CORRELATION OF SERUM FERRITIN, HEMOGLOBIN, AND PLATELET LEVELS IN PREGNANT WOMEN WITH GESTATIONAL DIABETES

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ABSTRACT

Background

Gestational diabetes mellitus (GDM) affects approximately 7% of all pregnancies. Pregnancy which is regarded as a pro-inflammatory state "mostly because of the mitochondria-rich placenta," is a condition that favors oxidative stress. A transitional metal, particularly iron, abundant in the placenta, is significant in producing free radicals. Various studies indicate that free radicals play a remarkable role in GDM. Iron storage and status in the body can be reliably assessed by serum ferritin as the standard measurement.

Objectives

The present study aimed to measure the serum ferritin level, hemoglobin, and platelet count in women with GDM and compare it with those of women experiencing a normal pregnancy.

Patients and Methods

This case-control study was conducted in Sulaimani Maternity Teaching Hospital in Sulaimani city, Iraq. Over 18 months, they were starting from Jan 1, 2020, till Jun 30, 2021. The study sample consisted of 160 pregnant women in the third trimester of their pregnancy. The participating women were divided into a study group and a control group. The study group consisted of 80 pregnant women with GDM, which OGTT detected from 24 to 28 weeks of their pregnancy. The control group consisted of 80 pregnant women who had a normal and healthy pregnancy, did not have GDM, and were in their third trimester. For both groups, mean platelet volume, platelet count, hemoglobin level, and serum ferritin level were measured, and the two groups were compared in terms of these variables.

Results

Compared to the control group, the group with GDM had a significantly higher level of mean serum ferritin (29.04±16.09 ng/ml versus 37.97±29.42 ng/ml) (P=0.02). However, the study and control groups were not statistically different regarding their mean hemoglobin levels (12.26±0.63g/dl versus 12.14±0.60g/dl) (P-value=0.19). In addition, the study group had a significantly higher mean platelet count than the control group (246.71x 103/µl±54.02 versus 203.52 x103/µl±54.1) (P<0.001). However, no significant difference was seen between the study group and the control group regarding their mean platelet volume (MPV) (9.50±1.25 1015/L versus 9.35±0.95 1015/L) (P=0.41).

Conclusion

Compared with women with normal pregnancy, GDM women have higher serum ferritin levels and platelet count; therefore, serum ferritin can be regarded as a marker for GDM pathogenesis. However, it is recommended that serum ferritin levels should be measured in early pregnancy to evaluate the risk of GDM development in those with high serum ferritin levels.

Keywords: *Gestational diabetes, serum ferritin, hemoglobin, platelet count.*

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INTRODUCTION

During the second and third trimesters of pregnancy, glucose intolerance might develop, referred to as gestational diabetes mellitus (GDM). GDM can result in hyperglycemia of variable severity and is regarded as the most common metabolic disorder of pregnancy. GDM confers an elevated risk of severe pregnancy complications and is accompanied by harmful effects on their offspring in the intrapartum, neonatal period, or later in life [1]. The worldwide prevalence of GDM remains to be discovered, as systematically synthesized data on this still need to be included. GDM prevalence varies mainly among countries and regions, ranging from 0.6 to 15% depending on individuals' race/ethnicity and socio-economic status. Aboriginal in Australia, Middle Eastern (Syrian, Lebanese, Iraqi, Iranian, or Afghanistan), and Pacific Islanders women are at significant GDM risk. Due to increasing obesity and advancing maternal age, GDM prevalence is increasing worldwide. [2] Pregnancy is a diabetogenic condition characterized by insulin resistance, with a compensatory increase in beta cell response and hyperinsulinemia. Insulin resistance usually begins in the second trimester and progresses throughout the remainder of the pregnancy. A steady reduction in insulin sensitivity occurs from 18 to approximately 28 weeks of gestation, reaching as much as eighty percent. Following delivery, insulin sensitivity returns to pre-pregnancy levels [1]. In response to glucose intake, insulin rises rapidly during normal pregnancy. Women with GDM cannot up-regulate insulin production relative to the insulin resistance degree and become hyperglycemic. Pregnancy is, therefore, a test of beta cell reserve. If there is a good function, insulin resistance will be overcome; otherwise, gestational diabetes results. [3]

Ferritin was discovered in 1937 by the French scientist Laufberger, who isolated a new protein from the horse spleen. It is an iron with a high molecular weight and contains protein that functions in the body as a compound of iron storage. It is found in all body cells and has exceptionally high concentrations in bone marrow, liver, and spleen. Ferritin is a well-defined molecule consisting of a protein shell surrounding an iron core. Consisting of a 24-subunit protein with two types of subunits, termed H and L, ferritin exists in most tissues as a cytosolic protein and a mitochondrial form [4, 5]. Storage of intracellular iron is mainly done by ferritin. Due to the high correlation between ferritin and bone marrow iron, ferritin concentration can be utilized as a representation of body iron stores. As an acute phase reactant, ferritin increases chronic and acute inflammation; therefore, increased serum ferritin levels have been documented in many inflammations-related diseases [6]. Iron is a crucial microelement that acts as a cofactor for several enzymes, and the main component of oxygen transport in the body and has important metabolic functions. Most of the iron in the human body is found in hemoglobin. About 70% of iron is in hemoglobin, and another 10% is in myoglobin (the oxygen-binding protein found in muscle). Much of the remaining iron is "storage iron" [7]. Storage iron comprises two components: soluble iron in ferritin and insoluble iron or hemosiderin [8]. Iron is an essential mineral. It is also an element of conflicting effects; it can be either beneficial or detrimental to the cell, depending on whether it serves as a micronutrient or a catalyst of free radical reactions [9]. Oxidative stress from excess iron accumulation can result in beta cell damage and apoptosis, consequently decreasing insulin secretion [10]. Mainly due to the mitochondria-rich placenta during pregnancy, this period is a condition that favors oxidative stress. Being especially abundant in the placenta, transitional metals, particularly iron, are essential in producing free radicals [11]. High levels of serum ferritin are linked with type-2 diabetes and GDM development. In normal pregnancy, maternal serum ferritin levels decrease as gestation advances, while GDM risk increases twofold in women in the highest quartile of serum ferritin [12,13].

As mentioned above, pregnancy is regarded as a pro-inflammatory state. It is reported that GDM is associated with sub-chronic inflammation. Platelet parameters, such as mean platelet volume (MPV) and platelet count, are associated with several inflammatory disease states and are used in the follow-up of patients. Like type 2 DM, GDM patients generally have different levels of insulin resistance and chronic low-grade inflammation, which trigger vascular injury, dysfunction, and subsequent platelet activation. Therefore, the level of platelet activation may be associated with the severity of GDM. [14,15].

The current study was conducted to measure serum ferritin level, hemoglobin level, and platelet count in GDM women and compare them with women with a normal pregnancy to know whether these markers differ among the two groups of pregnant women.

PATIENTS AND METHODS

This case-control study was carried out at Sulaimani Maternity Teaching Hospital over 18 months starting from Jan 1, 2020. A total of 160 pregnant women in the late second and third trimesters of their pregnancy participated in the present study. They were divided into a study group and a control group. The study group consisted of 80 pregnant women with GDM, which OGTT detected from 24 to 28 weeks of their pregnancy.

The control group included 80 pregnant women in their third trimester without GDM (normal healthy pregnancy). None of the participants was anemic (Hb> 11gm), and their iron supplementation was almost the same. Anemic pregnant women and those with type-1 and type-2 diabetes, hypertension, preeclampsia, renal, liver, and thyroid disease, and women with acute infections were excluded from the study. GDM was diagnosed by an oral glucose tolerance test using 75 gm oral glucose.

After informed consent from the participating women was obtained, a complete history was taken, and an examination, including BMI, was performed. Regarding gestational ages and BMI, the two groups were homogeneous. Then, 3 ml of venous blood was taken and sent to a private laboratory for assessment of serum ferritin, which Sand did with immunoluminometric assay procedure and by a CLIA technique (chemiluminescence immune assay) using Maglumi fully Auto analyzer and for complete blood count, which was measured by automated hematology analyzer. Data entry was performed via an excel spreadsheet then the statistical analysis was performed by the SPSS program, version 21 (IBM SPSS Statistical Package for the Social Sciences). P-values of 0.05 were used as a cut-off point for the significance of statistical tests.

RESULTS

regarding the age of the studied women, their gestational ages, gravidity, and family history of diabetes, the two groups were significantly different regarding their ages, gravidity and family history. The mean age of the GDM group was (33.38±5.54) years, compared to the mean age of controls, which was (29.03±6.27) years, p-value (<0.001). Parity was also significantly higher in the GDM group. Also, positive family history of diabetes was higher in GDM than in the control group (57.5% versus 26.3%), as shown in Table 1.

The mean serum ferritin level for the GDM group was higher than that of the control group (37.9± 29.42ng/dl versus 29.04± 16.09 ng/ml). However, the differences were statistically significant, as the p-value was 0.02, while the mean hemoglobin level for the GDM group was (12.26 ± 0.63 gm/dl), compared to the control group, which was (12.14 ± 0.60 gm/dl), the difference in mean Hb level between the two groups was not statistically significant (P-value =0.19), Table 2.

Analysis of serum ferritin levels concerning women aged within the GDM group revealed that the mean serum ferritin level is highest (40.16 ± 34.37 ng/ml) in the age group between 36-44 years and lowest (35.58 ± 25.09 ng/ml) in the age group between 27-35 years; however, the difference in serum ferritin among different age groups in GDM pregnant women was statistically not significant P-value=0.81, as shown in Table 3.

Analyzing serum ferritin levels concerning gravidity among the GDM group revealed that mean serum ferritin level is highest (55.49 ± 50.17 ng/ml) in primigravida, and lowest in multigravida (≥5), (25.39 ± 14.49 ng/ml), however, the difference was statistically non-significant, P- value= 0.07, as indicated in Table 4.

Regarding the platelet level, the mean platelet count in women with GDM was 246.71 X 103/µl ± 54.02, which is higher than the corresponding count in the control group (203.52 X103/µl ± 54.1), and the difference was statistically significant (p <0.001); while mean platelet volume (MPV) for GDM and control groups were 9.50 (1015/L)± 1.25 and 9.35 (1015/L) ± 0.95 respectively, the differences in MPV was statistically non-significant, as shown in figure (1) and figure (2).

Table 1. Clinical characteristics of study groups.

	GDM No=80	Normal No=80	Total No=160	P value
Age (years)				
Mean age ± SD	33.38 ± 5.54	29.03 ± 6.27	31.20 ± 6.29	< 0.001*
18 - 26 Years	9 (11.3%)	26 (32.5%)	35 (21.9%)	< 0.001 **
27 - 35 Years	41 (51.3%)	40 (50.0%)	81 (50.6%)	
36 - 44 Years	30 (37.5%)	14 (17.5%)	44 (27.5%)	
BMI (kg/m2)				
Mean BMI ± SD	26.71 ± 2.38	26.18 ± 2.56	26.44 ± 2.48	0.18
18.0 – 24.99 (Normal)	23 (28.7%)	32 (40%)	55 (34.4%)	0.14
25.0 – 29.99 (overweight)	55 (68.8%)	48 (60%)	103 (64.4%)	
30.0 – 35.0 (Obese)	2 (2.5%)	0 (0%)	2 (1.2%)	
Gravida and parity				
Mean gravida ± SD	3.61±1.87	2.81±1.49	3.21±1.73	0.003 *
Primigravida	11 (13.7%)	19 (23.8%)	30 (18.8%)	0.03 **
2 – 4 parity	45 (56.3%)	50 (62.5%)	95 (59.4%)	
≥ 5 parity	24 (30.0%)	11 (13.7%)	35 (21.8%)	
Gestational age(weeks)				
Mean gestational age ± SD	31.77 ± 3.54	32.91 ± 2.51	32.35 ± 3.11	0.12
24 - 28 Weeks	33(40.1%)	38(48.2%)	71(46.3%)	
29 - 35 Weeks	47 (59.9%)	42 (51.8%)	89(53.7%)	
Family history				
Positive	46 (57.5%)	21 (26.3%)	67 (41.9%)	< 0.001 **
Negative	34 (42.5%)	59 (73.7%)	93 (58.1%)	
Total	**80 (100%)**	**80 (100%)**	**160 (100%)**	

Table 2. Serum ferritin (ng /ml) and hemoglobin levels (g/dl) in study groups.

Laboratory results	Mean ± SD		Total (n= 160)	P value*
	Gestational Diabetes (study group) (n= 80) Mean ±SD	Normal (Control group) (n = 80) Mean±SD		
Serum ferritin(ng/ml)	37.97 ± 29.42	29.04 ± 16.09	33.45 ± 23.98	0.02
Hemoglobin(g/dl)	12.26 ± 0.63	12.14 ± 0.60	12.20 ± 0.62	0.19

* Performed by independent t-test

Table 3. The distribution of serum ferritin(ng/ml) concerning different age groups of women with GDM.

Age groups	Serum ferritin level(ng/ml) Mean ± Standard deviation
18 - 26 Years (n= 9)	38.16 ± 30.63
27 - 35 Years (n = 41)	35.58 ± 25.09
36 - 44 Years (n= 30)	40.16 ± 34.37
Total (n= 80)	37.59 ± 29.19
P value	0.81*

* Performed by ANOVA

Table 4. Serum ferritin level (ng/ml) among the GDM group according to the number of gravidities.

Gravida	Serum ferritin level(ng/ml) Mean ± Standard deviation
Primigravida (n = 11)	55.49 ± 50.17
gravida 2 - 4 (n = 45)	36.46 ± 27.32
gravida ≥ 5 (n = 24)	25.39 ± 14.49
Total (n= 80)	37.59 ± 29.19
P-value	0.07 *

* Performed by ANOVA

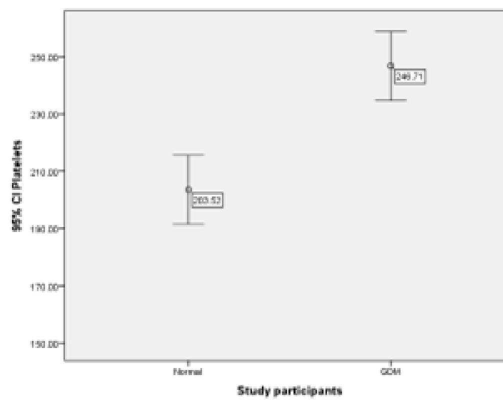

Figure 1. The mean platelet counts in the study (GDM) and control groups.

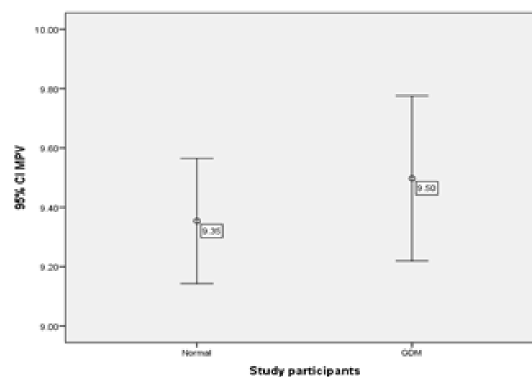

Figure 2. The mean platelet volume (fl) in the study (GDM) and control groups.

DISCUSSION

In the present study, most GDM patients are in ages above 27 years old, and there are a significantly higher number of GDM patients above 36 years in the study group than in the control group. This result demonstrates the possible increase in GDM risk as maternal age rises; however, the results of the present study indicated that the increased risk of GDM is not necessarily in a linear association with increases in maternal age. In their systematic review and meta-analysis of over 120 million participants in a maternal age of about 18-40 years, Li et al. (2020) [16] found similar results to ours, such that they found the risk of GDM increasing with the increasing age of the mother. However, they found a positive linear relationship between the number of mothers getting GDM with increasing ages.

In the present study, a significantly larger number of GDM women had a positive family history of DM than the control group. This finding aligns with the general opinion that GDM risk rises with a family history of DM. It might be due to hereditary factors that increase genetic susceptibility and induce GDM. This corresponds to a study by Yaping (2021) [17], who observed that one factor contributing to GDM development is parents with a diabetes mellitus history.

The GDM group had a significantly higher serum ferritin level than the control group. This result agrees with the results of Sharifi et al. (2010) [18], who did a case-control study on 128 pregnant women in their third trimester, and they observed that GDM women, regardless of their BMI, had a higher concentration of serum ferritin concentration than the control group.

Also, our result agreed with a systematic review and meta-analysis done on 170 pregnant women by Das et al. (2017) [19]. They reported that compared to the control group, the GDM group had a higher mean serum ferritin level. However, serum ferritin level was not significantly associated with maternal age or the number of gravidities.

The present study found no association between serum ferritin level and maternal age. This finding is in line with the study conducted on 561 pregnant women by Rasmussen et al. (2005) [20], who reported no significant association between maternal age and serum ferritin.

The current study showed no association between GDM and hemoglobin level, so the mean hemoglobin level in the study and control groups was within the normal range. This finding differs from Ho Yeon Kim et al. (2021) [21]. They explored the relationship between abnormal hemoglobin levels and the risk of GDM development in 14,799 GDM women. They found an association between high pre-pregnancy hemoglobin levels and the risk of the development of GDM. Moreover, they did not correspond to the result of Rostami et al. (2019) [22] in their study on 600 pregnant women in their second and third trimesters, that high hemoglobin levels were associated with a greater risk of developing GDM.

The platelet count in the GDM group was relatively higher than the control group but still within the normal range. However, this increase in count may raise a concern about the risk of abnormality in the hemostatic system, which puts GDM patients at risk of thrombosis and vascular complications .and our result corresponded to the results of Muhammet et al. (2012) [23] when he performed a retrospective study on 77 pregnant women their result was platelet count was significantly higher in GDM but against ours, in MPV as they found high MPV value in GDM rather than controls. Also, Erikçi et al. (2008) [24] 2008 were against ours; when they did a study on 90 pregnant women, they reported lower platelet counts in GDM and higher MPV values.

In conclusion, serum ferritin level was higher in GDM women than those with normal pregnancy. Maternal age and gravidity were not correlated with GDM development, either. Therefore, it is concluded that a high serum ferritin level might have a role in GDM development.

Recommendation

It is recommended that future studies should assess the level of serum ferritin at the beginning of the pregnancy and follow up with those with high serum ferritin levels to measure the risk of GDM development.

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