ORIGINAL ARTICLE

ASSOCIATION OF VITAMIN D AND INSULIN RESISTANCE IN GESTATIONAL DIABETES

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ABSTRACT

Objective: To determine the relationship between serum concentration of vitamin D and insulin resistance among patients of gestational diabetes (GDM).

Methods: This cross-sectional study was conducted from January to December 2021 at Combined Military Hospital (CMH) Lahore. Two hundred pregnant women with gestational diabetes in the age group 20-35 years were included. Blood specimens for fasting glucose, insulin and vitamin D were obtained and analyzed on Roche Cobas c501 and Cobas e411. Based on the vitamin D level they were classified as vitamin D sufficient and vitamin D deficient using cut off of 20 nmol/L. Homeostatic Model Assessment for Insulin Resistance (HOMA- IR) was used for gauging insulin resistance. Fasting glucose, fasting insulin and HOMA IR were compared between the two groups.

Results: The sample size for this study was of 200 pregnant women. Median age was 28 years (IQR 24-31). Median fasting plasma glucose, Vitamin D levels and HOMA-IR of the study population were 5.3 mmol/L, 19.5 nmol/L and 2.7 respectively. A significant difference ($p<0.001$) in serum vitamin D was seen among the insulin resistant and non-resistant patients. A strong association ($p<0.001$) was established between vitamin D and HOMA-IR by Chi-square test. Spearman correlation showed a negative correlation between the two ($r = -0.89$).

Conclusion: A strong association was found linking vitamin D and HOMA-IR. The negative correlation ($r=-0.89$) indicated that severe the deficiency of vitamin D, more pronounced the insulin resistance among pregnant women having GDM.

Key Words: Gestational Diabetes, Insulin Resistance, Vitamin D.

How to cite this article: Mahmood A, Sattar A, Shaheen S, Khalid UB, Ahmad S. Association of vitamin D and insulin resistance in gestational diabetes. Pak Postgrad Med J 2022;33(4): 108-111

DOI: https://doi.org/10.51642/ppmj.v33i04.507

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INTRODUCTION

Gestational diabetes is a type of diabetes that develops during the second or third trimester of the gestational period[1]. It has a worldwide prevalence of 14% and is fairly common in south east Asian population[2,3]. Both insulin insufficiency and insulin resistance contribute to the pathogenesis. Placental hormones increase insulin resistance during pregnancy which is then counteracted upon by increased insulin secretion by the beta cells[4]. Glucose intolerance develops when the maternal islet cells fail to adapt to the rising insulin resistance[5]. A pregnancy complicated with gestational diabetes poses an increased risk for adverse outcomes and these patients are likely to develop type 2 diabetes in future[6]. It also increases neonatal complications for the baby[7]. Researchers have shown keen interest to explore the

factors responsible for gestational diabetes and to find ways for it's prevention and better management.

Vitamin D has been of special interest as many researchers have emphasized the role of this vitamin in the development and prevention of GDM[8]. in addition to calcium regulation, Vitamin D is known to have many other effects in the body including immune system modulation and regulation of metabolic processes. These effects also seem to modulate glucose homeostasis by affecting both pancreatic secretion of insulin and insulin action on target tissues[9]. Evidence suggests that insulin secretion could be due affected by the action of vitamin D on calcium which has a pivotal role in secretion of insulin from the beta cells[10]. It is also speculated to affect insulin responsiveness by increasing the expression of peripheral insulin receptors[11]. Many studies conducted in different populations have given mixed results regarding this relationship.

The aim of this study was to better understand the effect of vitamin D on insulin resistance in GDM. An attempt to determine the association of vitamin D with insulin resistance among patients of gestational diabetes was made.

METHODS

An observational study was carried out from January to December 2021 at department of Chemical Pathology Combined Military Hospital (CMH) Lahore, after taking prior approval of the hospital's Ethical Review Board. Patients were selected for the research through non-probability sampling technique. Sample size of 184 was estimated at 95% confidence interval with 5% margin of error at 14% prevalence of GDM[2]. Two hundred pregnant women in the age group 20-35 years were diagbosed with GDM in the 75 grams glucose tolerance test. American Diabetic Association (ADA) 2021 guidelines were used for diagnosis[13]. No discrimination was done based on the gestational age or the parity of the women. Patients with BMI more than 30 and previous history of metabolic disorders like PCOS, thyroid, pituitary and adrenal disorders were excluded from the study in order to avoid bias from other factors affecting insulin resistance. All patients were enrolled during a period of 12 months at the department of Chemical Pathology, CMH Lahore. Informed written consent was taken prior to sampling. They were interviewed regarding their age, weight, height, family history of diabetes mellitus, history of previous gestational diabetes and past medical history. Information regarding smoking, chronic illness, drug intake and other metabolic conditions was also obtained. OGTT with 75 gm oral glucose was conducted in the Chemical Pathology department of CMH Lahore. All patients underwent the test after 8-10 hours overnight fasting. Fasting blood glucose specimens were drawn into sodium fluoride tubes. Approximately 4 mL blood was collected in clot activator tube simultaneously for measuring insulin and 25-OH vitamin D. All tubes were centrifuged for 10 minutes at 4000 revolutions per minute (RPM). Specimens for glucose estimation were analyzed immediately after separating plasma using Hexokinase method on a fully automated, random access chemistry analyzer, Roche Cobas c501. Serum specimens were stored at 04 degrees Celsius for subsequent analysis of insulin and 25-OH vitamin D on the next day using electrochemiluminesence immunoassay (ECLIA) on a fully automated random access immunoassay analyzer, Roche Cobas e411.

Based on the vitamin D level, patients were classified as "vitamin D sufficient" or "vitamin D deficient". Vitamin D concentration of 20 nmol/L was used to differentiate.[12] Homeostatic Model Assessment for Insulin Resistance (HOMA IR), was used to gauge insulin resistance, which was calculated for each patient using fasting serum insulin and fasting glucose values. Cut off for HOMA was 2.2. Fasting glucose, insulin and HOMA IR were compared among the two groups for any significant association.

Data was analyzed using SPSS version 21.0. Using the Shapiro- Wilk test the data was found to be non-parametric. For numerical variables, median (IQR) was calculated. For categorical variables, frequencies and percentages were computed. Comparison was done by Mann-Whitney U-test. Spearman's correlation was applied while considering p value ≤ 0.05 to be significant.

RESULTS

Median age was 28 years (IQR 24-31). Of these, 125 (62.5%) were less than 30 years of age while 75 (37.5%) were older than 30 years.

Table 1: Descriptive statistics

Parameter	Median	Interquartile range
Age (Years)	28.0	24.0 – 31.0
Body Mass Index (Kg/m^2)	23.7	21.0 – 25.8
Fasting plasma glucose (mmol/L)	5.3	5.0 – 5.6
Serum Vitamin D (nmol/L)	19.5	15.0 – 36.75
Fasting serum Insulin (mIU/L)	11.5	8.3 – 15.9
HOMA-IR	2.7	1.9 – 3.8

Vitamin D insufficiency (<20 nmol/L) was observed in majority of the study population as depicted in. Similarly, majority of the study population had HOMA-IR >2.2.

Mann Whitney U test showed a significant difference (p <0.001) in vitamin D concentrations of the two groups. A strong association in insulin resistance and vitamin D deficiency was established by Chi-square test.

Furthermore, a negative correlation was found between the two using Spearman correlation (r = -0.89). This correlation is shown in Figure 1. It implied that the pregnant women who developed GDM were deficient in vitamin D.

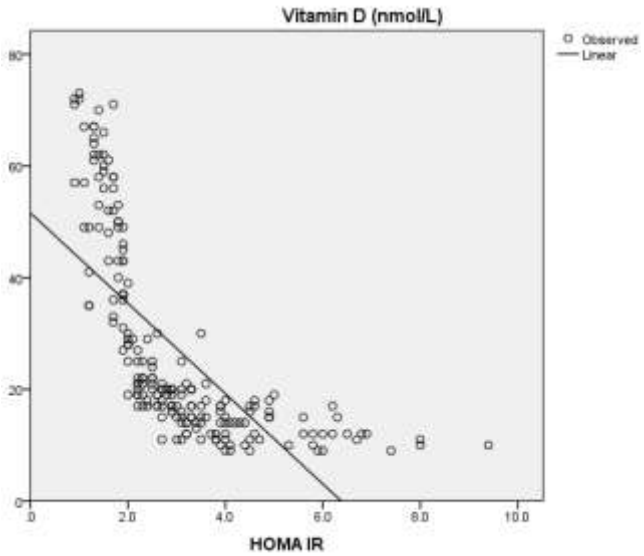

Figure 1: Correlation between HOMA-IR and Vitamin D (r= -0.89**)**

DISCUSSION

A lot of researches have proven vitamin D to be involved in the development of gestational diabetes[13]. Attempts have also been made to understand effect of vitamin D on the known risk factors contributing to gestational diabetes like, decreased insulin response and reduced beta cell function[14,15]. This study tried to focus on the association of vitamin D with HOMA IR in gestational diabetes and a significantly negative relation was found. In 2019, an article published by Wang et.al at Shijiazhuang First Hospital, China demonstrated similar results in patients of type 2 diabetes[16]. In 2018, McCormack et al, at the University of Adelaide Robinson Institute, Australia, also demonstrated increased insulin levels in vitamin D deficient women who had early miscarriages and also suggested a possible increase in risk of gestational diabetes in these patients[17]. Similarly, Chen et al carried out a study to claim a negative correlation of vitamin D with HOMA IR in women[18]. A current study by Azzam et al conducted in 2021 at University of Alexandria, Egypt could not prove deficiency of vitamin D to be a cause of gestational diabetes but did find an association between vitamin D and insulin resistance in gestational diabetes[19]. However, another study conducted at Royal Jubilee Maternity Hospital, Belfast, Northern Ireland by Casey et al failed to show any relation between the two[20].

Majority of these studies have consistently shown an association of vitamin D level in the body with the degree of insulin resistance, regardless of the target population. Our research adds further evidence to the possible role of vitamin D deficiency in the exacerbation of insulin resistance in GDM. Many clinical trials have showed a beneficial role of vitamin D supplementation on HOMA-IR in GDM[21,22]. Jahanjoo et al in 2018 concluded that vitamin D supplements remarkably improved fasting glucose and other metabolic parameters but had no effect on insulin levels or HOMA IR[23]. Maintaining optimum vitamin D concentration in the body can help prevent or even limit the extent of insulin resistance.

More reliable results were tried to obtain in this study by excluding bias from other disorders of increased insulin resistance, like obesity, PCOS and endocrine disorders. The majority of the patients in our study were severely deficient in vitamin D, while only few were moderately or slightly deficient. Hence it was difficult to comment on the degree of vitamin D deficiency that would cause significant insulin resistance. More research is advocated to ascertain the optimum serum concentration of vitamin D that is necessary to avoid significant increase in insulin resistance during pregnancy. Also, the correlation of vitamin D with other factors like inflammation and beta cell function still remains unclear that could possibly be involved in the development of GDM. A more clear understanding of the pathophysiology at molecular and genetic level along with better clinical results obtained with vitamin D supplementation could help decrease the incidence and complications related to gestational diabetes[24].

CONCLUSION

A strong association was found between vitamin D and HOMA- IR. The significant negative correlation (r=-0.89) indicated that severe the deficiency of vitamin D, more pronounced the insulin resistance among pregnant women having GDM; potentially, making vitamin D supplementation a possible adjunctive treatment and prevention of GDM.

CONFLICT OF INTEREST: None.

ETHICAL APPROVAL

The study was approved by the Research Review Board, Combined Military Hospital, Lahore, vide Reference No.243/2020.

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