

Assessment of Zinc Alpha-2 Glycoprotein Level in Gestational Diabetes Woman with Respect to Glycemic Status with or without Treatment

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Abstract:

Background: Gestational diabetes is a pathological condition that manifests between the 2nd and 3rd trimesters of pregnancy. It is distinguished by substantial insulin resistance induced by the secretion of placental hormone. Adipocytes secrete a particular type of adipocytokine called zinc $\alpha 2$ glycoprotein (ZAG), and numerous researches have suggested that ZAG is involved in crucial physiological processes such as glucose metabolism.

Objective: This study was designed to evaluate the ZAG level in GDM pregnant women on different therapeutic modalities, if it relates to the disease and whether it could be used as a biomarker in the diagnosis of GDM. Method: The research included 76 pregnant women within the age range of (18–40 years), from them 22 healthy pregnant women (group1), 30 newly diagnosed GDM pregnant women (group2), and 24 GDM on different therapeutic modalities (group3), in their 2nd or 3rd trimester; all the demographic and glycemic characteristics were measured.

Result: pregnant women with GDM in group 2 exhibited the greatest level of ZAG. But there was no substantial difference in ZAG levels between the study groups ($P \geq 0.05$). Significant variation in ZAG levels was observed among subgroups of treated GDM pregnant women ($p < 0.01$). The metformin group exhibited the lowest level of ZAG. There was significant increase in Fasting Blood Glucose and Glycated Hemoglobin in GDM pregnant women group 2 and 3 compared to group 1 pregnant women. Also, there was a slight increase in fasting plasma insulin level and Homeostatic Model Assessment of Insulin Resistance (HOMA IR) among group 2 and 3 compared to group 1 pregnant women, but without significant difference ($P \geq 0.05$). No statistically significant association was reported with ZAG and glycemic indices.

Conclusion: Pregnant women with GDM exhibit significant elevated in glycemic compared to those without GDM. ZAG level was increase among all pregnant women, particularly these with GDM. Hence, ZAG may be used as an indicator in GDM.

Keywords: Gestational diabetes GDM, Zinc alpha 2-glycoprotein ZAG, Glucose Metabolism, Correlation.



تقييم مستوى بروتين سكري الزنك ألفا-2 في الدم لدى النساء المصابات بسكري الحمل فيما يتعلق بحالة نسبة السكر مع أو بدون علاج

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خلاصة

الخلفية: سكري الحمل هو حالة مرضية تظهر بين الثلث الثاني والثالث من الحمل. ويتميز بمقاومة الأنسولين الكبيرة الناجمة عن إفراز هرمون المشيمة. تفرز الخلايا الشحمية نوعاً معيناً من البروتين يسمى بروتين سكري الزنك ألفا 2 (ZAG)، وقد أشارت العديد من الدراسات إلى أن ZAG يشارك في العمليات الفسيولوجية الحاسمة مثل تأبيض الجلوكوز. **الأهداف:** تم تصميم هذه الدراسة لتقييم مستوى ZAG لدى النساء الحوامل المصابات بسكري الحمل على طرائق علاجية مختلفة وما إذا كان يمكن استخدامه كمؤشر حيوي في تشخيص داء سكري الحمل. أيضاً لدراسة العلاقة بين ZAG وحالة نسبة السكر في الدم. **الطريقة:** شمل البحث 76 امرأة حامل (تتراوح أعمارهن بين 18 و40 عاماً)، ومن ثم تقسم إلى 22 امرأة حامل تتمتع بصحة جيدة (المجموعة 1)، و30 امرأة حامل تم تشخيصها حديثاً بسكري الحمل (المجموعة 2)، و24 امرأة حامل مصابة بسكري الحمل على طرق علاجية مختلفة (المجموعة 3)، في الثلث الثاني أو الثالث من الحمل. تم قياس جميع الخصائص الديموغرافية ومؤشرات السكر في الدم. **النتيجة:** لم تختلف مستويات ZAG في مجموعات الدراسة بشكل كبير عن بعضها البعض ($P \geq 0.05$)؛ لذلك، أظهرت النساء الحوامل المصابات بسكري الحمل في المجموعة 2 أعلى مستوى من ZAG. وقد لوحظ تباين كبير في مستويات ZAG بين المجموعات الفرعية من النساء الحوامل المصابات بسكري الحمل المعالجات. أظهرت مجموعة الميوقورمين أدنى مستوى من ($P < 0.01$) ZAG. كانت هناك زيادة كبيرة في نسبة الجلوكوز في الدم أثناء الصيام والهيوجلوبين السكري في مجموعة النساء الحوامل المصابات بسكري الحمل 2 و3 مقارنة بالنساء الحوامل في المجموعة 1، وفي الوقت نفسه، زيادة طفيفة في مستوى الأنسولين في بلازما الصيام وتقييم نموذج التوازن لمقاومة الأنسولين (HOMA IR) بين المجموعة 2 و3 مقارنة بالنساء الحوامل من المجموعة 1، وإن لم تكن ذات دلالة إحصائية ($P \geq 0.05$). لم يتم العثور على علاقة ذات دلالة إحصائية بين ZAG ومؤشرات نسبة السكر في الدم. **الاستنتاج:** لم يكن هناك اختلاف ذو دلالة إحصائية في مستوى ZAG بين مجموعات الدراسة ($P \geq 0.05$)، وبالتالي لا يمكن استخدام ZAG كمؤشر في تشخيص داء سكري الحمل.

الكلمات المفتاحية: سكري الحمل، بروتين سكري الزنك ألفا 2 (ZAG)، تأبيض الجلوكوز، الارتباط.

Introduction

Gestational diabetes mellitus (GDM) is characterized by varying levels of impaired glucose tolerance that occur for the first-time during pregnancy. Gestational diabetes is a condition that arises in the latter stages of pregnancy and is marked by a notable resistance to insulin due to the release of hormones by the placenta⁽¹⁾. It is a prominent cause of maternal and infant mortality⁽²⁾. (GDM) is the predominant medical condition linked to pregnancy. It is associated with negative consequences for both mothers and infants⁽³⁾. Efficient therapies should consistently control both fasting and postprandial blood glucose levels, while also decreasing the incidence of hypoglycemia and the presence of ketones in the bloodstream. Medications that do not cross

the placental barrier have an advantage since they are less likely to have adverse effects on the fetus⁽⁴⁾. Maintaining optimal blood glucose levels in GDM reduces the incidence of illness or disease in both the mother and the newborn⁽³⁾.

Zinc Alpha-2 Glycoprotein (ZAG) is an adipocytokine that is synthesized by adipocytes. It has been the subject of substantial research due to its involvement in the regulation of inflammation, cell adhesion, and melanin synthesis⁽⁵⁾. Moreover, several studies have shown that ZAG may serve as a biomarker for the prompt identification of cancer. Furthermore, it plays a crucial function in regulating the proliferation of malignant cells and the metabolic processes of glucose.⁽⁶⁾ There are limited investigation on the impact of ZAG on glucose

metabolism, but many reports have indicated that ZAG reduces the amount of glucose in the bloodstream and enhances the uptake of glucose into fat cells, and the expression of glucose transporter 4 (GLUT4), through the activation of the $\beta 1$ adrenergic receptor. It is worth to note that the level of ZAG in the blood does not show to be positively correlated to the level of glucose in the blood^(7, 8). ZAG potentially enhances glucose consumption, storage, and release, and adrenergic receptors likely have significant involvement in ZAG-mediated regulation of glucose metabolism. Nevertheless, further investigation is necessary to determine the exact mechanism by which ZAG influences glucose metabolism⁽⁹⁾. To the best search, plasma ZAG level was not measured among Iraqi GDM pregnant women, in order to evaluate if there is a variation in levels between GDM and non-GDM pregnant women and if it could be used as an indicator for GDM. Moreover, providing new evidence for existence of possible correlation between ZAG with glycemic parameters.

Patients and Methods

A cross-sectional study was performed between (December 2022 and May 2023), healthy pregnant women (group1) 30 newly diagnosed GDM pregnant women (group2), and 24 GDM on different therapeutic modalities (group3), who were divided into 3 subgroups 10 pregnant women were on diet control [group A], 7 pregnant women were taking insulin therapy [group B], and 7 pregnant women were taking metformin [group C].

Pregnant women were chosen to participate in the study when they visited the National Center for Diabetic Research to make an OGTT test or to seek for medical treatment. Pregnant women were in the 2nd and 3rd trimesters, and their age range was 18–40 years. The study excluded pregnant women with chronic disease and other pregnancy complications, on zinc supplements, with a

history of DM before pregnancy and pregnant women in the 1st trimester. All pregnant women submitted to demographic and glycemic measurements (FBG, HbA1C, FPI, and HOMA-IR). In addition to measuring fasting serum ZAG level.

FBG, HbA1C, FPI levels was determined using kits of Roche/ Germany by Cobas analyzer. FBG determined by enzymatic measuring method, HbA1C determination based on turbidimetric inhibition immunoassay, while FPI measured by automatic Sandwich principle.

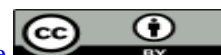
The serum ZAG level was determined using an enzyme-linked immunosorbent assay (Shanghai YL Biotech Co., China). The formula used to calculate insulin resistance index is $HOMA-IR = [FBG \text{ mg/dl} * FPI \text{ } \mu\text{U/mL}] / 405$ ⁽¹⁰⁾.

According to American Diabetes Association (ADA) diagnostic criteria, GDM is diagnosed when one or more of the following abnormalities are observed: FBG level exceeding 5.1 mmol/l (92 mg/dl), one-hour plasma glucose level exceeding 10.0 mmol/l (180 mg/dl), and 2-hrs glucose level exceeding 8.5 mmol/l (153 mg/dl) after an overnight fast and consumption of a 75g glucose load.⁽¹¹⁾.

Ethical Consideration

The methodology of the study was accepted via the Scientific Committee regarding Ethics in the College of Pharmacy at the University of Mustansiriyah. Additionally, an agreement was reached with the National Center for Diabetic Research .

Pregnant individuals were provided with information regarding the study and were asked if they were willing to participate in the ongoing research. The verbal and written consent was obtained after thoroughly explanation the objective of the study and confirming the reliability of the acquired information.



Data Collection

The study data was personally collected by the researcher. Upon the patients' arrival at the center, the researcher requested their consent to participate in the study after providing a concise explanation of its objectives. Upon receiving their assent, the researcher proceeded to provide them with a comprehensive description of the procedure. The subsequent data was documented; included demographic attributes (age, gestational age, parity, systolic and diastolic blood pressure). Also, Considerations associated with diabetes involve the duration of the disease, the therapy employed (Metformin, insulin, or diet), family history of DM, GDM history, and surgical history.

Results

Demographic Data

The mean age of groups was: group1 (26.5yrs), group 2 (31yrs) and group3 (31yrs). The variance within groups were statistically significant ($p < 0.05$). The mean gestational age between groups was as follows: group 1 (31.27 ± 1.16) weeks, group 2 (28.03 ± 0.88) weeks and group 3 (32.42 ± 0.80) weeks. Variations among groups were found to be statistically significant. Positive family history of diabetes mellitus was seen in (7) women within group 1, (24) women group 2 and (18) women in group 3. Also, Positive surgical history was seen in (7) women within group1, (18) women within group 2, and (11) women group 3. There was

a statistically substantial variance among groups in FH of DM and surgical history. While there was no noticeable difference regarding parity, GDM history, SBP or DBP between groups. The mean of parity was (2.2 ± 0.42) for group 1, (1.86 ± 0.28) for group 2, and (2.29 ± 0.36) for group 3. Positive GDM history was (6) in group 2 and (5) for group 3. The mean of SBP and DBP was (117.5, 77.5) mmHg for group 1, (115.71, 75.71) mmHg for group 2 and (117.29, 75) mmHg for group 3.

Glycemic and Metabolic Status of Study Groups

Table 1 present that ZAG levels of pregnant women, there was no noticeable variance in ZAG level between the 3 study groups, ($p \geq 0.05$), although the level is higher in pregnant women in group 2.

Regarding the glycemic status of pregnant women there was a statistically significant variance in FBG groups, ($p < 0.05$). There was highly significant difference in HbA1C among groups, ($p < 0.01$). About FBG the significant difference was between group 1 and 2. While in HbA1C the substantial variance was between group 1 and 2, and highly significant between group 2 and 3 according to post Hoc test.

About Insulin Resistance status, there was no variance among groups in FPI, ($p \geq 0.05$). Also, there was no differentiation among groups in HOMA-IR level as show, ($p \geq 0.05$), hence, slightly increase in FPI and HOMA IR in group 2 and 3 compared to group1.

Table 1 Glycemic and Metabolic Status of Study Groups

Study variable	Study group		
	group 1 (N=22)	group 2 (N=30)	group 3 (N=24)
ZAG mg/l	61.25±31 ^{aa}	71.67±31 ^{aa}	65.65±2.57 ^{aa}
FBG mg/dl	78.12 ± 18.7 ^{aa}	97.89 ± 25.8 ^{ab*}	89.41 ± 28.17 ^{aa}
HbA1c %	5.25 ± 0.65 ^{aa}	5.75 ± 0.69 ^{ab*}	5.15 ± 0.75 ^{bc**}
FPI μU/mL	3.74 ± 2.18 ^{aa}	4.58 ± 1.9 ^{aa}	4.31 ± 2.4 ^{aa}
HOMA IR	0.77 ± 0.6 ^{aa}	1.15 ± 0.57 ^{aa}	1.01 ± 0.7 ^{aa}

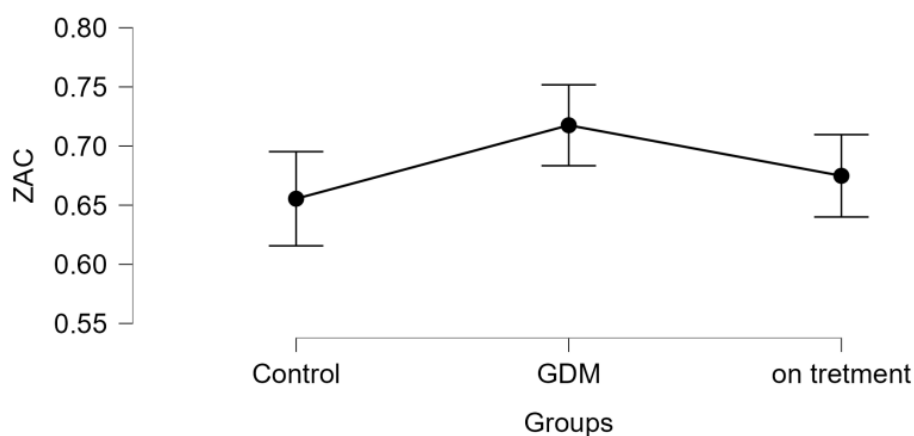
Data expressed as the mean ± SD, and number (n)

NS: non-significant ($p \geq 0.05$), *significant difference $p < 0.05$, **very significant difference $p < 0.01$, ***extremely highly significant difference $p < 0.001$.

aa = no significant difference among groups, ab=comparing between group 1&2, ac=comparing between group 1&3, bc=comparing between group 2,3.

To evaluate the difference in mean among the groups, an analysis of variance (ANOVA) test was used. Post Hoc test was used to evaluate the difference between two groups.

ZAG= zinc alpha-2 glycoprotein, FBG= fasting blood glucose, HbA1C= Glycated Hemoglobin, FPI= fasting plasma insulin, HOMA IR= Homeostatic model assessment of Insulin Resistance

**Figure 1 ZAG level among study groups**

Biomarker Level among GDM Women on Different Therapeutic Modalities

From the results, highly statistically significant differentiation in ZAG level among subgroups, ($p < 0.01$), according to post Hoc test, there was a highly difference in ZAG level between group A and C, and between group B and C, ($p < 0.01$), with highest level in group B women. ZAG levels were (73.9±9.9 mg/L) for group A, (79.9±2.3 mg/L) for group B, and (35.6±3.1 mg/L) for

group C. In addition, there was very high statistically significant difference in HbA1C, ($p < 0.01$), highly statistically substantial variance between group A and B, and between group A and C. The mean was (4.59±0.58%) for group A, (5.77±0.48 %) for group B, and (5.33± 0.66 %) for group C. Finally, there was no statistically significant difference among subgroups in (FBG, FPI, and HOMA-IR), ($p \geq 0.05$).

Table 2 Studied Biomarker among GDM women on Different Therapeutic Modalities

Study variable	Study group		
	group A (Diet) N=10	group B (Insulin) N=7	group C (Metformin) N=7
ZAG mg/L	73.9±9.9 ^{aa}	79.9±2.39 ^{bc**}	35.6±3.18 ^{ac**}
FBG mg/dl	80.48±32.09 ^{aa}	100.78±27.42 ^{aa}	90.81 ±21.47 ^{aa}
HbA1c %	4.59±0.58 ^{aa}	5.77±0.48 ^{bc**}	5.33±0.66 ^{ac*}
FPI µU/mL	3.86±1.73 ^{aa}	3.54±1.01 ^{aa}	5.72±3.64 ^{aa}
HOMA IR	0.84 ± 0.39 ^{aa}	0.89±0.39 ^{aa}	1.37±1.13 ^{aa}

Data expressed as the mean ± SD, and number (N)

NS: non-significant ($p \geq 0.05$), *significant difference $p < 0.05$, **very significant difference $p < 0.01$, ***extremely highly significant difference $p < 0.001$.

aa = no significant difference among groups, ab=comparing between group 1&2, ac=comparing between group 1&3, bc=comparing between group 2,3.

To evaluate the difference in mean among the groups, an analysis of variance (ANOVA) test was used. Post Hoc test was used to evaluate the difference between two groups.

ZAG= zinc alpha-2 glycoprotein, FBG= fasting blood glucose, HbA1C= Glycated Hemoglobin, FPI= fasting plasma insulin, HOMA IR= Homeostatic model assessment of Insulin Resistance

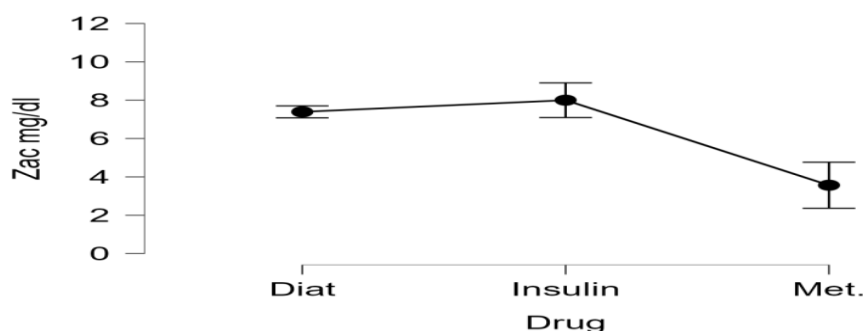


Figure 2: ZAG level among pregnant women on different therapeutic medications
Correlations between ZAG with Demographics and Glycemic Measures of Study Groups

Zinc a2 Glycoprotein correlation with patient demographic characteristics are shown in table 3 there was no substinital correlation between ZAG level with (gestational age, parity, and FH) in the all three groups, ($p \geq 0.05$).

Regarding The ZAG level correlation with laberatory biomrkers, there was no

statistically significant relation between ZAG level and (FBG and HbA1C) in the groups, ($p \geq 0.05$). There was statistically significant positive correlation between ZAG level and (FPI and HOMA-IR) in group 1, ($p: 0.03$, and 0.02 respectively), but no valuble correlation in group 2 and group 3, ($p \geq 0.05$).

Table 3 Correlation between ZAG with demographic and glycemic measures of study groups

Study variable	Study group		
	group 1 (N=22)	group 2 (N=30)	group 3 (N=24)
ZAG & Gestational Age			
Pearson's r	0.10	0.20	0.21
P-Value	0.65 ^{NS}	0.29 ^{NS}	0.32 ^{NS}
ZAG & parity			
Pearson's r	0.26	0.17	0.35
P-Value	0.24 ^{NS}	0.38 ^{NS}	0.10 ^{NS}
ZAG & FH			
Pearson's r	0.23	0.11	0.17
P-Value	0.30 ^{NS}	0.57 ^{NS}	0.42 ^{NS}
ZAG & FBG			
Pearson's r	0.33	0.10	0.06
P-Value	0.14 ^{NS}	0.59 ^{NS}	0.78 ^{NS}
ZAG & HbA1C			
Pearson's r	0.28	0.05	-0.01
P-Value	0.20 ^{NS}	0.79 ^{NS}	0.99 ^{NS}
ZAG & FPI			
Pearson's r	0.45	-0.01	-0.24
P-Value	0.03*	0.96 ^{NS}	0.26 ^{NS}
ZAG & HOMA IR			
Pearson's r	0.47	-0.08	-0.18
P-Value	0.03*	0.67 ^{NS}	0.41 ^{NS}

Data expressed as the mean \pm SD, and number (n)

NS: non-significant ($p \geq 0.05$), *significant difference $p < 0.05$, **very significant difference $p < 0.01$, ***extremely highly significant difference $p < 0.001$.

To evaluate the correlation between two parameter, pearsons correlation test was used.

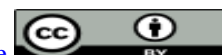
ZAG= zinc alpha-2 glycoprotein, FBG= fasting blood glucose, HbA1C= Glycated Hemoglobin, FPI= fasting plasma insulin, HOMA IR= Homeostatic model assessment of Insulin Resistance

Discussion

Demographic, Glycemic and Metabolic Status of Study Groups

In current study there was significant increase in maternal age in GDM women comparing to non-GDM pregnant women as in previous studies ^(12, 13). In present finding, GDM pregnant women had higher gestational age than non GDM pregnant. The prevalence of gestational diabetes rise with the progression of pregnancy on a global scale, rising from 25% in the 23rd week to 33% in the 3rd trimester ⁽¹⁴⁾. Insulin sensitivity increases during early pregnancy, which facilitates the absorption of glucose

into adipose tissue in anticipation of the increased energy requirements that occur later in pregnancy. Insulin resistance develops during pregnancy as a result of elevated levels of hormones produced locally and by the placenta, including placental growth hormone, estrogen, progesterone, leptin, cortisol, and placental lactogen ⁽¹⁵⁾. A significant correlation was observed between family history of DM and GDM in the present analysis, as in a previous investigation ⁽¹⁶⁾. Pregnant women who had first-degree, second-degree, or first- and second-degree relatives with diabetes had a higher risk of developing GDM than those without any FH ⁽¹⁷⁾. Nevertheless, the relation between a maternal family history of T2DM



and the development of GDM remains poorly understood and a subject of ongoing debate. The correlation between a familial predisposition to diabetes and GDM underscores the multifactorial character of the disease's pathophysiology and the influence of environmental and genetic factors. The literature that explaining the genetic and epigenetic causes of GDM, as well as the correlation between GDM and specific T2DM risk gene polymorphisms ⁽¹⁸⁾. There were no statistically significant differences between patient parity in the present study, which disagreed with previous study, may be due to small sample size. In a large international study, the analysis of the data revealed that the incidences of gestational diabetes increased significantly with increasing parity ⁽¹³⁾. The results of previous study reported that the incidence of GDM in primiparous women was significantly lower than that in multiparous women ⁽¹⁹⁾. About GDM history, there no difference among study groups, which disagreed with previous study that included 3587 singleton pregnancies complicated by GDM, 501 fell pregnant again and 367 (73.1%) developed GDM in their subsequent pregnancies ⁽²⁰⁾.

ZAG, an adipocytokine, is secreted by adipocytes. Extensive research has demonstrated that ZAG regulates cell adhesion, immunity, and melanin synthesis ⁽²³⁾. Additionally, a number of studies have identified ZAG as a potential indicator for the early detection of cancer, in addition to its role in controlling the proliferation of tumor cells and glucose metabolism ⁽²⁴⁾. Additionally, it was discovered that ZAG is in relation with the development of T2DM lipid metabolism disorder in addition to its role in regulating fat metabolism in obesity. ⁽²⁵⁾. In previous study, the cut off value for ZAG level in healthy subjects was $(43.8 \pm 19.5 \text{ mg/L})$ ⁽²⁶⁾.

In current study, ZAG level in healthy pregnant women was $(61.25 \pm 3.1 \text{ mg/L})$,

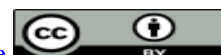
there was increase in ZAG level in GDM women, and in those GDM women who received treatment ZAG level was decreased to near that of healthy pregnant, still no significant difference among study groups. In previous study 207 pregnant women (130 with non-GDM and 77 with GDM) included in the beginning of third trimester, which noted that serum ZAG levels did not differ statistically between the GDM $(47.25 \pm 11.7 \text{ mg/L})$ and the non- GDM $(46.8 \pm 9 \text{ mg/L})$ as in current findings, There was no association between ZAG and gestational glucose metabolism ⁽²⁷⁾. An additional study comprised 80 newly diagnosed GDM patients. In comparison to pregnant without GDM, the case group exhibited a significantly lower serum ZAG level $(43.94 \pm 14.51 \text{ mg/L}$ vs. $62.57 \pm 19.05 \text{ mg/L}$, $P < 0.001$) ⁽²³⁾.

Limited research has been conducted on the link between serum ZAG and GDM. Such controversy in the level of ZAC in GDM and using ZAC as an initial indicator of metabolic irregularities in GDM require additional medical evidence.

In diabetic patients, ZAC was noticeably elevated in patients with T1DM than that in healthy subjects, ZAG might involve in T1DM pathogenesis ⁽²⁸⁾. In another study, levels of serum ZAG levels interval from 2.63 to 46.97 mg/liter. Interestingly greater concentrations of ZAG were seen in individuals with T2DM. The rise in ZAG in T2DM is believed to be a result of increased synthesis as a compensatory response to insulin and leptin resistance associated with obesity ⁽²⁹⁾. The metabolic disease patients had decreased levels of Plasma ZAG compared to the healthy controls. ⁽³⁰⁾.

Biomarker Level among GDM Women on Different Therapeutic Modalities

In the current study, pregnant with GDM on metformin treatment presented with the lowest ZAG level compared to those receiving insulin or diet controlled .A prior



investigation comprised 106 patients diagnosed with T2DM; of these, 50 were prescribed a combination of metformin and sulfonylurea, 18 were allocated sulfonylurea exclusively, and 25 were prescribed unspecified drug. Nevertheless, non-pharmacological control groups did not exhibit any statistically significant differences in serum ZAG level among the three treated groups, which disagreed with present study⁽²⁹⁾.

The FBG in GDM pregnant patients receiving metformin in the current study was lower than that pregnant patients on insulin therapy, and pregnant patients on diet, but there was no significant difference among them. Meanwhile, HbA1C was found to be lowest level in pregnant patients on diet control.

It is well known there is variation in response to different treatment of diabetes including GDM, A previous retrospective study comprised 45 women with GDM who were administered metformin, 45 women who were administrated insulin, and 83 women who did not take any medication (diet), women on diet exhibited the lowest HbA1c levels, while there was no variation in HbA1c levels between the insulin and metformin groups. Furthermore, the metformin group demonstrated a decrease in FBG compared to the insulin group⁽³¹⁾. Another previous study, assigned women with GDM (the 363 women on metformin and 370 received insulin), the metformin group exhibited the lowest FBG level⁽³²⁾. Also, in other previous study, GDM diagnosed women with WHO criteria were included, received oral metformin 500 mg, or were given insulin, higher HbA1C was noticed in insulin treatment as in current findings, and non-significant difference in FBG⁽³³⁾. Metformin may exert its effects indirectly via the reduction of insulin resistance and enhancement of insulin sensitivity⁽³⁴⁾. It enhances insulin sensitivity in peripheral tissues and the liver, leading to

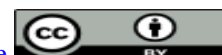
enhanced absorption and utilization of glucose induced by insulin⁽³⁵⁾.

Correlations between ZAG with Demographics and Glycemic Measures of Study Groups

In current study, there was no correlation between serum ZAG level and demographic characteristics (gestational age, parity and FH of DM). In previous study, ZAG was independently correlated with gastrointestinal age at delivery⁽²⁷⁾. No significant correlation was seen between ZAG level with glycemic parameters in the newly diagnosed GDM pregnant, and in other study groups. Unexplained significant positively correlation between ZAG level with resistant parameters in the control group, but no correlation between ZAG with (FPI and HOMA-IR) in GDM patient groups. In previous studies on T2DM patients, that's agreed with current study, resulted no association between ZAG and fasting glucose, and ZAG was shown to be inversely correlated with IR⁽²⁶⁾. In another study that's contract current finding, in metabolic syndrome patients enrolled in previous study, plasma ZAG was inversely related with glucose metabolic parameters (FBG, HbA1C, FPI, and HOMA)⁽³⁰⁾. Also, in newly diagnosed GDM patient's serum ZAG levels were inversely linked to FPG, FINS, and HOMA-IR⁽²³⁾. As previously reported, adrenergic receptors might play significant roles in ZAG-regulated glucose metabolism and Zinc- α 2 glycoprotein might contribute to glucose storage, utilization, and excretion.⁽³⁶⁾

Conclusion

Pregnant women with GDM exhibit significant elevated in glycemic parameters compared to those without GDM and these with GDM on treatment. ZAG level was increase among all pregnant women, particularly these with GDM.



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