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Research Article
Influence of Grand Multiparity on the Levels of Insulin, Glucose and HOMA-IR in Comparison with Nulliparity and Primiparity

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Abstract

Objective: It is to compare the levels of fasting glucose and insulin as well as insulin resistance in grand multiparas with primiparity and nulliparity. **Methodology:** Fasting blood samples were collected from 100 non-pregnant ladies as control group, 100 primiparity pregnant women and 100 grand multiparity pregnant women. Glucose (FBS) and insulin (FSI) concentrations were measured by Hitachi 912 full automated Chemistry Analyzer (Roche Diagnostics, Germany) as manufacturer procedure. Insulin resistance was calculated following the formula: FBG (mg dL^{-1}) × FSI (μU mL^{-1})/405. **Results:** This study found a significant reduction in glucose level in primiparity when compared to control group but it was increased significantly in multiparity comparing to primiparity and control. Insulin level showed significant high concentrations in pregnant women and increased significantly in grand multiparas comparing to primiparas and controls. As a result of that, HOMA-IR was increased significantly by increasing of parity. Also, there was a significant increase in fasting insulin and a decrease in insulin sensitivity with parity with association to age and obesity. **Conclusion:** Grand multiparity is associated with an increased risk of subsequent clinical insulin resistance (HOMA-IR).

Key words: Grand multiparity, primiparity, nulliparity, glucose, insulin, HOMA-IR

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Pregnancy involves marked alterations in vital parameters, involving reduced insulin sensitivity in peripheral tissues, incremented pancreatic production of insulin and accumulation and reallocation of body fat[1]. Meanwhile, women increase their energy intake, ameliorate the type and amount of their food and maintain or reduce regular physical activity: changes that may increase their risk for developing cardiometabolic diseases[2].

Pregnancy results in a state of insulin resistance that appears to include a decrease in maximum insulin sensitivity or responsivity[3]. Insulin resistance is defined as the decrease of the biological action of insulin and it mainly presents as hyperinsulinemia[4]. The resistance to insulin can be characterized as pre-receptor (insulin antibodies), receptor (decreased number of receptors on the cell surface) or post-receptor (defects in the pathway of intracellular insulin signals). The decreased insulin sensitivity in pregnancy is best characterized as a post-receptor defect resulting in the decreased ability of insulin to bring about glucose transporter (GLUT4) mobilization from the interior of the cell to the cell surface[5].

Gestational Diabetes Mellitus (GDM) is defined as a carbohydrate intolerance of varying severity with onset or first recognition during the present pregnancy[6]. The GDM has onset or discovery of glucose intolerance during pregnancy, commonly in the second or third trimester[7]. The GDM carries long-term repercussions for the development of type 2 diabetes in the mother and increased risk for obesity and glucose intolerance in the offspring[8]. The world health organization defines diabetes in pregnancy as a fasting glucose $\geq$140 mg dL^{-1} or a value >199 mg dL^{-1} 2 h after a 75 g glucose load[9]. Impaired Glucose Tolerance (IGT) was previously known as chemical diabetes or subclinical diabetes[10]. Therefore, the condition of IGT designed glucose tolerance results intermediate between normal glucose homeostasis and overt diabetes. It is diagnosed if fasting glucose $\geq$109 but <140 mg dL^{-1} or 2 h glucose >140 mg dL^{-1} and <200 mg dL^{-1}. About 25% of patients with IGT eventually become diabetic. In the last trimester, the carbohydrate tolerance is reduced due to reduced sensitivity to insulin[11]. Insulin resistance is a minimized ability of cells to respond to the insulin action in conveying glucose from bloodstream into muscle and other tissues[12]. However, a recent study reports that there is no relationship between parity and insulin resistance[13]. On the contrary, the influence of parity on metabolic syndrome in Chinese women reported that multiparity is a risk factor for metabolic syndrome[14]. A similar study in racially diverse population revealed that increased parity is associated with increase cholesterol levels[15] which may contribute to insulin resistance. Hence, it is not clear whether parity increases insulin resistance.

This study was carried to determine if there would be any changes in serum fasting glucose and fasting insulin levels as well as HOMA-IR in grand multiparas pregnant Sudanese women and to compare the results of these parameters with the results from age and sex-matched primiparas (first time pregnancy) and apparently healthy individuals non-pregnant females (nulliparas and control). The study was aimed to determine the effect of grand multiparity on insulin resistance in Sudanese women, as a representative of African women, on insulin resistance and to evaluate the influence of age and Body Mass Index (BMI) on insulin resistance.

MATERIALS AND METHODS

Study design: This study was designed as a cross-sectional study.

Study area: The study was carried in Khartoum state, in Al-Ajyal hospital, the fertility Center of Dr. Suraj and Dr. Amel Hospital for Obstetrics and Gynaecology.

Study period: The study was carried between August, 2013 and April, 2015.

Sample size: The study included 100 normal healthy non-pregnant ladies as control group (nulliparity), 100 pregnant ladies for the first time (primiparity) and 100 were pregnant for more than 5 times (grand multiparity). All pregnant women were between 20-30 weeks gestation during the time of collection of samples. The pregnant women those take drugs effect on estimation and/or with major hormonal disorder and those who refused to participate in this study were excluded.

Sampling: Informed consent was obtained from all study participants. Pre-prepared questionnaire including data concerning patients and their pregnancy information (such as age, tall, weight, health condition, complications during this pregnancy and number of pregnancies) was used. This study was approved by the ethical committee of Omdurman Islamic University.

The patients were asked to fast 8-10 h before the blood test. Seven milliliters of venous blood was obtained from each female using standard venipuncture technique in Serum

Separator Tubes (SST). After 15 min, serum specimens were collected in new and clean container after centrifugation at 3000 rpm for 5 min. The serum then assayed for fasting glucose (FBG) by glucose oxidase and for fasting insulin levels (FSI) by ECL standard method on a Hitachi 912 automated Chemistry Analyzer (Roche Diagnostics, Germany) as manufacturer procedure. Then homeostasis model assessment of insulin resistance (HOMA-IR) index was calculated using the equation[16]:

$$\text{HOMA-IR} = \text{FBG (mg dL}^{-1}) \times \text{FSI (}\mu\text{U mL}^{-1})/405$$

The primary outcome measure was HOMA-IR levels in both groups. The secondary outcome measures were the FBG and FSI. Additional analysis was performed on age and BMI.

Statistical analysis: The results were compared between multiparity with primiparity, multiparity with control and primiparity with control. Statistical analysis was performed using statistical package for social sciences (SPSS). Statistical significance was evaluated by student t-test in case between two groups and by one-way ANOVA followed by Tukey's test in case of comparisons of three groups, at which the p-value of less than 0.05 considers the significance.

RESULTS

The results showed that there was reduced level of glucose in primiparity when compared to control group but increased in multiparity to higher levels than control. Insulin level showed high concentration in pregnancy and increased significantly in grand multiparas comparing to primiparas and controls. The HOMA-IR was increased significantly in multiparity when compared to primiparity and nulliparity (Table 1).

The results of BMI, FBG, FSI and HOMA-IR in overweight multiparity subjects were similar to normal weight multiparity subjects when compared to respective overweight control (Table 2).

DISCUSSION

The high parity is hypothesized to be associated with insulin resistance and type 2 diabetes, few researchers have studied this association in diverse racial samples or geographical areas. The relationship between parity and risk of diabetes remains unclear[11].

This study showed that pregnant women suffer from obesity. The body mass index in the present study increased with increasing the parity. Bogaerts *et al.*[17] stated that maternal obesity and excessive gestational weight gain are both important health care issues especially in multiparity.

Fasting blood glucose in this study showed significant decrease in primiparity pregnant women when compared to nulliparity, but increased significantly in multiparity in comparing to both groups (nulliparity and primiparity). While, the concentration of fasting serum insulin was increased significantly as increase of parity, showing the highest level in grand multiparity. This is the same results of HOMA-IR, which also displayed the highest level in grand multiparity. This may suggest that increased parity promotes earlier development of diabetes rather than increasing lifetime diabetes risk. Few studies have discussed the relationship between parity and either IGT or IFG. After adjusting for obesity and age, Gunderson *et al.*[18] study showed increased risk of diabetes

Table 1: Comparison of FBG, FSI and HOMA-IR levels between control, primiparity and multiparity

Parameters	Control	Primiparity	Multiparity
Number	100	100	100
Age (years)	30.250±5.025	28.750±4.499	32.500±5.715**
Body mass index (BMI)	22.301±1.055	24.158±6.394*	28.729±4.915***$^{\#}$
Fasting Blood Glucose (FBG) (mg dL^{-1})	86.904±12.877	77.833±8.316***	109.890±12.424***$^{\#\#\#}$
Fasting Serum Insulin (FSI) (μU mL^{-1})	16.761±2.099	24.108±5.051***	27.223±4.329***$^{\#\#\#}$
Homeostasis model assessment of insulin resistance index (HOMA-IR)	3.597±0.834	4.633±1.00***	7.387±0.9130***$^{\#\#\#}$

The results were expressed as Mean±SD, *p<0.05 when compared to control, **p<0.01 when compared to control, ***p<0.001 when compared to control, $^{\#}$p<0.05 when compared to primiparity, $^{\#\#\#}$p<0.001 when compared to primiparity

Table 2: Comparison of FBG, FSI and HOMA-IR levels between control (overweight) and multiparity (overweight)

Parameters	Control	Multiparity
Number	30	80
Age (years)	33.250±5.671	32.110±3.028
Body Mass Index (BMI)	27.115±3.800	29.323±3.217**
Fasting Blood Glucose (FBG) (mg dL^{-1})	90.600±5.441	111.400±6.736***
Fasting Serum Insulin (FSI) (μU mL^{-1})	18.220±2.404	28.810±3.007***
Homeostasis model assessment of insulin resistance index (HOMA-IR)	4. 082±2.055	7.828±1.992***

The results were expressed as Mean±SD, **p<0.01 when compared to control, ***p<0.001 when compared to control

with increasing of multiparity. The study of Green *et al.*[19] revealed that there is a relationship between risk of diabetes and parity that may vary with age, showing more diabetes with grand multiparity among younger but not among older women.

Consistent with these findings, an earlier study of Kritz-Silverstein *et al.*[20] examined the relationship between parity and glucose homeostasis in middle-aged to older women, exhibited each pregnancy was associated with increased fasting insulin and decreased insulin sensitivity that was not explained by obesity and body composition measures. That study suggested that changes in insulin sensitivity related to parity persist many years after childbearing. On the other hand, Manson *et al.*[21] report suggested that women with high parity had a 50% higher risk of incident diabetes over 12 years of follow-up.

The finding of the present study explicated the insulin resistance in multiparity pregnant women leads up to outcrop of gestational diabetes with all its complications in the long term. The results of this study will also help in understanding of factors such as race, socioenvironmental factors that may be contribute to insulin resistance as and when more studies from subjects of other background are available. Moreover, the results of the present study reaffirm that parity is directly associated with insulin resistance and is contradictory to the recent report that parity does not influence insulin resistance[13].

CONCLUSION

Grand multiparas are a high-risk obstetric group of patients liable to develop a number of antepartum and intrapartum complications with adverse neonatal outcome. Despite a diabetogenic effect become clear during pregnancy, parity is associated with an increased risk of subsequent clinical insulin resistance (HOMA-IR). This result is contributed by age and obesity.

SIGNIFICANT STATEMENTS

- Gestation diabetes is common and occurs due to insulin resistance
- The number of multiparity cases is one decline throughout the world due to birth control measures. However, multiparity is very common in the African continent
- The present study evaluates the effect of multiparity on insulin resistance in the Sudanese women
- The results of the present study can be extrapolated to the African women and will help in preventing complications due to diabetes

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