunger caused by insulin resistance. This insulin resistance

leads to compromised function of adipose tissue and consequently excess fat is out sourced to other organs like skeletal muscle and liver leading to lipotoxicity accelerating the other related complications such as diabetes, cardiovascular diseases, and PCOs[22]. In contrast to this, in normal women excess fat is deposited in conditionally enlarged adipocytes with reduction in adipokines compared to obese women who maintain their adiponectin level[23]. Thus, major contributor to IR is the visceral adipose tissue. Its function as a metabolic buffer is compromised due to hypertrophy of the adipocytes, decrease in adipogenesis and angiogenesis[24]. In our previous study, BMI and lipid profile showed no significant association with body fat percentage[25]. Differences in the sample size, techniques and patients characteristics along with ethnicities may possibly explain the results of the previous study.

During pregnancy or postnatally, GDM create complications for the mother[26]. Expectant mothers are at higher risks of preeclampsia, C-section, macro-somia, neonatal hypoglycemia, and hyperbilirubinemia if exposed to GDM. Increased IR during this period may cause defects in β-cell response and faster deterioration of secretory capacity of β-cells. Consequently, during following pregnancies, deterioration of beta-cell function leading to insulin insensitivity is accelerated in these women[27]. Other possible complications in women with previous GDM include metabolic impairments involving dyslipidemia and vascular dysfunction[28]. Thus, compared to women who do not experience GDM, risk of postpartum diabetes and other complications occur at a much earlier age in women with a history of GDM[29]. In accordance with study by Alina Sokup, other parameters such as age, parity, BMI and body fat were not found statistically significant[11].

In this study, due to small sample size, we were unable to calculate HOMA IR cut off values and comparison of IR among healthy and GDM pregnant women. Future studies with bigger sample size are required to calculate HOMA IR and its cut off values for pre-diabetic risk among Pakistani population.

## CONCLUSION

Linear positive correlation was found between insulin resistance and GCT in the second trimester. Patients with significantly higher GCT values are at risk for developing GDM. Pregnant women at risk should be counseled during antenatal visits for lifestyle changes with guidance regarding healthy diet, physical activity and weight loss. Future research on bigger sample size should be done to further establish HOMA IR cut off values for our population.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## ETHICS APPROVAL

Ethics review committee of Ziauddin University Pakistan approved this study.

## PATIENT CONSENT

Verbal and written signed consent was taken from patients.

## AUTHORS' CONTRIBUTIONS

HA conceived the idea and did bench work and statistics.SI contributed in sample collection/patient counseling. SB contributed in sampling and manuscript writing. STA and RR contributed in writing and overall formatting.

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