Journal of Progressive Medical Sciences
ISSN: 3052-8518
J.P.M.S
DOI: https://doi.org/10.63939/80aaz067

Vol. 2 , No. 5 , May 2026

RESEARCH Open Access

Diagnostic Performance of Maternal Serum Visfatin in Predicting Preterm Labor: Evidence from ROC Curve Analysis

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Abstract

Background: Spontaneous preterm birth remains a leading cause of neonatal morbidity and mortality worldwide. Growing evidence suggests that inflammatory pathways play a significant role in the pathophysiology of spontaneous preterm birth. Phesfatin, a multifunctional adipokine with immunometabolic properties, has emerged as a potential biomarker associated with inflammatory activation during pregnancy. PTL is defined as birth occurring prior to the 37th week of pregnancy. It is one of the leading causes of neonatal morbidity and mortality worldwide. **Objective:** The present research explored the potential use of maternal serum visfatin as an early biomarker for diagnosis of spontaneously occurred PTL and evaluated its relationship with inflammation. **Methodology:** hospital-based case–control study was conducted between March and June 2025 in Basrah governorate, Iraq. Ninety pregnant women in the third trimester were enrolled, 60 of them with spontaneously occurred PTL and 30 healthy pregnant as a control matched according to their gestational age. Maternal serum concentrations of visfatin, were determined via enzyme-linked immunosorbent assay), and addition to the C-reactive protein estimated by biochemical analyzer and Total white blood cells (WBC) counts obtained with an automated hematology analyzer (markers of inflammation). **Results:** Concentration of visfatin was significantly higher in patients compared to control women (39.63 ± 8.35 vs. 21.15 ± 5.93 ng/mL; $p < 0.001$). The ROC curve indicated high diagnostic performance of maternal serum visfatin (area under the curve [AUC]: 0.962). The optimal cutoff value of visfatin of 27.7 ng/mL allowed predicting PTL with sensitivity and specificity equal to 93.3% and 90.0%,

respectively. In addition, there were strong correlations between visfatin levels and CRP and WBCs. According to multivariate analysis, visfatin was found to be an independent biomarker of spontaneously occurred PTL. **Conclusions:** The case study concluded that maternal serum visfatin levels are strongly associated with spontaneous preterm birth and activation of systemic inflammation. The diagnostic findings suggest that visfatin may be a promising adjunctive biomarker for identifying women at risk of spontaneous preterm birth. Large-scale, prospective, multicenter studies are needed to validate these findings and determine their clinical relevance.

Keywords: Visfatin; Preterm Labor; Adipokine; Inflammation; Biomarker; ROC Analysis; Pregnancy.

Introduction

Preterm labor (PTL), which is the delivery occurring before 37 weeks of gestation, is one of the main causes of neonatal morbidity and mortality globally [1,2]. Although there have been advancements in the management of obstetrics and neonatal complications, the burden of preterm birth in various parts of the world, especially in low-and-middle-income countries, still remains high due to various neonatal complications such as respiratory distress syndrome, sepsis, and intraventricular hemorrhage [1–3]. Therefore, early detection of at-risk pregnant women and providing them with prevention and treatment options can contribute significantly to maternal and neonatal outcome improvement. Currently used methods in predicting spontaneous PTLs, such as measurements of cervical length and fetal fibronectin, are inefficient and cannot provide accurate predictions [3,4]. As a result, researchers have started paying attention to various biomarkers such as inflammatory factors.

Visfatin is an adipocytokine playing multiple roles in metabolic and inflammatory processes [5,6]. Normally, visfatin concentrations gradually increase with the progression of pregnancy; however, a high level of the substance can lead to different obstetrical conditions like gestational diabetes mellitus and preeclampsia [7–9]. Furthermore, according to scientific evidence, visfatin activates inflammatory pathways leading to preterm labor through increased cytokine production and NF-κB pathway activation [10–12]. Based on the above considerations, the aim of the current study is to explore the role of maternal serum visfatin as a marker of spontaneous

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preterm labor and investigate its correlation with CRP, WBC, and other inflammatory markers using receiver operating characteristic (ROC) curve analysis.

Materials and Methods

This case–control study was carried out at the Department of Obstetrics and Gynecology, College of Medicine, University of Basrah, in cooperation with Al-Imam Al-Sadiq Hospital, Basrah, Iraq, from March to June 2025. Ninety pregnant women during the third trimester (28-40 weeks of pregnancy) were recruited and assigned into two groups. Preterm labor (PTL) group contained 60 pregnant women with spontaneous PTL at gestational ages between 28^+0 and 36^+6 weeks. It was mentioned that the spontaneous preterm labor was characterized as regular uterine contractions along with cervical effacement and dilatation prior to 37 weeks. No cases of PPROM (preterm premature rupture of membranes) were included because PPROM may have the effect on the level of inflammatory mediators caused by inflammation due to PPROM. All PTL cases had no medical induction.

Control group represented 30 women without symptoms of labor. Most of control cases were recruited from outpatients' antenatal clinic. They were matched to the case group based on gestational age, especially 32-36 weeks window. In addition, the gestational age of the controls was confirmed by dating first trimester ultrasound or the history of last menstrual period. It is important that controls delivered their infants at term (≥37 weeks) without any obstetric complications. Age, parity, and gravidity were estimated for all subjects, and gestational age was confirmed by first trimester ultrasound or menstrual period dating.

Inclusion criteria: included the following features of participants: age between 18-40 years, single intrauterine pregnancy, and confirmation of spontaneous PTL in the case group. Some exclusion criteria were used to exclude potential factors that might independently influence the serum visfatin levels and inflammatory state of women. **Exclusion criteria:** included multifetal pregnancies, major fetal malformations, placental abruption, placenta previa, hypertensive disorders of pregnancy, gestational diabetes mellitus necessitating pharmacological management, clinical chorioamnionitis, infection, chronic inflammatory or autoimmune diseases, and uncontrolled metabolic disorders. Besides, women with anti-inflammatory medication

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intake, such as corticosteroids and NSAID (non-steroidal anti-inflammatory drug) use not less than one week ago, were not considered [13].

Sample Collection and processing:

Blood samples from all subjects were drawn prior to commencement of any medical interventions. Blood samples in the PTL group were obtained right after admission to the hospital and before administering tocolytics, corticosteroids, antibiotics, or intravenous fluids to avoid changes due to pharmacological therapy in laboratory values. Maternal venous blood about 5 mL in volume was taken in plain glass tubes from the antecubital vein. The samples were allowed to clot at room temperature, followed by 10 minutes of centrifugation at 3000 rpm. Then the separated serum was aliquoted and kept frozen at −20°C until analysis. To reduce variations between assays, samples were analyzed in one batch at the end of data collection period.

Laboratory Measurements:

Serum Visfatin estimation:

For determining concentrations of visfatin in maternal serum, a sandwich enzyme-linked immunosorbent assay (ELISA) was used in accordance with the manufacturer's guidelines. Specifically, we used a high-sensitivity Human Visfatin (NAMPT) ELISA kit (Elabscience, USA). Each sample was analyzed in duplicate and the average values were used in further analysis. Assay sensitivity and intra- and inter-assay coefficients of variation were within acceptable ranges, established by the manufacturer.

Serum C-reactive protein assessment:

Concentration of inflammatory markers was analyzed to assess systemic inflammatory activity in pregnant women. Serum C-reactive protein (CRP) level was measured with a high-sensitivity immunoturbidimetric test (Biotech Co., Korea) in an automated biochemical analyzer.

White blood cells count detection:

Total white blood cells (WBC) counts (×109/L) obtained with an automated hematology analyzer (Mindray BC-3000, China) were considered as indicators of systemic inflammatory activity. Concentration of hemoglobin was determined to characterize the study subjects, but not to include these data in our analysis. Calibration

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was routinely performed in laboratory instruments and daily quality controls were run to provide accuracy of results. Routine biochemical tests, including tests for renal and liver function, were performed in order to rule out the presence of clinical condition which can affect the results of inflammation biomarkers' measurement. Urine analysis was additionally performed to eliminate the possibility of urinary tract infection or marked proteinuria. This made sure there were no baseline disturbances which can be responsible for the changes in inflammation biomarker concentrations [14].

Statistical Analysis

The data were statistically analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Normality tests were performed by applying the Kolmogorov–Smirnov test. For continuous data, normal distribution was expressed by mean ± standard deviation (SD), whereas for non-normal distribution by median with interquartile range (IQR). For categorical data, percentages and frequencies are presented. Group differences were evaluated based on Student's t-test for continuously normally distributed variables (e.g., age, gestational age, biomarkers concentrations). For non-parametric data group differences, Mann-Whitney U test was applied. Group differences among categorical variables (e.g., parity, previous preterm history) were assessed with Chi-Square or Fisher's Exact Test.

Pearson's Correlation Coefficient (r) was performed in order to investigate the association of maternal serum visfatin levels with inflammatory markers (CRP and white blood cells count) and gestational age during delivery. Statistical significance was accepted for p values < 0.05 (two-tailed). Diagnostic efficacy of maternal serum visfatin in predicting preterm labor (PTL) was determined via receiver operator characteristics (ROC) curves. Diagnostic discriminatory accuracy was indicated by calculating Area Under the Curve (AUC). The optimal cutoff point of visfatin serum level was estimated using Youden Index (sensitivity+specificity−1). In addition, sensitivity, specificity, positive and negative predicted values along with 95% Confidence Intervals (CI) were calculated for each test.

In order to determine that maternal visfatin independently predicts PTL, multivariate logistic regression was applied. Multivariate logistic regression analysis adjusted for potential confounding factors such as maternal age, BMI, parity. Adjusted ORs and 95% CI for each test with p value < 0.05 were considered significant.

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Ethical approval:

Ethical approval was gained from the Institutional Review Board of University of Basrah, and informed consents were collected from all participants

Results

Participant Characteristics

In the current investigation, there were a total number of 90 pregnant women, including 60 patients with spontaneous preterm labor (PTL) and 30 healthy pregnant women. Information on clinical and demographic features of these two groups is provided in Table 1. There was no difference observed between the two groups as concerns maternal age. The mean maternal age was 28.1 ± 5.0 years in the PTL group, as compared with 27.6 ± 4.3 years in the control group ($p = 0.74$). Likewise, the parity distribution showed similar values with 38% of the patients being primiparous in the PTL group and 40% of the participants being primiparous in the control group ($p > 0.05$). Around 10% of the women belonging to the PTL group had experienced a spontaneous preterm birth, while there was no one having this experience in the control group. The mean gestational age at the moment of the procedure was 34.2 ± 1.5 weeks in the PTL group and 33.9 ± 2.8 weeks in the control group, and these two values did not differ significantly ($p = 0.87$). All healthy control women delivered babies at term delivery after blood collection (gestational age at delivery: 38.5 ± 1.2 weeks).

Inflammatory Markers: WBC Count and CRP

There were statistically significant differences in inflammatory markers between women with spontaneous preterm labor (PTL) and the group of pregnant healthy subjects indicating the existence of the activated systemic inflammatory reaction in women with spontaneous PTL. The mean maternal WBC counts were higher in PTL cases compared to control ones (11.86 ± 2.23 vs. 8.02 ± 1.49 × 109/L, respectively; $p < 0.001$). A vast majority of women with PTL were leukocytes (>10 × 109/L), while only few subjects from the control group showed increased counts of white blood cells.

The same trend was revealed when the mean CRP serum levels in different groups were analyzed. There were considerably elevated serum levels of CRP in the PTL group compared to control one (5.56 ± 1.13 vs. 2.97 ± 0.91 mg/L, respectively; $p < 0.001$).

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The majority of PTL women had the CRP level more than 5 mg/L, while most control women demonstrated the CRP level less than 5 mg/L.

Table 1. Clinical Characteristics of Study Groups

Characteristic	Control (n = 30)	Preterm Labor (n = 60)	p-value
Maternal age (years)	27.6 ± 4.3	28.1 ± 5.0	0.74
Primiparous (%)	40%	38%	0.85
Prior spontaneous PTL (%)	0%	10%	0.07
Gestational age at sampling (weeks)	33.9 ± 2.8	34.2 ± 1.5	0.87
Gestational age at delivery (weeks)	39.1 ± 1.1 (term)	34.2 ± 1.5 (preterm)	NA
WBC count (×10⁹/L)	8.02 ± 1.49	11.86 ± 2.23	<0.001
CRP (mg/L)	2.97 ± 0.91	5.56 ± 1.13	<0.001
Visfatin (ng/mL)	21.15 ± 5.93	39.63 ± 8.35	<0.001

NA: not applicable for statistical comparison (by definition, control deliveries were term vs. PTL preterm).

Visfatin Levels in Preterm Labor with. Controls

In accordance with the hypothesis underlying this study, maternal serum visfatin concentration was significantly elevated in pregnant women with spontaneous preterm labor in comparison with healthy control participants. Thus, the average concentration of serum visfatin in the former was 39.63 ± 8.35 ng/mL, which was almost two times higher than in the latter (21.15 ± 5.93 ng/mL, $p<0.001$).

Correlation of Visfatin with CRP and WBC

Significant positive correlations have been established between the maternal serum levels of visfatin and various inflammatory markers during spontaneous preterm labor (PTL). Maternal serum visfatin levels showed a highly positive correlation with C-reactive protein (CRP) concentrations ($r = 0.734$, $p < 0.001$). In addition, the presence of a high correlation between visfatin and total white blood cell (WBC) counts ($r = 0.679$, $p < 0.001$) confirms an association between the elevation of serum visfatin levels and leukocytes' activation. An analysis of the relationship between other factors also

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revealed a negative correlation between serum visfatin levels and gestational age at delivery ($r \approx -0.45$, $p = 0.002$).

ROC Curve Analysis of Visfatin for PTL Prediction

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of maternal serum visfatin in distinguishing women with spontaneous preterm labor from healthy pregnant controls. The analysis demonstrated excellent discriminatory ability, with an area under the curve (AUC) of 0.962 (95% CI: 0.92–0.99), indicating a highly accurate predictive performance for visfatin as a biomarker of PTL. The optimal cutoff value for maternal serum visfatin was identified at 27.7 ng/mL using Youden's index. At this threshold, visfatin achieved a sensitivity of 93.3% and a specificity of 90.0%. In addition, the positive predictive value (PPV) and negative predictive value (NPV) were 93.3% and 90.0%, respectively.

Table 2. ROC Curve Analysis of Maternal Serum Visfatin for Prediction of Preterm Labor

Parameter	Value
Area under the curve (AUC)	0.962 (95% CI: 0.92–0.99)
Optimal cutoff (ng/mL)	27.7
Sensitivity (%)	93.3
Specificity (%)	90.0
Positive predictive value (%)	93.3
Negative predictive value (%)	90.0

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The diagnostic accuracy of visfatin was further illustrated by the ROC curve, which confirmed excellent discriminatory ability (Figure 1).

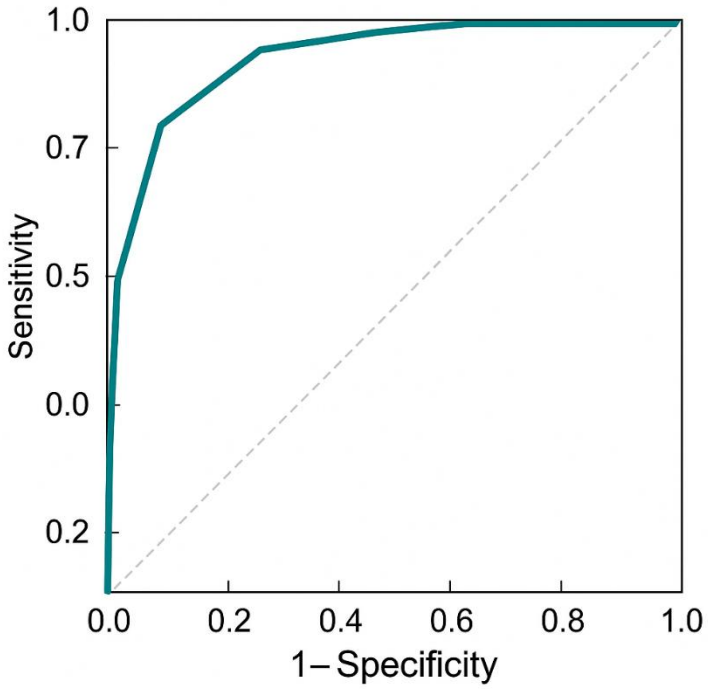

Figure 1. The ROC test performed on maternal visfatin for early detection of preterm labor is highly discriminatory with an AUC of 0.962 (CI: 0.92–0.99). Using the best cut-off point of 27.7 ng/mL, visfatin has been found to have a sensitivity of 93.3% and specificity of 90.0%.

According to the results of ROC analysis, the accuracy and sensitivity of predicting PTL in women was very high. Specifically, the area under the curve reached 0.96, whereas the cutoff point at the level of 27.7 ng/ml provided sensitivity and specificity higher than 90%.

Discussion

As the results of our study show, visfatin levels in maternal sera were considerably increased in patients with spontaneous PTL compared to the controls of gestational age-matched subjects. These changes took place concurrently with elevated levels of markers of the inflammatory process, like CRP and WBC, and, therefore, prove the participation of visfatin in the inflammatory profile of PTL. Also, our study demonstrates specific diagnostic value of the marker, which emphasizes its prospective use for PTL diagnostics. The pronounced elevation of visfatin concentration in PTL patients implies the active participation of the substance in the pathogenesis of preterm labor rather than being a secondary phenomenon. Therefore, this study provides

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evidence of a link between elevated maternal serum phosphatine levels and spontaneous preterm labor. Distribution analysis shows that the vast majority of patients who experienced spontaneous preterm labor had significantly higher serum phosphatine levels than their healthy counterparts. Specifically, serum phosphatine concentrations in 90% of pregnant women experiencing preterm labor were above 30 ng/mL, while the concentration in the control group did not reach this level. Interestingly, the lowest concentration recorded in women experiencing preterm labor was very close to the highest concentration recorded in the control group.

To rule out any potential influence of gestational age differences on plasma visfatin levels, given that previous studies have indicated a gradual increase in this cytokine throughout pregnancy and a steady rise in visfatin levels during the last months of pregnancy due to physiological mechanisms [7], the ages of the participants were deliberately matched. In normal circumstances, the observed increase in visfatin levels in women with preterm birth reflects a pathological process resulting from an inflammatory mechanism or related to stress. Several factors may contribute to the elevated visfatin levels, including placental inflammation, oxidative stress, decidual membrane damage, and the release of inflammatory cytokines.

It has been previously suggested that visfatin is a multifunctional adipokine with pro-inflammatory and metabolic effects. Experimental research has shown that visfatin enhances IL-6 expression and other inflammatory mediators involved in the process of cervical ripening and uterine contractility [19,20]. In other words, the increased levels of visfatin not only reveal inflammatory activation in PTL but are also capable of contributing to it, which is confirmed by the obtained positive correlation of the substance with inflammatory markers CRP and WBC count. It is worth noting that previous research revealed elevated visfatin levels in patients with PTL and intra-amniotic infection [10]. Also, increased salivary visfatin levels were found in spontaneous preterm labor patients [11]. Our study adds new data to existing literature by proving the existence of increased serum levels of visfatin together with high diagnostic value determined by ROC curve analysis.

As was mentioned above, individuals who had the highest serum levels of visfatin also had the highest levels of CRP and WBCs. In contrast, patients whose serum visfatin levels were low had much lower CRP and WBC levels compared to the rest of the study

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participants. Such results confirm the hypothesis that visfatin levels are correlated with spontaneous PTL due to their association with inflammation. Despite the fact that a previous preterm birth can be considered as a risk factor for subsequent preterm births, the low percentage found in this sample would not likely affect comparison results. Laboratory examinations (renal and liver function tests) demonstrated normal physiological values in all subjects involved. None of the women had any signs of infection (including UTI, fever, or chorioamnionitis), thus suggesting that the group under study consisted of generally healthy pregnant women who differed from each other in the presence of spontaneous preterm labor. Furthermore, higher levels of maternal serum visfatin in PTL patients compared to control subjects correlated with earlier gestational age at the time of delivery, implying that pronounced visfatin elevation occurred mostly in severe cases of PTL. It seems reasonable to assume that exaggerated inflammation is one of the causes of very early preterm births, and, therefore, visfatin may be considered as an indicator of the intensity of the process.

This particular study design included strict matching for gestational age to eliminate its influence on the physiological levels of circulating visfatin. Given the similarity of gestational age sampling, this result suggests that visfatin elevation is mainly due to spontaneous PTL and not to gestational physiological changes. Thus, considering the nature of spontaneous PTL as an inflammation-related condition, one can assume that elevated maternal serum visfatin concentration in PTL cases was probably a consequence of inflammatory processes occurring during the development of spontaneous preterm labor.

Interestingly, serum visfatin concentrations recorded in healthy control participants corresponded to physiologically expected levels for late pregnancy, while the values found in PTL participants were well above this level. Thus, the result provides further evidence that high maternal serum visfatin may play a role in immunometabolic processes involved in PTL development. Notably, the link between high maternal serum visfatin and spontaneous PTL was confirmed even after adjustment for age, BMI, and parity. Also, the values of BMI in these two groups were similar, which means that the contribution of maternal adiposity to this effect could be negligible. Thus, the conclusion about maternal serum visfatin being an important biomarker associated with PTL seems highly plausible.

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High correlation between visfatin and CRP is especially noteworthy since CRP is considered a reliable biomarker of systemic inflammation. The simultaneous increase in the levels of these factors indicates that the biological pathway responsible for the inflammatory process during PTL involves visfatin. Moreover, the association of the elevated visfatin serum level with an increased number of white blood cells suggests that increased activation of the immune system during spontaneous PTL is also mediated by visfatin.

Though mild increase of CRP occurs in late pregnancy, elevated values indicate a more pronounced inflammatory response accompanying preterm labor. It may be stated that there is a link between enhanced inflammatory response in spontaneous preterm labor regardless the presence of the infection. Though mild physiological leukocytosis is a characteristic feature of late pregnancy, high leukocyte levels in patients with PTL reflect a pathological reaction instead of physiological changes caused by gestational age progression. Moreover, there was no clinical infection or chorioamnionitis confirmed in all the recruited individuals. It seems that the subclinical or sterile inflammation plays an important role in preterm labor initiation. Thus, equal gestational ages of the compared groups prove that increased counts of WBC are connected with the process of spontaneous preterm labor. Thus, the elevated level of WBC together with high serum CRP concentration proves that a specific systemic inflammatory reaction exists in women with spontaneous preterm labor. However, it should be noted that there were no any baseline medical conditions that could cause such an inflammation in both groups of patients. Hence, it can be concluded that inflammatory changes found in the analysis are related to PTL only and are not affected by some other diseases. Consequently, it will facilitate the understanding of the possible association of serum visfatin and its levels.

The obtained data also prove that visfatin participates in the same inflammatory process as CRP. The production of CRP is regulated by IL-6 [18], whereas visfatin was shown to increase IL-6 expression via activation of inflammatory pathways, such as NF-κB and TLR4-dependent ones [19,20]. From this point, visfatin may be viewed both as a biomarker and a mediator of PTL inflammation. From the practical point of view, high sensitivity and specificity of visfatin imply its potential application as a non-invasive biomarker for early PTL prediction. Unlike currently used predictive techniques (e.g., fetal fibronectin testing), visfatin revealed excellent performance

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among other potential markers of the disease [17,22]. Furthermore, incorporating visfatin into combined predictive algorithms along with other clinical and biochemical parameters may increase their diagnostic ability and enhance patient management. However, several limitations of our study should be mentioned. Namely, we used relatively small sample sizes and conducted the experiment in only one hospital, which decreases the reliability of our results. Also, while major inflammatory and metabolic factors that might distort our results were taken into account, the possibility of presence of subclinical inflammation cannot be fully excluded. Further multicenter research will be required to validate our conclusions and establish reference values for visfatin. High serum visfatin levels corresponded to low gestational age during delivery, thus showing that more premature deliveries exhibited higher serum visfatin levels than other participants. This finding may indicate a proportional relationship between visfatin levels and the premature stage of spontaneous PTL. To sum up, the presented data provide new evidence of the connection between visfatin and inflammation-related processes occurring in spontaneous PTL. Thus, the concurrent relationship between visfatin and CRP, WBC count, and gestational age during delivery can be regarded as biologically relevant for PTL.

Although inflammatory markers such as CRP and WBC count were positively associated with visfatin, combining these markers with visfatin did not significantly improve the overall predictive performance compared with visfatin alone. This finding suggests that maternal serum visfatin may independently capture a substantial proportion of the inflammatory activity associated with PTL. Overall, the ROC analysis supports the potential value of maternal serum visfatin as a highly sensitive and specific biomarker for the early prediction of spontaneous preterm labor. Maternal serum visfatin concentrations of patients who were suffering from spontaneous preterm labor (PTL) were approximately 1.8 times higher than those found in the control healthy pregnant women of the same gestational age, which demonstrated statistical significance and high importance. The levels of inflammatory indicators, such as white blood cell (WBC) count and C-reactive protein (CRP) values, were considerably higher in the experimental group of women suffering from PTL, which indicated that their bodies were under the influence of inflammation. Moreover, maternal serum visfatin levels correlated positively with the values mentioned above and revealed a direct link between the substance and the factors responsible for PTL.

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Recent study findings indicate that maternal serum visfatin has a high ability to correctly identify women with PTL while maintaining a low false-positive rate among healthy controls. The ROC findings further demonstrated that most women with spontaneous PTL exhibited visfatin concentrations above the identified cutoff value, whereas the majority of controls remained below this threshold. This strong separation between groups highlights the potential clinical utility of visfatin as a non-invasive biomarker for early detection and risk stratification of preterm labor. Additional regression analysis demonstrated that elevated visfatin levels remained independently associated with PTL after adjustment for maternal age, body mass index (BMI), and parity. The adjusted odds ratio remained significantly elevated (adjusted OR ≈ 6.7, $p < 0.001$), indicating that increased maternal serum visfatin was a strong independent biomarker of spontaneous preterm labor. Taking into account the results mentioned above, one can suggest that maternal serum visfatin is a good predictor of PTL, whose predictive potential does not depend on age, BMI, and other characteristics. More specifically, a correlation between visfatin concentration and PTL at different stages is likely, which means that the substance appears in larger quantities with a growing intensity of inflammatory processes.

Numerous studies have analyzed the effect of adipokines, namely leptin, adiponectin, and resistin, on the development of various pregnancy-associated pathologies and preterm delivery. At the same time, visfatin, which belongs to the adipokine group, has received little attention in terms of predicting and explaining the phenomenon of spontaneous PTL. Nasri et al. established increased visfatin levels in the saliva of patients with spontaneous PTL, which was supposed to confirm visfatin involvement in triggering inflammation. This research adds another important finding concerning visfatin by showing increased levels of this adipokine in maternal blood. Ormindean et al. found altered adipokine blood levels in mothers of complicated pregnancies in relation to particular pathological factors. Despite this information, data related to the role of visfatin in the process of PTL are insufficient. As shown, the elevated inflammatory markers in this study correspond to existing knowledge regarding increased levels of various inflammatory mediators, such as IL-6, CRP, and procalcitonin, in pregnant women with PTL. Nevertheless, visfatin differs from other mediators because it is associated not only with inflammatory processes but also with metabolism. While the role of CRP is limited to the inflammatory response, visfatin is

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involved in metabolic functions, as well. It might explain why visfatin demonstrated higher accuracy of ROC curve compared to CRP. In general, visfatin might provide a more complex assessment of changes in both metabolic and inflammatory processes in pregnant women at risk of PTL.

From a mechanistic perspective, there are data on the role of visfatin in physiological pathways associated with premature birth. Musilová et al. revealed the correlation between increased eNAMPT concentrations in amniotic fluid and intra-amniotic inflammation as the cause of PPROM, thus confirming the participation of visfatin in inflammation-induced prematurity. Moreover, pharmacological experiments confirmed the ability of inhibitors of visfatin activity (for example, FK866) to inhibit inflammation and extend pregnancy. It indicates that visfatin can act not only as a marker but also as a molecule responsible for activating inflammation in women experiencing PTL. There are numerous markers that might be used in the prediction of PTL, including fetal fibronectin, IL-6 in the cervix, matrix metalloproteinases, and cell-free fetal DNA. Most of these molecules, despite being informative, show poor diagnostic accuracy when different clinical settings are considered. In addition, visfatin is characterized by both sterile and inflammation pathways, which might increase its clinical usefulness. Also, Tokgöz Çakır et al. noted the ability of systemic inflammatory indexes, such as NLR, in predicting spontaneous PTL. Thus, our results confirmed the presence of an inflammatory component in the pathogenesis of PTL; however, a more specific molecular marker of this process was revealed.

One of the advantages of visfatin in the context of biomarker is that it can integrate metabolic pathways with inflammatory mechanisms. Pregnancy is a state of both metabolic and immunological adaptation, and abnormalities in these mechanisms might lead to PTL [22]. In light of its metabolic-inflammatory nature, visfatin can be considered an adequate marker for the detection of inflammatory imbalance and disease activity. From the standpoint of clinical application, measuring maternal serum visfatin in pregnant women at risk of preterm delivery might help to stratify their risk. Particularly, in high-risk patients (especially those with a history of preterm birth), repeated testing during mid-to-late gestation may allow detecting signs of inflammatory activation before manifesting clinical symptoms [21]. In patients with active uterine contraction, assessment of serum visfatin level can be used as additional information for the decision on hospitalization and administration of steroid therapy [24].

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Development of obstetric research field leads to the creation of multi-marker algorithms aimed to predict poor pregnancy outcomes. In accordance with these advances, visfatin seems to be one of the promising components in future predictive algorithms because of its strong individual diagnostic value as well as the connection between visfatin and inflammatory activation [22]. Combination with other known markers such as CRP, IL-6, and fetal fibronectin can potentially increase the sensitivity of prediction in future studies. Moreover, understanding the mechanism of action of visfatin in relation to premature labor opens the perspective of its use in the prevention and treatment of preterm delivery. Based on experimental studies, it can be stated that targeting visfatin-related pathways can reduce inflammatory responses in preterm labor [20]. At present, there are no clinical applications for such strategies in the management of pregnant women, but maternal serum visfatin may become a surrogate biomarker.

As to the limitations of this study, first of all, it is necessary to mention that the small sample size may reduce the validity of obtained results (cut-off points and estimates). Second, this study is limited by its monocentric design; moreover, the study population belongs to the Iraqi ethnic group. It is possible that different genetic and environmental factors affect visfatin baseline levels; therefore, multicenter investigations should be performed. It is also worth noting that the results of this study concern visfatin as a biomarker specific for PTL. Nevertheless, it was shown earlier that increased visfatin concentration can be found not only in women with PTL, but also in pregnancy-related disorders, such as gestational diabetes mellitus or preeclampsia [8, 9]. Therefore, visfatin specificity requires confirmation in patients with different complications. Last but not least, this study is limited by its exclusive attention to PTL without membrane rupture. In light of this, the results cannot be extrapolated to other causes of preterm delivery, including PPROM and infection-related cases. Further investigations are necessary to reveal visfatin profile in PPROM and infectious PTL.

Conclusion

In conclusion, the current study has demonstrated significant elevation of visfatin levels in maternal serum in the presence of spontaneous preterm labor and its close association with inflammatory activity in the body. The correlation between visfatin, CRP and white blood cells count confirms the involvement of this protein in inflammation-related metabolic and immune processes which trigger premature labor.

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Finally, high levels of sensitivity and specificity achieved through ROC analysis confirm high potential of visfatin as a predictor of premature labor (PTL). The results of the study indicate the fact that visfatin might be used not only as an inflammatory marker. Its inflammatory and metabolic activity suggests some role in the pathogenesis leading to uterine premature activity. Clinical usefulness combined with high diagnostic efficacy makes visfatin a promising biomarker of the process under investigation.

Clinically, the use of visfatin might become helpful in early diagnosis of women who are more prone to preterm delivery. In addition, visfatin might become a crucial element of multi-marker models used for the prediction of premature parturition. However, the necessity of further investigations cannot be ruled out at this point. Large scale prospective studies should be conducted to prove the validity and efficacy of the current findings. Further research should focus on the timing of the phenomenon, biological source of the protein and its exact role in PTL, as well as its potential value for therapy. Overall, the current study adds valuable data about maternal serum visfatin being a relevant inflammatory and metabolic biomarker in premature labor and the related pathogenetic mechanisms.

References

1. Cao G, Liu J, Liu M. Global, regional, and national incidence and mortality of neonatal preterm birth, 1990–2019. JAMA Pediatr. 2022;176(8):787–796.
2. World Health Organization. Born Too Soon: Decade of Action on Preterm Birth. Geneva: WHO; 2023.
3. Pascoal E, Wessels JM, Aas-Eng MK, et al. Strengths and limitations of diagnostic tools for endometriosis and relevance in diagnostic test accuracy research. Ultrasound Obstet Gynecol. 2022;60(3):309–320.
4. MacDonald TM, Walker SP, Hannan NJ, Tong S, Kaitu'u-Lino TJ. Clinical tools and biomarkers to predict preeclampsia. EBioMedicine. 2022;75:103780.
5. Dakroub A, Nasser SA, Kobeissy F, et al. Visfatin: an emerging adipocytokine bridging the gap in the evolution of cardiovascular diseases. J Cell Physiol. 2021;236(9):6282–6296.

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6. Abdalla MMI. Role of visfatin in obesity-induced insulin resistance. World J Clin Cases. 2022;10(30):10840–10851.

7. Cortés-Salim P, González AP, Gómez-Ojeda A, et al. Serum levels of visfatin and vaspin in healthy and complicated pregnancies and their association with anthropometric measures of their offspring. Clin Chim Acta. 2025 (in press).

8. Jiang YK, Deng HY, Qiao ZY, et al. Visfatin level and gestational diabetes mellitus: a systematic review and meta-analysis. Arch Physiol Biochem. 2021;127(5):468–478.

9. Amiri-Dashatan N, Koushki M, Hosseini H, et al. Association between circulating visfatin and pre-eclampsia: a systematic review and meta-analysis. J Matern Fetal Neonatal Med. 2022;35(13):2606–2618.

10. Cho HY, Lee JE, Park KH, et al. Identification and characterization of plasma proteins associated with intra-amniotic inflammation and/or infection in women with preterm labor. Sci Rep. 2024;14:14654.

11. Nasri K, Mehrabi M, Bayani M, Almasi-Hashiani A. Maternal saliva visfatin level in term and preterm labor: a case control study. PLoS One. 2023;18(7):e0288786.

12. Musilova I, Kolackova M, Andrys C, et al. Nicotinamide phosphoribosyltransferase and intra-amniotic inflammation in preterm prelabor rupture of membranes. J Matern Fetal Neonatal Med. 2021;34(5):736–746.

13. Tokgöz Çakır B, Aktemur G, Karabay G, et al. Evaluation of complete blood count parameters and inflammation markers in spontaneous preterm labor. Am J Reprod Immunol. 2025;93(2):e70051.

14. Morisaki N, Piedvache A, Nagata C, et al. Maternal blood count parameters of chronic inflammation by gestational age and their associations with risk of preterm delivery in the Japan Environment and Children's Study. Sci Rep. 2021;11:14690.

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15. Cui H, Du X, Liu C, et al. Visfatin promotes intervertebral disc degeneration by inducing IL-6 expression through the ERK/JNK/p38 signalling pathways. Adipocyte. 2021;10(1):110–121.

16. Yao S, Jiang C, Zhang H, et al. Visfatin regulates Porphyromonas gingivalis LPS-induced proinflammatory/prodegradative effects in periodontal cells partially via the NF-κB pathway. Biochim Biophys Acta. 2021;1867(2):166047.

17. Sezginer EK, Kirlangiç ÖF. Analysis of changes in serum levels and gene expression profiles of novel adipocytokines (omentin, vaspin, irisin, visfatin) and their correlation with serum C-reactive protein levels in endometriosis. Turk J Obstet Gynecol. 2022;19(3):204–212.

18. Gomez-Lopez N, Galaz J, Miller D, et al. The immunobiology of preterm labor and birth: intra-amniotic inflammation or breakdown of maternal–fetal homeostasis. Reproduction. 2022;164(2):R11–R39.

19. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. N Engl J Med. 2008;358(20):2166–2175. doi:10.1056/NEJMra0707600.

20. Gong YY, Peng HY. Correlation analysis of epicardial adipose tissue thickness, C-reactive protein, interleukin-6, visfatin, JAZF1 and type 2 diabetic macroangiopathy. Lipids Health Dis. 2021;20(1):70.

21. Semerena E, Nencioni A, Masternak K. Extracellular nicotinamide phosphoribosyltransferase: role in disease pathophysiology and as a biomarker. Front Immunol. 2023;14:1268756.

22. Romero R, Dey SK, Fisher SJ. Preterm labor: one syndrome, many causes. Science. 2014;345(6198):760–765. doi:10.1126/science.1251816.

23. Kurban Y, Alan Y, Uyar I, Atak Z, Aydemir O. Investigation of neutrophil/lymphocyte ratio and mean platelet volume in patients diagnosed with preterm labor. Paediatr (Turkish). 2021; [Epub ahead of print].

24. Menon R. Fetal inflammatory response at the fetomaternal interface: a requirement for labor at term and preterm. Immunol Rev. 2022;308(1):149–167.

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