

# Correlation between maternal weight and insulin resistance in second half of pregnancy

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## ABSTRACT

**Background:** In pregnancy, routine measurement of maternal weight gives a crude assessment of maternal and foetal well-being. Excess weight gain in pregnancy is related to increased risk for gestational diabetes mellitus (GDM), hypertension in pregnancy and foetal macrosomia. In the Nigerian context, lack of knowledge of pre-pregnancy weight coupled with late booking of women in pregnancy hinders accurate assessment of weight gain in pregnancy. The absolute maternal weight is often used as surrogate. This study evaluates the relationship between absolute weight in the second half of pregnancy and insulin resistance. **Patients and Methods:** The weight of hundred pregnant women was measured between 24 to 32 weeks of pregnancy and their insulin resistance was measured using Homeostatic Model Assessment (HOMA-IR) from fasting serum glucose and fasting serum insulin. **Results:** Twenty-six women had weight  $\geq 95$  kg and 74 women had weight of  $< 95$  kg. There was a significant positive correlation between weight and HOMA-IR ( $r = 0.248$ ), fasting glucose ( $r = 0.198$ ), and fasting insulin ( $r = 0.228$ ), ( $P < 0.05$ ). The mean weight, HOMA-IR, fasting glucose and fasting insulin were higher in women with weight  $\geq 95$  kg compared to those with less weight. Also maternal weight  $\geq 95$  kg was associated with severe insulin resistance, (Odds Ratio = 3.1). **Conclusion:** Absolute weight in pregnancy correlates well with insulin resistance. Women having weight  $\geq 95$  kg between 24-32 weeks of gestation were more likely to have severe insulin resistance with implications for increased risk of GDM and other complications.

**Key words:** Fasting glucose, fasting insulin, insulin resistance, obesity, overweight

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## INTRODUCTION

Weight is a routinely measured clinical parameter used for assessing the state of well-being including risk for developing a number of adverse health conditions. Whereas normal weight often reflects good health, extremes of weight are usually a predictor or sign of disease conditions. Overweight and obesity for instance are associated with a constellation of clinical features like increased blood pressure and abnormal biochemical findings such as increased insulin resistance, increased glucose intolerance, and dyslipidaemia that conspire to increase the risk for cardiovascular disease.<sup>1,2</sup> Evidently, the incidence of overweight and obesity is on the increase

globally, assuming pandemic proportions.<sup>3,4</sup> The inevitable result is a likely increase of these conditions in pregnancy.

In the context of pregnancy, overweight and obesity are associated with complications for both the mother and her foetus, these include gestational diabetes mellitus (GDM), gestational hypertension, increased risk of caesarean section, macrosomic babies and neonatal hypoglycaemia.<sup>5,6</sup> Assessment of these risks is commonly done by determining the body mass index (BMI) early in pregnancy or weight gain in pregnancy with respect to the pre-pregnancy weight.<sup>7</sup> However, when a safe estimate of the body mass index (BMI) or weight gained in pregnancy cannot be done, as a result of lack of knowledge of pre-pregnancy weight and/or late antenatal booking as commonly the case in Nigeria, absolute weight measurement is often used as a crude surrogate.

Absolute weight of  $> 90$  kg at booking has been advocated for classifying women as overweight or obese in pregnancy.<sup>8,9</sup> However, this is most appropriate in early pregnancy. Studies suggest that women in Nigeria commonly book at gestational age ranging from 24 to 30 weeks of gestation.<sup>10-13</sup>

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This period coincides with the establishment of increased insulin resistance in pregnancy.<sup>14,15</sup> The association between absolute maternal weight particularly at higher weight categories and insulin resistance, a harbinger of abnormal glucose metabolism in pregnancy has not been well examined in the Nigerian setting. This study is an attempt to assess the relationship between maternal weight in second half of pregnancy and insulin resistance.

## PATIENTS AND METHODS

This study was a cross-sectional study involving 100 women with singleton pregnancy at 24-32 weeks of gestation referred for oral glucose tolerance test (OGTT) at the metabolic clinic of the Jos University Teaching Hospital, located in Plateau State, north-central Nigeria. The gestational weight was dated from the first day of the last menstrual period (LMP) and confirmed by booking ultrasound scan. The booking scan dating was used in cases of unsure LMP date or whenever there was  $\geq 10$  days difference in LMP and booking scan dating. The weight of the subjects was measured using a Harrison's weighing scale. The subjects included 26 overweight subjects (classified as  $\geq 95$  kg) and 74 lean/normal weight subjects ( $< 95$  kg) matched for gestational age. Glucose and insulin were measured in fasting blood of the subjects and used to compute their (HOMA-1R) with HOMA2 Calculator v2.2 software. Subjects with severe insulin resistance were classified as those with (HOMA-IR)  $\geq 1.9$  (corresponding to the 80<sup>th</sup> percentile of HOMA-IR).<sup>16</sup>

Serum glucose was assayed within 4 hours of sampling. Serum for insulin assay was stored at  $-20^{\circ}\text{C}$  and insulin assayed within 30 days of collection. Blood samples were analysed for glucose using commercial kits on the Roche/Hitachi 902 automatic analyser. Insulin was assayed using DRG Human insulin ELISA kits (DRG International, Inc. U.S.A). The intra-batch and inter-batch coefficient of variation (CV) were 2.4% and 4.3%, respectively for glucose as well as 1.9% and 5.4%, respectively for insulin. The collected data were compiled, tabulated, and analysed using Statistical Package for Social Sciences (SPSS Incorporated Chicago Version 15.0) software.  $P < 0.05$  was set as the level of significance.

### Ethical consideration

This study was conducted after due approval from the Ethical Committee of our Hospital. Informed consent was obtained from all subjects in the study.

## RESULTS

The mean age and gestational age of all the subjects were 31.5 years and 28.5 weeks, respectively. The mean fasting glucose (FPG), fasting insulin (FPI), and HOMA-1R were higher in the overweight subjects compared with their

lean/normal weight counterpart, although the observed differences were not statistically significant ( $P > 0.05$ ). The mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) were, however, significantly higher in the overweight subjects compared to the lean or normal weight subjects ( $P < 0.05$ ), see Table 1.

Table 2 shows the Pearson's correlation coefficient between the weight and clinical as well as biochemical variables. There was a significant positive correlation between weight and HOMA-IR ( $r = 0.248$ ), fasting glucose ( $r = 0.198$ ), and fasting insulin ( $r = 0.228$ ), ( $P < 0.05$ ). Also, both systolic and diastolic blood pressures correlated significantly with weight ( $P < 0.05$ ).

The association between overweight and severe insulin resistance as well as  $\text{FPG} \geq 5.1$  mmol/L was assessed as shown in Table 3. The overweight subjects ( $\geq 95$  kg) were more likely to have severe insulin resistance compared to their lean/normal weight counterpart (OR = 3). Also

**Table 1: Mean (S.D) values of some clinical and biochemical parameters compared among overweight and normal weight groups using unpaired student's t-test**

Variable	Overweight ( $\geq 95$ kg) $n = 26$	Normal weight ( $< 95$ kg) $n = 74$	P-value
FPG* (mmol/L)	4.8 (1.1)	4.3 (1.3)	0.073
FPI† (mIU/L)	12.5 (7.0)	10.7 (5.2)	0.187
HOMA-1R	1.6 (0.9)	1.3 (0.6)	0.095
SBP‡ (mmHg)	118.5 (14.3)	109.6 (11.7)	0.002
DBP§ (mmHg)	75.1 (8.2)	70.1 (8.9)	0.013

\*FPG – Fasting glucose; †FPI – Fasting insulin; ‡SBP – Systolic blood pressure; §DBP – Diastolic blood pressure

**Table 2: Correlation between maternal weight and clinical/biochemical parameters**

Variable	Pearson's correlation coefficient (r)	P-value
FPG (mmol/L)	0.198	0.048
FPI (mIU/L)	0.228	0.022
HOMA-1R	0.248	0.004
SBP (mmHg)	0.407	0.000
DBP (mmHg)	0.285	0.004

**Table 3: The association between severe insulin resistance and overweight**

Weight category	Overweight ( $\geq 95$ kg) $n = 26$ (%)	Normal weight ( $< 95$ kg) $n = 74$ (%)	Odds ratio (95% CI) (%)	Adjusted odd ratio* (95% CI) (%)
Severe IR†	11 (44.0)	14 (18.9)	3.1 (1.2-8.3)	3.2 (1.2-8.2)
Normal IR	15 (56.0)	60 (81.1)		
FPG $\geq 5.1$ mmol/L	9 (34.6)	11 (14.9)	3.0 (1.1-8.5)	3.1 (1.1-8.6)
FPG $< 5.1$ mmol/L	17 (65.4)	63 (85.1)		

\*Adjusted for family history of diabetes mellitus and age  $\geq 25$  years; †IR – Insulin resistance

overweight subjects are more likely to have three times of FPG  $\geq 5.1$  mmol/L. These associations remained significant even after controlling such factors as positive family history of DM and age  $\geq 25$  years.

## DISCUSSION

The results from this study show that maternal weight in second half of pregnancy correlates positively and significantly with fasting glucose, fasting insulin and insulin resistance as well as systolic and diastolic blood pressure. Although, the weak strength of the association with these parameters suggests that factors other than weight may influence changes in the level of the assessed variables, it is clear from this study that increase in maternal weight is associated with increased insulin resistance, glucose and insulin levels as well as blood pressure. This is consistent with reports in literature.<sup>17,18</sup>

Rising insulin resistance puts more strain on the compensatory insulin secretion resulting in increased insulin and glucose levels.<sup>14,15</sup> This constellation of associations bears a resemblance to the metabolic syndrome pointing to the fact that increasing maternal weight in pregnancy may herald impaired glucose tolerance and hypertensive disorders in pregnancy.<sup>18,19</sup> These pregnancy-related conditions would likely resolve clinically after delivery. However, in many overweight pregnant women, particularly those with increased postpartum weight gain, subclinical underlying metabolic disorder often persist and may manifest as features of metabolic syndrome in later life.<sup>5,20</sup>

This study also demonstrated that women with weight of 95 kg and above in the early second half of pregnancy were about three times more likely to have severe insulin resistance and FPG  $\geq 5.1$  mmol/L. It is remarkable that this association was independent of whether the subjects had family history of DM or were  $\geq 25$  years old (both risk factors for GDM).<sup>21</sup> It also worthy of note that a FPG  $\geq 5.1$  mmol/L would be enough to make a diagnosis of GDM, according to the recent International Association of Diabetes in Pregnancy Study Groups (IADPSG) recommendations for diagnosis of GDM.<sup>22</sup>

An absolute weight of  $>90$  kg at booking has been used to classify pregnant women as being overweight. However, in obstetric practice in many developing countries in Africa, most women present late for antenatal booking raising questions for the use of this classification in the Nigerian setting. The findings from this study implies that a weight of  $\geq 95$  kg at or before 32 weeks gestation should flag women with singleton pregnancy for increased risk of severe insulin resistance and impaired glucose tolerance.

A limitation of this study is that the records of pre-pregnancy or first trimester weight of most of the women in

this study were not available due to late booking. However, it is likely that women who weighed  $\geq 95$  kg at 24-32 weeks of gestation would have weighed above 90 kg had they booked in the first trimester. Thus having weight of  $>90$  kg in first trimester may also portend increased risk for severe insulin resistance. It would therefore be appropriate that this cutoff weight ( $>90$  kg) or the estimated BMI should continue to be used for women who present in the first trimester. However, in antenatal clinics were women generally present late, absolute weight of  $\geq 95$  kg at or before 32 weeks should be considered high risk for metabolic complications and screening for GDM should be encouraged. This should also apply to women who were booked in first trimester with normal weight, but recorded weight  $\geq 95$  kg at any other point prior to or at 32 weeks.

More significantly, appreciation of the abnormalities associated with increased absolute weight in pregnancy as demonstrated in this study reinforces the call for preventive measures pre-pregnancy. For instance, pre-conception planning provides for opportunity to address the issue of weight control prior to conception. Furthermore, checking excessive weight gain during pregnancy may prevent excessive postpartum weight retention. These lifestyle modifications not only would benefit the woman and her offspring in the index pregnancy, but also provide subsequent long-term benefits for both.

## CONCLUSION AND RECOMMENDATIONS

It is clear from this study that increase in weight is associated with increased risk for insulin resistance and higher glucose levels. Women with booking weight of above 90 kg in the first trimester or early second trimester as well as women with weight of 95 kg and above in second half of pregnancy should be screened for abnormality in glucose metabolism using OGTT and receive counseling about weight gain and nutrition. Awareness of the challenges of obesity in pregnancy should be raised among the general public and women should be encouraged to pursue weight reduction before pregnancy.

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