

## ASSOCIATION BETWEEN MATERNAL BASAL GLUCOSE LEVEL AND INTRAUTERINE GROWTH RESTRICTION: A COMPARATIVE CROSS-SECTIONAL STUDY

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### Abstract

**Background:** Intrauterine life is the most pivotal period of development that determines vital outcomes in postnatal life. Diabetes Mellitus may lead to disturbed fetal growth and maternal vasculopathy resulting in placental insufficiency with subsequent development of intrauterine growth restriction (IUGR). This study aims to find an association between hyperglycemia and the risk of IUGR, comparing pregnancies with IUGR with those with adequate for gestational age pregnancies.

**Methods:** This cross sectional study was conducted in Federal Post Graduate Medical Institute (FPGMI) from January 2015 to January 2016, including 106 pregnant women using non-probability convenient sampling technique. Participants were divided into two groups: Group A comprises of pregnant women with adequate for gestational age pregnancies (n=53) and groups B includes pregnant women with intrauterine growth restricted pregnancies (n=53). Random blood sugar level was estimated by glucose/oxidase test and IUGR was confirmed by ultrasonography at 28-35 weeks of gestation. Shapiro-Wilk test was used to examine data normality and independent t-test was used to compare statistically significant difference. A p-value of <0.05 was considered significant.

**Results:** Mean basal sugar level of group A was  $98.9 \pm 7.1$  mg/dL and that of group B was  $97.9 \pm 6.0$ mg/dL. This mean difference was not statistically significant (p-value= 0.566).

**Conclusion:** We found no statistically significant association between raised maternal basal glucose level and the occurrence of intrauterine growth restriction at 28-35 weeks of pregnancy.

**Key Words:** Intrauterine Growth Restriction, glucose level, hyperglycemia

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Intrauterine period of fetal growth is the most important period as during this time life long and strong health foundations are laid.<sup>1</sup> A thirty percent reduction

in cases of low birth weight (less than 2.5 kilograms) by the year 2025 is one of the goals of 2012 World Health Assembly.<sup>2</sup> Intrauterine growth restriction (IUGR) is second most common reason of low birth weight neonates; first being premature birth. Both these may end in early as well as with lifelong complications.<sup>3</sup> IUGR is labelled when velocity of fetal growth does not match with the normal fetus growth potential. It is usually considered when the birthweight is less than 10<sup>th</sup> percentile of normal weight.<sup>4</sup> In clinical setting, besides physical examination and ultrasonography, umbilical artery Doppler scan is also used as a differentiating tool for intrauterine growth restriction, constitutionally small fetus and normal pregnancy.<sup>5</sup>

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IUGR is a public health concern as it overburdens the health care facilities. It increases the risk of stillbirth around 10 percent in addition to increasing the susceptibility of hypoxia at birth and neurodevelopmental problems,<sup>6</sup> metabolic disturbances like diabetes mellitus, fatty liver, etc in adult life.<sup>7</sup> The incidence rate of IUGR in developing and underdeveloped countries is about six times higher as compared to developed countries.<sup>4</sup> Globally, IUGR complicates around 10-15% of pregnancies.<sup>7</sup> The rate of occurrence of IUGR in Pakistan is estimated to be around 10-25 %, which is quite alarming.<sup>8</sup>

Diabetes Mellitus is becoming a major burden on health care resources as number of individuals suffering from diabetes mellitus is expected to jump from 171 million in 2000 to 366 million by 2030.<sup>9</sup> World Health Organization (WHO) defines Diabetes Mellitus as a metabolic condition exhibiting elevated blood glucose levels and disturbance in metabolism of carbohydrates, fats and proteins due to abnormalities in Insulin secretion, its action or both. The individuals suffering from Type I diabetes mellitus have Insulin deficiency while insulin resistance is found in Type-2 diabetes mellitus.<sup>10</sup> Diabetes Mellitus is diagnosed if fasting blood glucose is more than or equal to 126 mg/dl or random blood glucose is more than or equal to 200 mg/dl or HbA1c is  $> 6.5\text{mg/dl}$ .<sup>11</sup> A common type of diabetes mellitus in pregnant women is gestational diabetes. It is defined as first time detection of disturbance in glucose tolerance during pregnancy. Although it does not rule out underdiagnosed cases of diabetes mellitus.<sup>12</sup> Diabetes is generally associated with large for gestational age fetus; it is also associated with restricted fetal growth as well.<sup>13</sup> Exposure of placenta to hyperglycemia plays a significant role in development of placenta and later development of fetus. It is hypothesized that the degree of hyperglycemia adversely affect placental function, hence, affecting fetal growth. In diabetic women long -term uncontrolled hyperglycemia could result in placental insufficiency which plays a vital role in supplying oxygen and nutrients to the fetus.<sup>14</sup> Long-term maternal distress like hyperglycemia, dyslipidemia and hyperinsulinemia lead to

exhaustion of compensatory abilities of placenta resulting in dysfunction of placenta and fetal outcomes like IUGR. The reduced blood supply due to chronic hyperglycemia results in hypoxia-restricted growth of the fetus leading to IUGR.<sup>15</sup> The objective of the study was to examine an association of maternal basal sugar level with intrauterine growth restriction, comparing those pregnancies with adequate for gestational age and pregnancies with IUGR at 28-35 weeks of pregnancy.

## METHODS

A comparative cross-sectional study was conducted in Physiology Department, Federal Postgraduate Medical Institute, Lahore in collaboration with Department of Obstetrics and Gynecology, Shaikh Zayed hospital, Lahore during January 2015 through January 2016. A formal permission was obtained from the departments and from Ethical Review Boards of these institutes. We included 106 pregnant women using non-probability convenient sampling technique. These women were divided into two groups: Group A (n=53) comprises of pregnant women aged between 20-40 years of age, having adequate for age uncomplicated normal pregnancy with duration of pregnancy between 28-35 weeks. Group B (n=53) includes pregnant women (aged between 20-40 years) with intrauterine growth restricted pregnancy with duration of pregnancy between 28-35 weeks. These pregnant women were recruited from department of obstetrics, Shaikh Zayed Medical Complex, Lahore. After taking informed consent, a detailed history was obtained from participants using a semi-structured questionnaire. A blood sample was drawn and random blood sugar level was estimated by glucose/oxidase test in Pathology Laboratory of Shaikh Zayed Medical Complex, Lahore. Data were managed and analyzed using Statistical Package for Social Sciences (SPSS) version 17.0. Shapiro Wilk test was used to check whether data in both groups are normally distributed. We used independent t-test to compare mean basal glucose level in both groups and to examine the mean difference. A p-value of  $<0.05$  was considered statistically significant difference between the groups.

## RESULTS

The mean basal glucose level of group A was  $98.9 \pm 7.1$  mg/dL and mean basal glucose level of group B was  $97.9 \pm 6.0$  mg/dL. Range of basal glucose level in group A was 85-111 and that of group B was 85-110 mg/dL Shapiro Wilk test showed that the data were normally distributed in both groups. There was no statistically significant difference in mean basal glucose level between both groups ( $p = 0.55$ ).

## DISCUSSION

In this study we studied the effect of basal sugar level in pregnant women in age group between 20-40 years with intrauterine growth restricted pregnancy

**Table 1:** Comparison of Basal glucose level between Group A and Group B

	Basal glucose level			
	Mean±SD	Minimum	Maximum	P
Group A	98.9 ± 7.1	85	111	0.55
Group B	97.9 ± 6.0	85	110	

**Abbreviations:** SD, standard deviation; p-value was calculated using independent t-test Group A represents pregnancies with adequate for gestational age and Group B represent pregnancies with intrauterine growth restrictions

evaluated by physical examination and ultrasound at 28-35 weeks of gestation with age and duration of pregnancy matched group of pregnant women having adequate for gestational age fetuses evaluated by both physical examination and ultrasound.

Our result differs from multiple studies showing significant association of maternal diabetes mellitus and IUGR. In a study conducted by Brand J. et al. positive association of maternal diabetes and IUGR was suggested in 12-16 weeks of gestation especially in South Asian population owing to chronic malnutrition of mothers.<sup>16</sup> Our findings are also not in accordance with study conducted by Gutaj and Wender reporting relation of diabetes mellitus with IUGR suggesting that coexistence of diabetes and insufficient perfusion because of vascular impairment can result in unfavorable conditions for optimum fetal growth.<sup>13</sup> The study conducted by Langmia et al. also suggested the association of IUGR with maternal diabetes since uncon-

trolled maternal hyperglycemia results in insufficiency of placenta, contributing to fetal malnutrition and ultimately IUGR.<sup>14</sup> However, studies conducted by Nhandi et al. and Kamana et al. differ and reported that maternal diabetes leads to large for gestational age fetuses. Even in normal pregnancies, maternal insulin resistance promotes transfer of glucose to fetus however in case of diabetes this transfer is exaggerated and resulting in fetal overgrowth.<sup>17,18</sup> Limitation of this study is the small sample size and inadequate analyses. Regression analyses should have been employed to investigate the effect of confounding factor in examining the association between hyperglycemia and IUGR.

## CONCLUSION

Intrauterine growth restriction is an underdiagnosed condition. We conclude that there is no association between maternal basal glucose level and occurrence of IUGR. However, considering the importance of monitoring fetal growth and findings of previous reports showing positive association between higher basal glucose level and placental insufficiency, regular glucose level monitoring throughout pregnancy would prevent low birth weight neonates.

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