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A CROSS-SECTIONAL STUDY OF BONE TURNOVER MARKERS IN GESTATIONAL DIABETES MELLITUS

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ABSTRACT

Background and Aim: Bone turnover markers (BTMs) can be used to monitor bone formation and bone resorption activity. Maternal age, Vitamin D, obesity, parathyroid hormone (PTH), and prior history of diabetes mellitus are various risk factors for gestational diabetes mellitus (GDM). The objective of the current study aimed to explore the bone turnover markers in gestational diabetes mellitus.

Patients and Methods: This cross-sectional study investigated 102 gestational diabetes mellitus patients in the departments of Endocrine and Gynecology, Fatima Memorial Hospital, Lahore from January 2023 to December 2023. All the pregnant females aged 18-45 years having 24 weeks gestational age with no prior history of diabetes mellitus were included. Patients were classified into two groups; Group-I (Pregnant female with GDM) and Group-II or Control group (Pregnant female without GDM). All the patients underwent detailed history, physical examination, and bone turnover markers in terms of Vitamin D, serum ALP, parathyroid hormone, and serum-ionized calcium were measured and compared with the control group. Data analysis was done using SPSS version 27.

Results: The number of patients in Group-I and Group-II was 60 (58.8%) and 42 (41.2%), respectively. The overall mean age in Group-I and Group-II was 27.8 ± 2.8 years and 26.32 ± 2.86, respectively. The mean BMI, Ionized calcium, Vitamin D, and Serum PTH in both groups were as follows; (25.86 ± 3.51 kg/m2 vs. 23.98 ± 2.62 kg/m2, 4.58 ± 0.379 m-Eq/L vs. 4.59 ± 0.349 m-Eq/L, 31.256 ± 8.41 ng/ml vs. 20.98 ± 9.52 ng/ml, and 36.28 ± 8.13 pg/ml vs. 70.391 ± 35.192 pg/ml, respectively). Serum ALP in Group-I and Group-II was 8.9 ± 4.61 KA U/dl and 6.99 ± 2.1 KA U/dl, respectively.

Conclusion: The present study observed that pregnant female with gestational diabetes mellitus (GDM) are more susceptible to obesity, lower parathyroid hormone, and lower vitamin D levels as compared to control group. This provide a justification for the assessment of bone turnover markers at early stages for better positive and health outcome.

Keywords: Gestational diabetes mellitus, Bone turnover biomarker, Bone metabolism

INTRODUCTION

Gestational diabetes mellitus (GDM) represents a common congenital condition. This includes impaired glucose tolerance or any type of diabetes diagnosed during pregnancy, GDM affects approximately 2%–20% of pregnant women with pre-diabetic conditions, the need for insulin therapy, or persistent abnormal glucose metabolism after delivery is irrelevant [1]. For certain ethnic groups, the incidence is associated with type 2 diabetes mellitus (T2DM) [2, 3]. Recent findings of increased risk as osteoporotic fractures in patients with diabetes emphasize the importance of bone health [4]. Despite extensive research on bone metabolism in diabetes, bone metabolism in women with GDM has been completely overlooked. However, one study showed an increase in bone turnover in pregnant women [5-7].

Pregnancy and lactation increase calcium requirements due to fetal bone growth and lactation. During these reproductive stages, bone acts as a reservoir of calcium. There is a perception that pregnancy may affect the attainment of maximum bone mass and may increase the risk of developing osteoporosis later in life [8]. Bone chemical markers of bone turnover increase gradually during pregnancy, peaking in the third trimester. This period marks a dramatic increase in bone formation and remodeling, which is important for maternal bone health and fetal growth [9]. Bone loss can occur during pregnancy and lactation, resulting in a condition called pregnancy/lactation osteoporosis. This condition can show symptoms such as back pain, height loss and spinal fractures [10]. A recent densitometric study of women with gestational diabetes mellitus (GDM) reported and additionally found decreased vertebral bone mineral density compared with non-diabetic pregnant women that 40% of women with GDM experienced greater than normal bone loss after childbirth [11].

Parathyroid hormone (PTH) regulates vitamin D synthesis. During pregnancy the placenta also synthesizes 1,25 dihydroxyvitamin D (1,25(OH)2D), which can have autocrine or paracrine functions [12]. Maternal vitamin D status directly affects fetal growth via insulin. Normal serum levels of PTH and calcium are a useful indicator of adequate vitamin D supplementation during normal pregnancy [13]. Some studies suggest that total 1,25(OH)2D is an accurate measure of maternal vitamin D status, as accurate estimation of PTH threshold is challenging. Clearly, there are other indications for improved fasting glucose and insulin levels in women receiving calcium and vitamin D supplementation [14].

METHODOLOGY

This cross-sectional study investigated 102 gestational diabetes mellitus patients in the departments of Endocrine and Gynecology, Fatima Memorial Hospital, Lahore from January 2023 to December 2023. All the pregnant females aged 18-45 years having 24 weeks gestational age with no prior history of diabetes mellitus were included. Patients were classified into two groups; Group-I (Pregnant female with GDM) and Group-II or Control group (Pregnant female without GDM). All the patients underwent detailed history, physical examination, and bone turnover markers in terms of Vitamin D, serum ALP, parathyroid hormone, and serum-ionized calcium were measured and compared with control group. The women underwent an oral glucose tolerance test (OGTT) in which they drank a tablet containing 50 g of glucose and their blood glucose levels were measured 1 hour later and a cutoff point of 140 mg/dL was set. After an overnight fast of 8 to 14 hours, the OGTT was conducted. Data analysis was done using SPSS version 27. Baseline characteristics between groups with gestational diabetes (Group-I) and those without gestational diabetes (Group-II) were analyzed using paired t-tests. In addition, body mass index (BMI), 25-hydroxyvitamin D (25(OH)D), alkaline phosphatase (ALP), and serum ionized calcium Correlations with parathyroid hormone (PTH) were assessed using the Pearson test.

RESULTS

Number of patients in Group-I and Group-II was 60 (58.8%) and 42 (41.2%), respectively. The overall mean age in Group-I and Group-II was 27.8 ± 2.8 years and 26.32 ± 2.86, respectively. The mean

BMI, Ionized calcium, Vitamin D, and Serum PTH in both groups were as follows; (25.86 ± 3.51 kg/m2 vs. 23.98 ± 2.62 kg/m2, 4.58 ± 0.379 m-Eq/L vs. 4.59 ± 0.349 m-Eq/L, 31.256 ± 8.41 ng/ml vs. 20.98 ± 9.52 ng/ml, and 36.28 ± 8.13 pg/ml vs. 70.391 ± 35.192 pg/ml, respectively). Serum ALP in group-I and group-II was 8.9 ± 4.61 KA U/dl and 6.99 ± 2.1 KA U/dl, respectively. Comparison of baseline and general characteristics are shown in Table-I. Different laboratory of both groups are compared in Table-II. Correlation of PTH, Serum ionized calcium, ALP, and BMI in group-I are shown Table-III.

Table-I Comparison of baseline and general characteristics

Variables	Group-I (N=60)	Group-II (N=42)	P-value
Age (years)	27.8 ± 2.8	26.32 ± 2.86	0.23
Gestational age (weeks)	24.69 (22.92–25.56)	24.69 (24.31–25.72)	0.615
Body mass index (Kg/m2)	25.86 ± 3.51	23.98 ± 2.62	0.591
Neonatal weight (Kg)	3.21 ± 0.47	3.35 ± 0.38	0.118

Table-II Comparison of different laboratories of both groups

Parameters	Group-I (N=60)	Group-II (N=42)	P-value
Hemoglobin (g/dl)	10.9±0.89	11.2±0.69	0.572
TLC/mm3	6198±1454.8	6097±1082.6	0.59
Blood urea (mg/dl)	26.183±5.89	27.31±3.87	0.28
Serum creatinine (mg/dl)	0.79±0.145	0.791±0.162	0.246
PLT/mm3	223,598±61,524.8	241,148±50,078.8	0.146
Ionized Calcium (m-Eq/L)	4.58 ± 0.379	4.59 ± 0.349	0.429
ALP (KA U/dl)	8.9 ± 4.61	6.99 ± 2.1	0.0039
Vitamin D (ng/ml)	31.256 ± 8.41	20.98 ± 9.52	<0.0001
PTH (pg/ml)	36.28 ± 8.13	70.391 ± 35.192	<0.0001

Table-III Correlation of PTH, Serum ionized calcium, ALP, and BMI in group-I

Parameters	r	ρ (Significance)
Vitamin D	−0.8926	0 (S)
ALP	0.6781	0 (S)
BMI	0.7921	0 (S*)
Ionized calcium	0.1325	0.2984 (NS**)

*S Significance **NS Non-significance

DISCUSSION

The present study mainly focused on the bone turnover biomarkers in gestational diabetes mellitus and reported that pregnant female with gestational diabetes mellitus (GDM) are more susceptible to obesity, lower parathyroid hormone, and lower vitamin D levels as compared to control group. Several previous studies have shown that obesity is a widely accepted risk factor for 25-hydroxyvitamin D deficiency. Vitamin D plays an important role in maintaining bone metabolism and mineral homeostasis. Vitamin D deficiency as known to affect bone density, neonatal vitamin D and calcium status, increasing the risk of childhood fractures [15-17].

Lee et. al., [18] demonstrated that maternal serum levels of 25-hydroxyvitamin D (25(OH)D) at 24-28 weeks of gestation were significantly lower in women with gestational diabetes mellitus (GDM) compared with pregnant women without GDM. Another study showed that pregnant women without hyperglycemia had a normal 25(OH)D level of 25 [19]. Parathyroid hormone (PTH) levels were significantly elevated in pregnant women with severely low OH)D levels, and PTH levels were significantly elevated in women with GDM compared with controls. In addition, several studies have shown that primary or secondary elevated PTH levels in other disorders were associated with impaired glucose tolerance [20, 21].

Several previous studies have reported elevated levels of alkaline phosphatase in diabetes mellitus, which often leads to osteoporosis [22, 23]. Wang et al. [24] reported a pregnancy complicated by

gestational diabetes and hypertension, where the bone-specific iso-enzyme of alkaline phosphatase was found to be significantly elevated during delivery. This increased total serum alkaline phosphatase levels, which could not do not assume only from placenta.

Parathyroid hormone (PTH) regulates vitamin D synthesis. Vitamin D is mediated by the maternal state of insulin directly affects the growth of the fetus [25]. Vitamin D from calcium is broken down during pregnancy, causing increase in blood levels post first trimester, and there is no concomitant change in blood calcium levels.

Numerous studies observed that Vitamin D had inverse association with insulin resistance and calcium level [26, 27]. There has been inconsistency in results indicating calcium supplementation effected by Vitamin D. Some trials showed no effect or improvement in insulin action with supplementation, while others demonstrated a significant decrease in fasting glucose and insulin levels among women supplemented with calcium and Vitamin D [28]. During pregnancy, the fetus receives calcium from the mother's blood through the placenta to support bone growth [29].

CONCLUSION

Pregnant female with gestational diabetes mellitus (GDM) are more susceptible to obesity, lower parathyroid hormone, and lower vitamin D levels as compared to control group. This provide a justification for the assessment of bone turnover markers at early stages for better positive and health outcome. Additional bone markers that do not inhibit glycosylation could be explored to provide more accurate estimates of bone health.

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