

Resistin Levels And Many Physiological Variables As Early Indicators For Detecting Gestational Diabetes In Obese Women In Kirkuk City.

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Abstract :

DM is a higher risk factor for cardiovascular disease in the future and has long been linked to obstetric and neonatal problems, mainly involving high birth weight babies. Due to epidemiological variables such as rising rates of obesity among women of reproductive age and advancing maternal age, GDM is still on the rise globally. The regulation of human glucose metabolism may be significantly influenced by resistin. Additionally, carnitine is essential for maintaining cell membrane integrity, avoiding the buildup of fatty acids, and regulating the processes of gluconeogenesis and ketogenesis.

Keywords: Resistin , L-carnitin, Cortiso , GMD, Insuli, C-peptid.

INTRODUCTION

Chronic metabolic conditions like diabetes, which involves consistently high blood sugar levels, can negatively impact a person's quality of life and raise the risk of death (Hasan et al., 2024), Diabetes results from either insufficient insulin production or improper insulin use. It can result in numerous severe health issues if left untreated (Sulaiman et al., 2022) .Pregnancy is a complex physiologic condition that require the body to alter many hormones and other biological processes in order to maintain the the progression of the pregnancy. Pregnancy has a high energy demand since it involves a number of intricate and energy-intensive physiological processes. One of the vital nutrients, fatty acids are needed for the oxidation-based energy source and carry out vital biological processes like antioxidant and anti-inflammatory actions that have a significant impact on human health. Along with several pregnancy-related conditions that can impact both the mother's and the fetus's health, a disruption of fatty acid metabolism can result in anomalies in the growth and development of the fetus (Cao et al., 2024) . Gestational diabetes The most prevalent metabolic disorder in pregnancy, in which the pregnant woman does not have a previous history of hyperglycemia neither any degree of impaired glucose tolerance test.. The symptoms of GD may spontaneously resolve after birth, however, mothers with GD are more likely to develop disorders such as type II diabetes, cardiovascular and obesity, diseases. Moreover, GD can cause macrosomia in infants, obesity or even the risk of developing diabetes in early childhood (Gu et al., 2023).

Adipose tissue and its derivatives (adipose) have been identified as a unique endocrine organ that plays a specific role in maintaining insulin and glucose homeostasis. Resistin, a newly discovered cysteine-rich hormone secreted mostly by human adipocytes, is one of the adipogenic cytokines that decreases adipocytes' uptake of glucose, increases plasma glucose levels, and thus decreases insulin sensitivity.(Yura et al., 2003 ; Chen et al., 2005). It is thought to be linked to the pathophysiology of GD and insulin resistance (Ferdousi et al., 2025), Resistin is a may play an important role in regulation of glucose metabolism in human. High resistin levels induce insulin resistance and exert inflammatory effects. The regulation of human glucose metabolism may be significantly influenced by resistin. Elevated levels of resistin cause inflammation and insulin resistance. Numerous metabolic, inflammatory, and autoimmune disorders have been repeatedly demonstrated to be significantly impacted by resistin. Additionally, it has a role in the pathophysiology of the byt that controls glucose metabolism and is aberrantly expressed in the blood of patients with gestational diabetes mellitus (GDM). Under normal circumstances, it consistently works with insulin to improve immune function and control the body's inflammatory response. Nevertheless, as its levels rise, it may contribute to insulin resistance and lose some of its

regulating ability (Acquarone et al., 2019). Carnitine is well-known for its function in fatty acid oxidation and is an essential component for healthy mitochondrial activity. Additionally, carnitine is essential for preserving cell membranes, avoiding the buildup of fatty acids, controlling the processes of ketogenesis and gluconeogenesis, and getting rid of harmful metabolites.(Virmani and Cirulli, 2022).

In contrast, cortisol raises lipid metabolism, which raises blood glucose levels and the quantity of free fatty acids in the bloodstream, and encourages gluconeogenesis, which is the process by which glucose is produced from non-carbohydrate sources. Through the excessive release of free fatty acids, which can activate protein kinase C (PKC), which phosphorylates IRS-1 on a serine residue, high cortisol levels contribute to insulin resistance and the pathophysiology of GD. Serine phosphorylation of IRS-1 prevents it from efficiently promoting insulin signaling, which exacerbates insulin resistance and further impairs glucose absorption.(Du et al., 2024). The current study were designated to assess some adipocytokines in pregnant women during various gestational phases and their relation to the development of GD.

MATERIALS AND METHODS

Samples collection:-

Samples were collected in Kirkuk city for the period from March 2024 to February 2025. The patients were those who came to the Obstetrics and Gynecology Department at Al-Nasr Maternity Hospital, in addition to private clinics. Each participant received a questionnaire to complete and sign, along with a consent form. Every patient received a questionnaire with demographic data like age, body mass index (BMI), cycle pattern, number of births, and other pertinent information, as well as a medical examination and an interview with a gynecologist.

Inclusion criteria

Two groups of pregnant women in the first trimester who are obese with a BMI ≥ 30 . The groups are followed up and divided according to the incidence of gestational diabetes into 2 subgroups in the second trimester of pregnancy.

Exclusion criteria

Pregnant women who had type 1 or type 2 diabetes, women who used medications that raise blood sugar levels such as Metformin drug and cortisol, women with frequent miscarriages and those with chronic high blood pressure.

Study procedure

All participants who fit the inclusion criteria were viewed at Gynecology Ward and participants followed up from the 1st trimester throughout the 2nd trimester. A panel of blood tests were performed on the subjects blood after collecting 4ml of whole blood, these tests included oral glucose tolerance test after 12 hour fasting, HbA1c and C-peptide. According to the test result of those biochemical tests the participants in the 2nd trimester.

Biochemical analysis

Whole blood 5ml was extracted from all participants After 12 hours of fasting, One ml of whole blood was kept into an EDTA tube for the HbA1c test, while the remaining 4 ml was poured into sterile gel tubes.. The serum was separated via centrifugation at 3000 rpm for 20 min and transferred to an Eppendorf tube, and each tube was labeled. with the patient's code and stored at -20°C. OGTT was performed to assess the glycemic levels of the donors after 12 h fasting via ingestion of 50g of pure glucose solution. Further biochemical tests were done including serum glucose, insulin, cortisol, and C-peptide, as well as resistin levels. The biochemical tests were measured via an automated autoanalyzer for chemiluminescence (Elecsys, Cobas e411, Roche Diagnostic GmbH, Mannheim, Germany). As for serum resistin and L-carnitin an ELISA kit was utilized to assess the level in those participants (SunLong Biotech Co., LTD). The insulin resistance index was estimated by multiplying the fasting blood sugar (FBS) mg concentration by the fasting insulin level and dividing by 22.5 which will provide the Homa IR index (Ma and Lu, 2024)

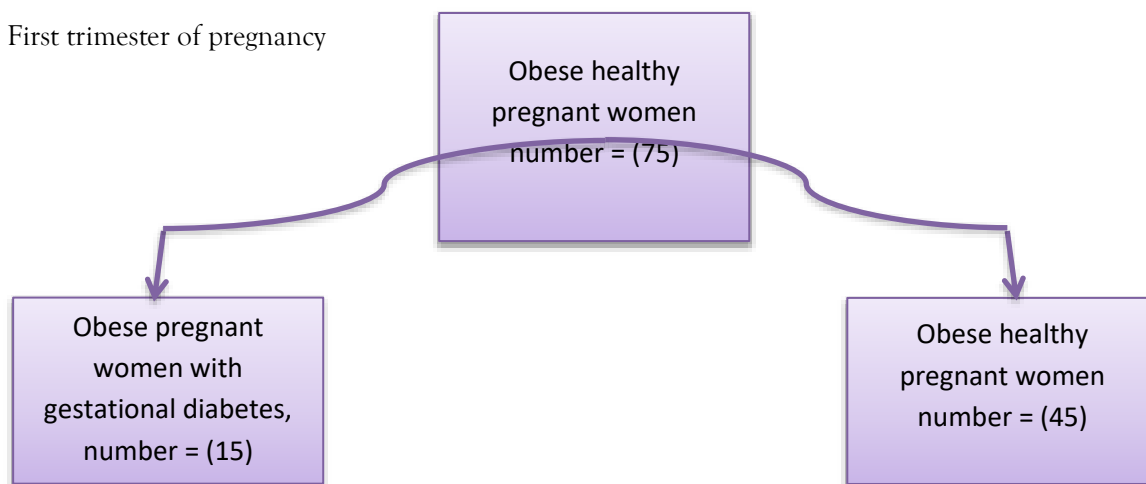
Statistical analysis

One-way anova were used to analyze the data, and SPSS version 27 was used to test for mean differences using Duncan's multiple range test.

RESULTS

(75) blood samples were selected from pregnant women in the (10-12) week of pregnancy with a body mass index (BMI) ≥ 30 . After following up on the cases in the second half of pregnancy (20-24) weeks, a number of samples that did not meet the conditions were excluded, specifically those taking sugar-lowering medications such as metformin and others. It was found that (45) samples did not show any symptoms of gestational diabetes.. (15) samples were selected that suffered from an increase in most of the studied variables that have a close relationship with the sugar level and all related analyses, and they were diagnosed as cases of gestational diabetes.

First trimester of pregnancy

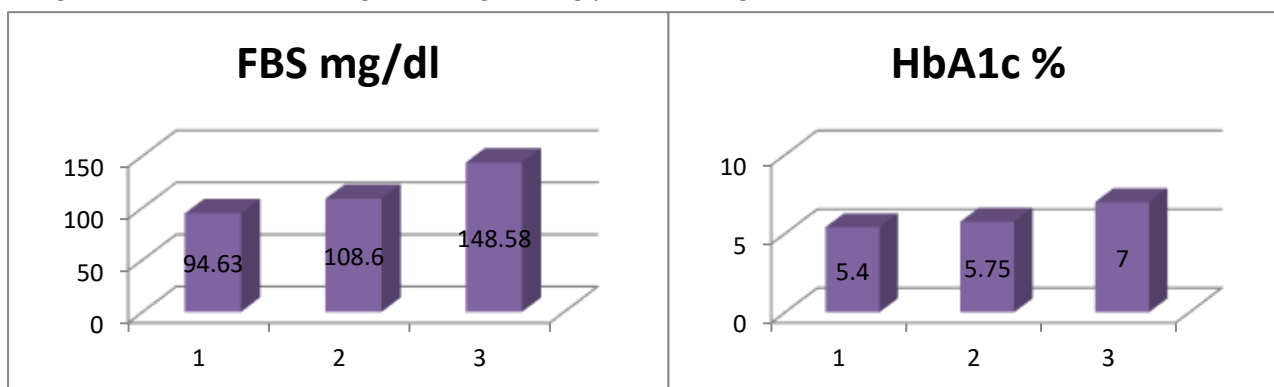


Second trimester of pregnancy

Figure (1) A chart showing the distribution of groups.

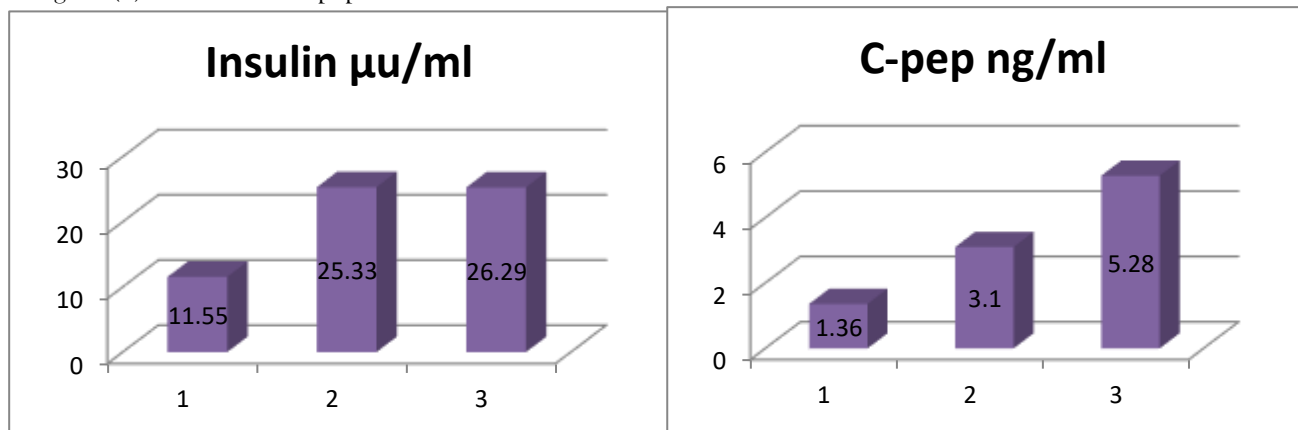
A progressive increase in FBS levels was observed across the groups. The mean FBS in Group 1 was 94.63 ± 14.64 mg/dl, rising to 108.6 ± 8.32 mg/dl in Group 2, and reaching a significantly higher value of 148.58 ± 15.01 mg/dl in Group 3. The variations were statistically significant ($p < 0.05$). HbA1c levels were notably elevated in Group 3 ($7 \pm 0.51\%$) compared to Group 2 ($5.75 \pm 0.32\%$) and Group 1 ($5.4 \pm 0.30\%$), indicating statistically significant differences ($p < 0.05$). As shown in Figure (1)

Figure (1) Variables of fasting blood sugar and glycated hemoglobin.



Both Group 2 (25.33 ± 5.94 μ U/ml) and Group 3 (26.29 ± 8.71 μ U/ml) demonstrated significantly higher fasting insulin levels compared to Group 1 (11.55 ± 4.71 μ U/ml), with clear statistical significance ($p < 0.05$). C-peptide levels increased markedly among the groups, with Group 1 showing a mean of 1.36 ± 0.63 ng/ml, Group 2 at 3.1 ± 0.88 ng/ml, As shown in Figure (2).

Figure (2) Insulin and C-peptide levels.



Lipid profile parameters were compared among three study groups (G1, G2, G3), as illustrated in Figure 1. The findings revealed the following:

Total Cholesterol: Showed a gradual increase from G1 to G3, with G1 recording 185.77 mg/dL, G2 at 222.46 mg/dL, and the highest level in G3 at 234.11 mg/dL. **Triglycerides:** Demonstrated a notable rise from G1 (187.3 mg/dL) to G2 (272.4 mg/dL), followed by a slight decrease in G3 (268.1 mg/dL) compared to G2. **High Density Lipoprotein (HDL):** Was highest in G1 (44 mg/dL), and showed a clear reduction in G2 (37.13 mg/dL) and G3 (38.47 mg/dL). **Low-Density Lipoprotein (LDL):** Increased from 106.15 mg/dL in G1 to 132.85 mg/dL in G2, with a slight decrease observed in G3 (142.02 mg/dL). **Very Low-Density Lipoprotein (VLDL):** Rose from 37.15 mg/dL in G1 to 52.48 mg/dL in G2, and remained elevated in G3 at 53.62 mg/dL.

These results indicate a progressive pattern of lipid imbalance across the groups, which may reflect an increased metabolic risk or a potential association with gestational diabetes or other metabolic disturbances (depending on the study hypothesis).

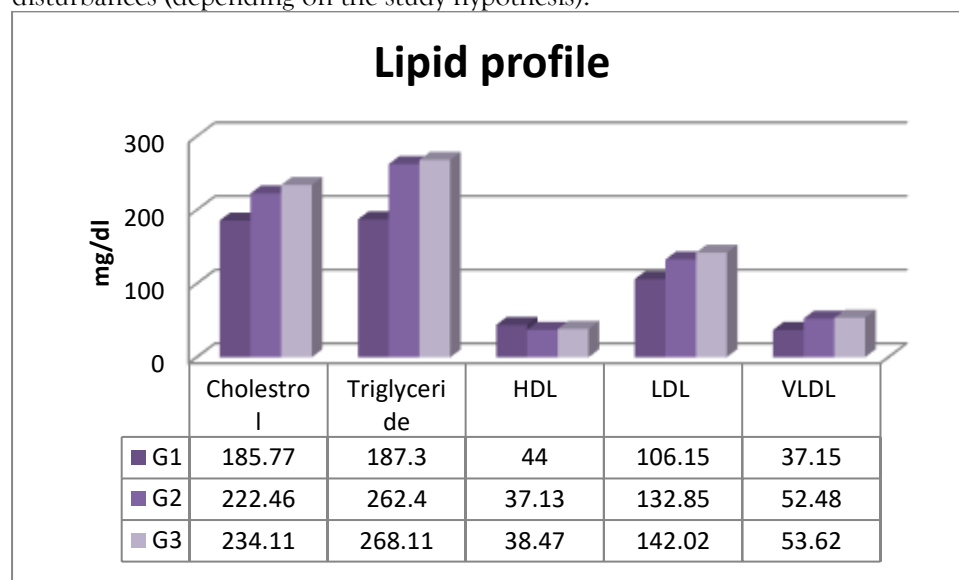


Figure 3: Comparison of lipid profile parameters (Cholesterol, Triglycerides, HDL, LDL, VLDL) among the three study groups.

In figure :4 **Cortisol Levels:**The results demonstrated a progressive increase in mean cortisol levels across the three groups. Group 1 (G1) recorded a mean of 7.84 mcg/dl, which rose to 10.84 mcg/dl in Group 2 (G2), and reached 13.31 mcg/dl in Group 3 (G3).

This trend suggests a potential dysregulation in hormonal balance among women with gestational diabetes mellitus (GDM), as cortisol is known to exert anti-insulin effects by promoting gluconeogenesis and reducing tissue sensitivity to insulin—mechanisms that can exacerbate insulin resistance during pregnancy.

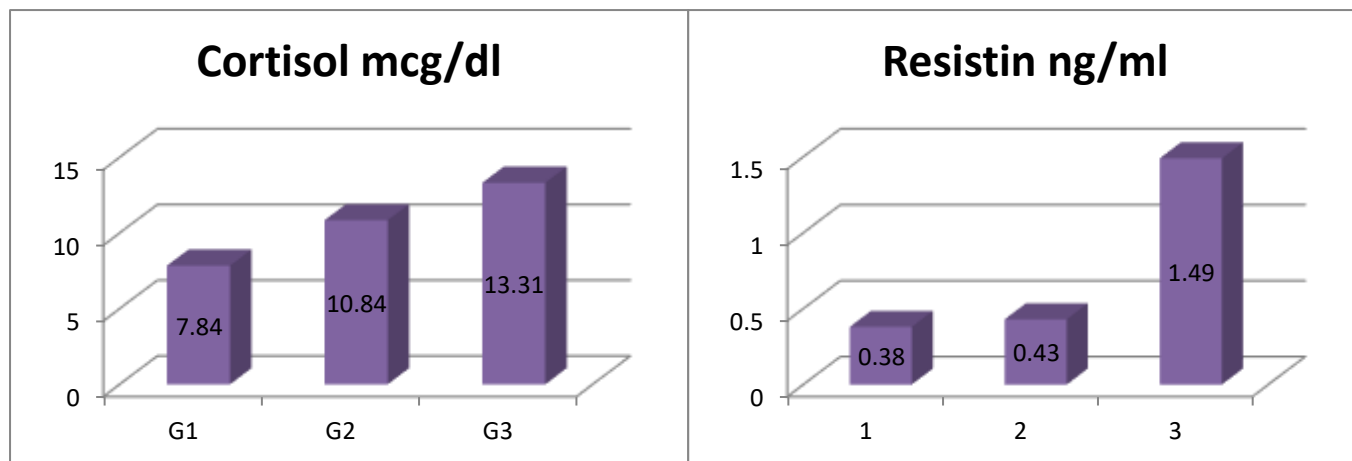


Figure: (4) Cortisol and resistin levels.

L-carnitine Levels:in Figure: (5) The data shows that L-carnitine levels dropped in the third group (217.85 ± 27.05 ng/ml) compared to the first group (263.56 ± 84.15 ng/ml), then second group to (220.54 ± 29.37) ng/ml. This inconsistent pattern might reflect how the body responds to metabolic changes during pregnancy, especially with the development of gestational diabetes.

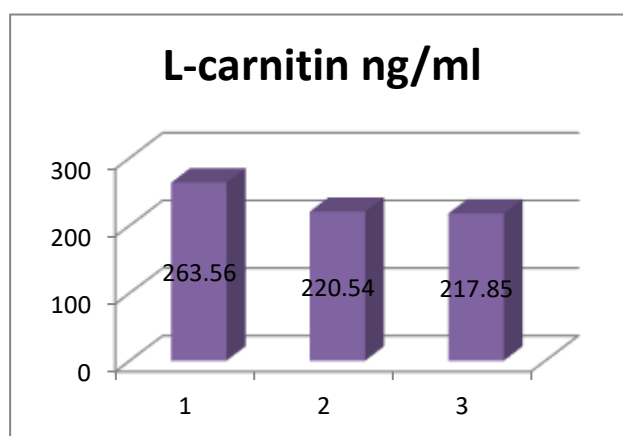


Figure: (5) Carnitine level.

DISCUSSION

Diabetes mellitus is quickly becoming one of the major health challenges of the 21st century. The number of people affected by it continues to rise steadily in both developed and developing countries (Mijwil and Jasim, 2025). Gestational diabetes, marked by decreased glucose tolerance that develops or is identified during pregnancy, which is regarded as a serious public health issue. Insulin is the usual treatment when food and lifestyle changes don't result in standardized glucose levels (30% of women) (Bodier et al., 2025), Gestational weight gain (GWG), gestational diabetes mellitus (GDM), and pre-pregnancy body mass index (BMI) are all related to one another and may have complex effects on fetal development (Lyu et al., 2024). The incidence of Globally, GDM has increased. Although a number of factors, including lifestyle choices and weight management, influence the development of GDM, in addition reduction of processed sugar sources which any play crucial roles in prevention strategies (Mellem et al., 2024).

Overall, our findings indicated that a sedentary lifestyle and a high body mass index raise the risk of acquiring GDM. The high incidence of GDM in our group may be associated with women's high rates of obesity and sedentary lifestyles. Obesity and other pregnancy-related issues, hypertension and gestational diabetes are well-known risk factors that assume in elevation of morbidity and mortality in pregnant women. GDM as a solo condition can be associated with maternal postpartum metabolic and cardiovascular morbidity in addition to over illness that may influence the wellbeing of the fetus and neonate. Hence, there is a pivotal need to identify this clinical condition as early as possible (Li et al., 2022; Song et al., 2022). Recent research indicates that the mother's weight or obesity, preterm premature rupture of the membranes, cesarean birth, hemorrhage, and preeclampsia may account for around 25% of the risk of pregnancy problems (Zhang et al., 2022). Song et al (Song et al., 2022) examined the pregnancy problems and outcomes of obese or GDM-afflicted women in over 15,000 moms, and found that obesity or overweight was responsible for 16% and 4% of the development of GDM in the entire study group. GDM prevalence was 12.3%. Additionally, the investigators noted that participants with a BMI of 30 kg/m² or greater were more likely to develop GDM. The results of the current study are consistent with what Mellem et al. (2024) found, as they found that excessive inactivity, sedentary time during pregnancy, and an unhealthy lifestyle lead to increased obesity, which in turn leads to gestational diabetes.

On the other hand, pregnancy is regarded as an inflammatory state because of the mother's physiological changes to provide the right conditions for the fetus's growth, and resistin is categorized as a pro-inflammatory adipokine. During pregnancy, mononuclear cells, adipose tissue, and placental trophoblastic cells are the main sources of the pro-inflammatory adipokine resistin (Nava-Salazar et al., 2022). Additionally, it has been demonstrated that resistin reduces cell surface glucose transporters and, consequently, glucose uptake into cells, raising blood glucose levels and lowering insulin sensitivity. The results of the current study were similar to those of Ferdousi et al. (2025), who explained that the level of resistin is higher in women with gestational diabetes than in women without gestational diabetes, and therefore resistin is a good indicator of gestational diabetes.

The main stress hormone, cortisol, has the opposite impact of insulin in that it raises blood glucose levels. For any pregnant woman, pregnancy is an extremely trying time in her life, and is associated with increased secretion of cortisol, thus leading to an increase in the level of glucose in the bloodstream of pregnant woman (AlShaibani et al., 2024). In this study, compared to pregnant women without GDM, pregnant women with GDM had noticeably higher blood cortisol levels. There is clear variation in the association between cortisol levels and GDM, and this was similar to what was stated in the study of AlShaibani et al., 2024. Nonetheless, it is widely acknowledged that the pathophysiology of GDM involves increased amounts of stress hormones, such as cortisol (Martin et al., 2021). Cortisol is a potent insulin antagonist. It interferes with insulin signaling, suppresses insulin secretion, and increases glucagon secretion (Exton, 1979). Pregnancy-related hormonal alterations are believed to be the cause of GDM (Yang et al., 2023). It is yet unknown what mechanism underlies the formation of GDM. The pathophysiology of GDM may be influenced by elevated cortisol levels in pregnant women's blood. Chronically elevated cortisol levels keep the body in a general state of insulin resistance. A vicious cycle gradually emerges as blood glucose levels rise, cells are unable to use blood glucose, and the pancreas fights to maintain insulin production (Tien et al., 2023). Recent research on this relationship, however, has produced conflicting results. According to a 2024 study, women with and without GDM did not significantly differ in their cortisol levels, suggesting that the association may be indirect or impacted by mediating factors like body mass index (BMI) or chronic low-grade inflammation (Shen et al., 2024). Resistin Levels: In contrast, resistin levels showed a modest increase between Groups 1 and 2 (from 0.38 to 0.43 ng/ml), followed by a sharp rise in Group 3, reaching 1.49 ng/ml. This pronounced elevation aligns with current evidence emphasizing resistin's role in promoting inflammation and insulin resistance—two key pathophysiological components of GDM. These findings are consistent with a 2023 study which highlighted resistin as a promising biomarker for distinguishing women at risk of GDM, supporting its potential use for early diagnosis (Feng et al., 2023).

Integrated Analysis: The simultaneous elevation of both cortisol and resistin levels in Group 3 suggests a possible synergistic interaction between hormonal stress and immune-mediated inflammation in enhancing insulin resistance during pregnancy. While resistin appears to be a more reliable and consistent marker based on recent evidence, the exact contribution of cortisol remains uncertain and warrants further longitudinal studies to clarify its direct role in the development or progression of GDM.

The altered of acylcarnitine levels may contribute to the pathophysiology of gestational diabetes by disrupting insulin secretion and sensitivity. Long-chain acylcarnitines, such as palmitoylcarnitine, have been shown to interfere with insulin signaling pathways. Specifically, these compounds induce dephosphorylation of the insulin receptor (InsR) at Tyr1151 through a mechanism dependent on protein tyrosine phosphatase 1B (PTP1B). This reduces phosphorylation of protein kinase B (Akt) at Ser473, a key step in insulin signaling, limiting cellular responsiveness to insulin and contributing to insulin resistance. (Vilks et al., 2021). L-carnitine is essential for transporting fatty acids into mitochondria to produce energy. In early stages of gestational diabetes, insulin resistance and metabolic stress could lead to increased use of L-carnitine, which may explain the decrease in Group 2. Later in pregnancy, the body may try to compensate by increasing L-carnitine levels to improve fat metabolism and energy balance. This could explain the sharp rise seen in Group 3. (Zhang et al., 2023)

C-peptide levels in the early stages of pregnancy are linked to the chance of developing gestational diabetes later on, according to data gathered from prospective studies. Pancreatic beta-cells release C-peptide into the bloodstream in equimolar levels to insulin. Because it has a longer half-life than insulin and is hardly cleared by the liver, it is a valuable biomarker for estimating beta-cell function. Because of physiological changes in hormonal and metabolic homeostasis, pregnancy causes an increase in insulin resistance. Hyperglycemia is caused by islet beta-cells' inadequate compensation. (Milionis et al., 2024)

CONCLUSIONS

The increase incidence if GDM is strongly associated with hormonal imbalance that can increase the risk developing early insulin resistance and hence the occurrence of GDM . Patients with gestational diabetes had statistically and substantially greater levels of resistin than a sample of pregnant women without the condition. One reliable marker of gestational diabetes is resistin.

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