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Characteristics of Asprosin and Some Biochemical in Prediabetic Pregnant Women Presenting with UTIs

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Abstract

Diabetes can exacerbate the infection since pregnant women with diabetes had a higher incidence of UTI (29.9%) than pregnant women without diabetes (11.1%). This study investigated the percentage of patients who had a urinary tract infection (UTI) in order to evaluate the function of paternal genetics in the development of DM and ascertain the effect of DM on the urinary system. The study comprised 90 pregnant women, ages 25 to 50, with and without diabetes mellitus (DM) in comparison to control pregnant women. The blood sugar levels and diabetes mellitus were determined both clinically and in a private, specialized laboratory. There was information on the age, etiology, and family history of diabetes. Bacterial species were isolated and identified using culture media and biochemical assays. Patients with UTIs were mostly female (73%) in proportion. To sum up, type 2 diabetes is the most prevalent, particularly in women, and it rises with age. Family genetic susceptibility and abrupt shocks were the primary causes of diabetes mellitus. The majority of diabetes individuals, particularly women, experienced UTIs, and the primary reasons of UTI inflammation were also shown by the current study. Insulin-resistant mice and humans have pathologically elevated levels of asprosin, a new hormone that has been found to be concentrated in white adipose tissue. However, there is currently no information available about asprosin's involvement in type 2 diabetes mellitus (T2DM). The aim of our study was to determine whether there might connection between prediabetic pregnant women presenting with and circulating asprosin levels.

Introduction

Hyperglycemia in pregnancy (HIP) affects about 16% of pregnancies globally, which can result from either pre-existing diabetes (defined as any kind of diabetes diagnosed prior to the index pregnancy) or hyperglycemia first recognized in pregnancy (HFDP) (Nicolaou, 2021). HFDP is the primary cause of HIP (International Diabetes Federation, 2019), includes both diabetes during pregnancy and gestational diabetes mellitus (GDM), which is diagnosed in pregnant women with blood glucose levels that fall between those of diabetes outside of pregnancy (López Stewart, 2014). Pregnancy rates with pre-existing diabetes are thought to be less than or approximately (Albrecht et al., 2010). On the other hand, women who already have diabetes need close clinical supervision and assistance (Kitzmiller et al., 2008). to maximize glycemic control and lower the risk of diabetes-related pregnancy problems both before and during pregnancy (Mondestin et al., 2002).

From an evolutionary perspective, the physiology of insulin resistance during pregnancy is intriguing because it is meant to restrict the mother's ability to use glucose and divert enough of it toward the developing baby, which needs glucose as its primary energy source.

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Consequently, the degree of maternal insulin resistance that develops during pregnancy is connected with the amount of glucose flow from the mother to the fetus (Luo etal., 2024).

The fasting-induced adipokine asprosin, which controls the release of glucose, was initially identified in 2016. Adipose tissue produces this protein hormone, which is subsequently delivered to the liver once the C-terminal region of profibrillin is cleaved. Upon entering the liver, it triggers the cAMP/PKA pathway, which causes glucose to be synthesized quickly and released into the bloodstream. Surprisingly, the glucagon and catecholamine axis have little bearing on asprosin's actions (Romere et al., 2016). Furthermore, asprosin can directly excite orexigenic neurons by crossing the blood–brain barrier via a process that relies on cAMP activation. This stimulation raises appetite, which increases the significant risk of weight gain and obesity (International Diabetes Federation, 2019; López Stewart, 2014). Because of these qualities, asprosin is a possible option for new therapies that target type 2 diabetes (T2D) (Shabir et al., 2021; Al-Sultan & Al-Issa, 2023).

Urinary tract bacterial contamination, or "bacteriuria," is a common occurrence that can occasionally lead to microbial invasion of the tissue that forms, transports, and stores urine (Colella et al., 2023). Aside from host-related factors that have been identified as having a specific role in the likelihood of infection recurrence, pathogen-related conditions (like invasion or virulence factors) also impact the severity of the infection and its resistance to antibiotic therapy (Chin et al., 2020).

A urinary tract infection can affect either the upper or lower urinary tracts. The syndrome characterized by dysuria, frequency, and sometimes suprapubic tenderness is referred to as cystitis (Fried, 2022). A single factor causes more than 95% of urinary tract.

Methods

The study included one hundred pregnant women with type 2 diabetes and was conducted in Baghdad. Study design and patients Diabetes patients who were not inpatients participated in the current study. In biomedical hematology and bacteriology laboratories, we obtained blood and urine samples, along with pertinent medical records, from one hundred patients diagnosed with diabetes. Every patient gave the following details: name, gender, age, duration of diabetes, and family history of the disease pregnancy and urinary tract infection

Sample collection and preparation

Patients had a 3-5 cc blood sample taken, in two tube EDTA to measured HbA1c and plain tube and allowed to clot for 5–10 minutes. The serum was then separated from the blood sample by centrifuging it for five minutes at a speed of 3000 revolutions per minute used to clinical parameters. Additionally, sterile urine caps bearing the patient's information were used to collect urine samples.

Methods for testing blood sugar

The HbA1c test, a test that used blood before separating serum, and a serum sugar test that was performed while fasting were the two test types used to determine the blood sugar level. Blood sugar levels were assessed following an overnight fast (no food) in a fasting blood sugar test. The criterion for prediabetes was 100–125 mg/dL, the threshold for diabetes was 126 mg/dL, and the threshold for normal fasting blood sugar was 99 mg/dL or less. Hormonal analysis for insulin resistance was also carried out.

Hormones

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Numerous hormonal axes are impacted by the placenta during pregnancy. During pregnancy, the placenta releases hormones into the mother's bloodstream. In some cases, the hormones secreted by the placenta either bypass or even replace the mechanisms that normally regulate hormones. Because placental hormones and hormones found in the nonpregnant state share structural similarities, placental hormones may also affect hormone secretion.

Pregnancy-specific hormones include prolactin, progesterone, and estrogen, cortisol, and estradiol, which are all present in the mother's blood in increasing concentrations during pregnancy. Hyperinsulinemia, reduced insulin-stimulated glucose uptake and glycogen synthesis, and a diminished capacity of insulin to inhibit hepatic gluconeogenesis are some of the diabetogenic effects that prolactin may potentially have. It has previously been reported that progesterone, estrogen, and cortisol act as mediators of the shift in insulin sensitivity that occurs during pregnancy.

Diagnosis of urinary tract infections

In outpatient laboratories, urinary tract infections were found in patients, the majority of whom had bacterial infections. Others experienced damage from bladder defects or sand and kidney stones. All of the patients were prescribed antibiotics, and many of them experienced repeated UTIs. Culture media and biochemical tests were used to isolate and characterize different species of bacteria. Table One

Statistical Analysis

Excel and the Statistical Package for Social Sciences (Graph pad Prism 9.5.0) program were used to analyze the data, and a P-value of less than 0.05 was deemed to be statistically significant. Pearson’s correlation coefficients (r) and their significant were used for analyzing results between all biochemical and biological parameters.

Results and Discussion

Thirty of the pre diabetes mellitus patients in this study tested positive for UTIs, while thirty tested negative. UTI positivity was absent in patients without pre diabetes [Table 2]. Due to complications that can pose a risk to both the mother and the unborn child, urinary tract infections (UTIs) are especially important in pregnant women with diabetes mellitus (DM) (Alhaj et al., 2024).

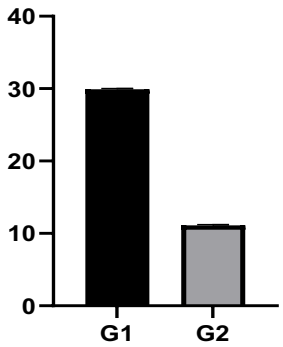

Figure1: relationship between prediabetes and UTIs

Urinary tract infections have long been thought to be predisposed by diabetes mellitus (Rochon et al., 2024). 100% of the prediabetic patients in this study who were married women tested

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positive for UTIs. This study sheds light on the relationship between diabetes mellitus (DM) and the prevalence of urinary tract infections (UTIs) in married women. Previous research has demonstrated that married women with prediabetic are more likely to experience UTIs (Fageräng et al., 2024; Raatz et al., 2024) discovered in his research that asymptomatic pyuria is becoming more common in female diabetics who have complications from retinopathy and nephropathy.

Table 1. the comparison of some clinical parameters in three groups

Parameters	Control	Pregnant without D.M	Pregnant with D.M
FSH mg/dl	88.9±0.10	92.4±0.10	146.4±0.20
HbA1c	5.1±0.15	5.4±0.10	6.7±0.24
HOMA IR (mg /dl)	1.3±0.34	1.48 ± 0.57	2.23±0.12
Prolactin (ng /mL)	8.60 ± 1.62	20.32± 2.10	23.76± 2.15
Progesterone (ng /mL)	0.42± 0.18	1.02±0.06	1.18±0.09
Estrogen (ng /mL)	12.05±1.47	15.53±2.4	17.05±2.52
Asprosin (ng /mL)	25.42±1.03	27.69±1.12	29.07±1.26

P-value 0.001*** when compared pregnant without D.M with pregnant with D.M and control groups in all parameter and there is no statistically significant when compared pregnant without D.M with control. The results of this study demonstrated that metabolic deficits predated gestational diabetes mellitus (GDM) by showing statistically significant relationships between pre-diabetic FBG and HOMA-IR in pregnancy. These associations persisted even after controlling for a number of possible confounders. As a result, they would be regarded as separate indicators for GDM prediction. Our findings reveal that in women who develop GDM, pathophysiological alterations linked to glucose control that may result in GDM are not only brought on by pregnancy but also exist prior to conception (Savona-Ventura et al., 2024; Cetin et al., 2024; Alwash et al., 2023). Increased blood levels of reproductive hormones, including progesterone, estrogen, and prolactin, are linked to several physiological changes associated with pregnancy (Noyola-Martínez et al., 2019).

Throughout pregnancy, estradiol levels gradually increase; by the third trimester, they have multiplied 100 times from prenatal levels. Progesterone and 17-hydroxyprogesterone levels are likewise obviously and consistently rising. The sex hormone-binding globulin levels rise by approximately five times during pregnancy. Elevated estrogen levels initiate neo-angiogenesis, the development of tissues that support lactation and eventually become the placenta. The typical pregnancy symptoms of weakness, vomiting, bowel motions, and headache are brought on by these endocrine changes (Fuhler, 2020). Sex hormones such as estrogen, progesterone, androgens, and prolactin can influence multiple aspects of immune system function and potentially impact MS development, activity, and risk because immune cells have hormone receptors. The effects of sex hormones will vary depending on the kind of target cell, the receptor subtype expressed on that cell type, and the hormone concentration. Therefore, to understand how gender affects MS and autoimmunity in general, it is crucial to understand the complex interactions between sex hormones, sex chromosomes, and immune response genes (Ysrraelit & Correale, 2019).

A recently identified glucogenic adipokine is asprosin (Mazur-Bialy, 2021) that rises with insulin resistance (Diao et al., 2023). Abnormal insulin resistance is linked to gestational diabetes mellitus (GDM), a dangerous illness that has numerous negative implications on both

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the mother and the fetus (Nakshine & Jogdand, 2023). Asprosin may be a predictor of DM diagnosis and a potential treatment target for type 2 diabetes and prediabetes (Diao et al., 2024). Since there is debate over asprosin's involvement in gestational diabetes, we looked into how asprosin levels changed in pregnant rats compared to pregnant women in order to understand its physiological function during a typical pregnancy.

Furthermore, we investigated the function of asprosin in the pathophysiology of gestational diabetes by assessing the plasma asprosin levels in pregnant-induced diabetic rats, presuming that it has a predictive function in the diagnosis of the condition.

Adipose tissue acts as an endocrine organ, controlling metabolism and preserving energy balance, as demonstrated by asprosin (Wondmkun, 2020). Excessive body fat can cause insulin resistance, which is a key contributing factor to the development of type 2 diabetes mellitus. To far, a great deal of study has been done to look into the molecules that influence insulin secretion and insulin resistance. White adipose tissue (WAT) secretes asprosin, a recently discovered adipokine that is essential for promoting the release of glucose from hepatic cells to sustain blood glucose levels in a normal state. The researcher also discovered that asprosin levels were higher in people with insulin resistance. Asprosin was identified as a possible novel therapeutic target for type 2 diabetes mellitus as a result of these studies (Hekim et al., 2023).

The impact of sex hormones on immune cells is described in Figure 2

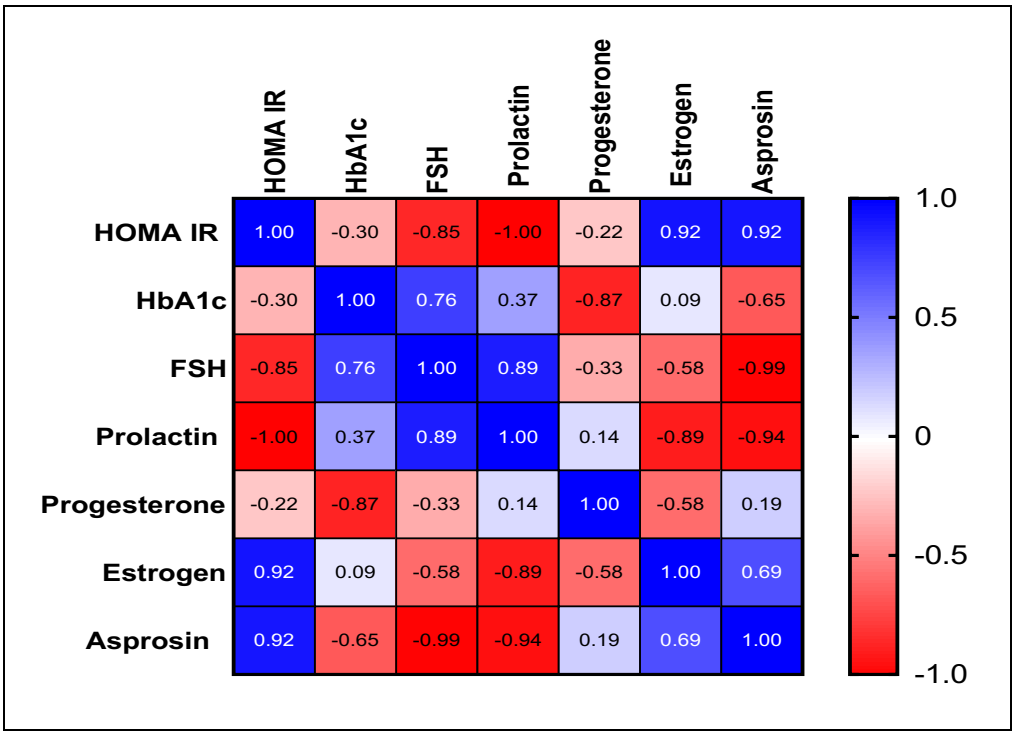

Figure 2. Correlation HOMA IR and asprosin with six hormones in prediabetic pregnant

In is table HOMA IR correlation negatively with FSH, prolactin and positively correlation with estrogen. But there is no correlation with progesterone. FSH correlation positively with HbA1c and prolactin, and negatively with estrogen and progesterone, prolactin negatively with estrogen will progesterone is negatively correlation with estrogen. In the other hand asprosin positively correlation with insulin resistance and estrogen will negatively with HbA1c, FSH, and prolactin.

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Area under the curve ROC for asprosin

The ROC curves were analyzed for asprosin in circulation to investigate its predictive value. The optimal cutoff value for circulating asprosin to predict prediabetes mellitus in pregnant was found to be > 27.39 ng/ml (sensitivity: 90%, specificity: 95%, and AUC: 0.987) at a 95% confidence interval of (0.968 ~ 1.000), and > 25.85 ng/ml (sensitivity: 70%, specificity: 75%, and AUC: 0.787) at a 95% confidence interval of (0.638 ~ 0.937), P <0.001 figure (3).

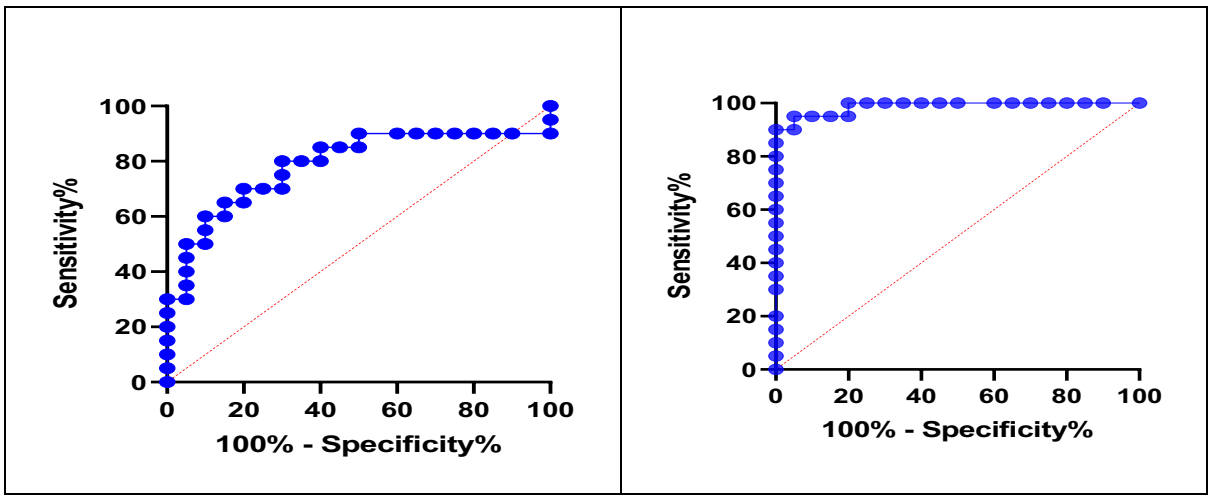

Figure 3. ROC-curve of asprosin Control- pregnant with and without D.M

According to the study, compared to DM patients without UTI, the majority of UTI patients had G+ve bacteria [Table 3].

Gram-negative enteric bacteria were found to be the primary etiologic agents of UTIs in various general population studies.

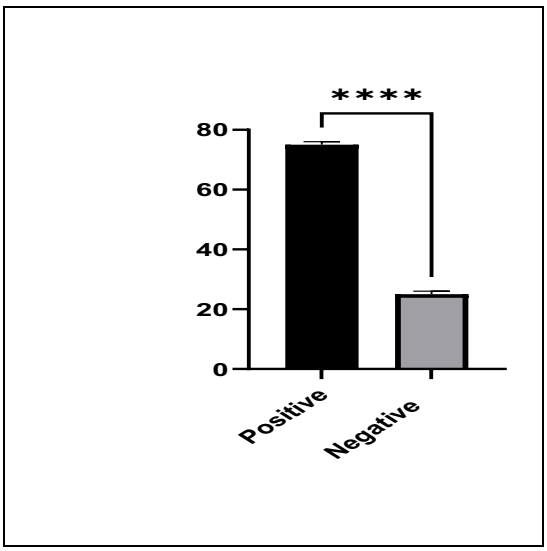

Figure 4. Results of urine culture among study groups.

Pregnancy also, encourages the occurrence of urinary tract infections (pregnancy) as a result of the sudden hormonal and anatomical changes, in addition to the increase in the result of pregnancy and diabetes, which contributes to supporting the growth of bacteria in the urine and thus the occurrence of infection Bacterial species belonging to the family Enterobacteriaceae can cause infection due to their possession of many virulence factors, the most important of

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which is their production of hemolysin, which acts as a cytotoxic agent by forming holes in the host's membranes, which leads to the release of iron, hemoglobin and other components necessary for bacterial growth. The produced hemolysin also lyses E. coli lymphocytes from bacteria and inhibits the process of phagocytosis and chemotaxis (Karunarathna et al., 2024). Studies indicate that 10% of pregnant women develop urinary tract infections due to the colonization of the urinary tract by these bacteria. These bacteria have many virulence factors that enable them to cause infection, and infection with these bacteria often leads to premature delivery (Mititelu et al., 2024).

Table 2. Antibiotic Sensitivity Distribution of Gram-Positive Bacteria Isolated from Married Women

Type of antibiotic	***Escherichia coli***	***S. epidermidis***	***Staphylococcus aureus***	***Klebsiella pneumoniae***	***Proteus mirabilis***	***P. aeruginosa***
Ciprofloxacin	75.3	50.3	82.5	55.6	77.4	72.3
oxacillin	0	89.7	87.3	0	0	26.7
Trimethoprim	6.46	52.6	74.7	23.66	15.6	43.45
Gentamicin	34.6	85.62	81.7	43.9	75.7	62.4
Amoxicillin	24.77	83.66	0	13.72	85.82	65.71
Nitrofurantoin	85.65	52.77	45.77	85.8	90.42	85.77
Ceftazidim	78.78	73.74	40.43	57.86	74.87	72.94
ampicillin	5.63	0	0	0	0	22

The antibiotics used to treat urinary tract infections in pregnant women should be safe for the mother and fetus. Ampicillin is always the best choice for pregnant women, but due to the emergence of resistance by bacterial pathogens that cause urinary tract infections, there are alternative drugs such as the cephalosporin group. However, nitrofurantoin, cephalosporins, and quinolones for the Tetracyline group have been found to have a toxic effect on the fetus, so these antibiotics should be avoided during pregnancy (Mandal, 2024). Pregnant women, especially those with diabetes, have a high probability of recurrence of urinary tract infection. Therefore, urine should be examined monthly (recurrent UTI) and a urine culture should be done because early treatment with antibiotics leads to avoiding many complications that a pregnant woman with urinary tract infection may be exposed to, including the development of the infection into acute pyelonephritis and nephritis, in addition to labor (Acutephlonephritis) (Pacheco & Omere, 2024).

Conclusion

The study's findings showed that asprosin had strong associations with pregnancy, both with and without D.M., when compared to healthy people. It also found that D.M and UTI were strongly correlated, with S. aureus and E. coli being the primary offenders. Asprosin was predicted to cause D.M. disease in pregnant patients based on the ROC statistical findings. According to the correlation statistical result, sex hormones and asprosin are closely related in pregnant women with and without D.M. In order to identify risk factors for D.M., it may be concluded that the study examines the probable connection between asprosin hormone and prediabetic pregnancy.

Financial Disclosure

No financial disclosure occurs.

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Conflict of Interest

Nothing to declare.

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