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CORRELATION ANALYSIS OF SERUM PAPP-A2, PIGF WITH THE PROGNOSIS OF GESTATIONAL DIABETES MELLITUS

ANALIZA KORELACIJE SERUMSKOG PAPP-A2 I PLGF SA PROGNOZOM GESTACIJSKOG DIJABETES MELITUSA (GDM)

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Summary

Background: To assess the diagnostic efficacy of the detection of serum Pregnancy-Associated Plasma Protein A2 (PAPP-A2), placental growth factor (PIGF), and SFRP5 for the detrimental effects of gestational diabetes mellitus (GDM) on pregnant patients.
Methods: 242 patients who received a GDM diagnosis at this hospital between January 2023 and December 2024 were chosen to be the GDM group. The control group consisted of 156 healthy expectant mothers who received prenatal care at this hospital during the same time frame. Patients in the GDM group were divided into the well-controlled diabetes, poorly controlled diabetes, and high-risk groups based on glycated haemoglobin (HbA1c) levels. Based on their follow-up results, patients in the GDM group were divided into two groups: those with poor pregnancy outcomes and those with favourable outcomes. Serum PAPP-A2, PIGF, Adipokine SFRP5, and urine microalbumin (mAlb) levels varied between the GDM and normal pregnancy groups. Univariate and multivariate analyses were used to examine the factors influencing pregnancy outcomes and the relationships between serum PAPP-A2, PIGF, Adipokine SFRP5, and urine mAlb levels, and the

Kratak sadržaj

Uvod: Clj je bio da se ispita dijagnostička efikasnost određivanja serumskih nivoa proteina A2 u vezi sa trudnoćom (PAPP-A2), vaskularnog/placentarnog faktora rasta (PlGF) i SFRP5 u proceni štetnih efekata gestacijskog dijabetesa melitus (GDM) kod trudnica.
Metode: U GDM grupu su uključene 242 pacijentkinje kojima je dijagnostikovan GDM u našoj ustanovi u periodu od januara 2023. do decembra 2024. Grupu normalnih trudnoća činilo je 156 zdravih trudnica koje su u istom periodu obavljale prenatalne preglede u našoj ustanovi. Pacijentkinje iz GDM grupe su, prema nivou glikozilisanog hemoglobina (HbA1c), podeljene u grupu dobro kontrolisanog dijabetesa, loše kontrolisanog dijabetesa i u grupu visokog rizika. Na osnovu praćenja ishoda trudnoće, GDM grupa je dodatno podeljena na grupu sa nepovoljnim i grupu sa povoljnim ishodima. Upoređivani su nivoi serumskog PAPP-A2, PIGF, adipokina SFRP5 i urinarne mikroalbuminurije (mAlb) između GDM i kontrolne grupe. Jednostruka i multivarijantna analiza korišćene su za procenu faktora koji utiču na ishod trudnoće i veze nivoa PAPP-A2, PIGF, SFRP5 i mAlb sa stepenom kontrol glikemije i nepovoljnim ishodima trudnoće. Takođe je pro-

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degree of blood glucose control and adverse pregnancy outcomes. In addition, it has diagnostic efficacy for adverse pregnancy outcomes in patients with GDM.

Results: Serum PAPP-A2, PIGF, and Adipokine SFRP5 levels were considerably lower in the GDM group than in the group with a normal pregnancy (P<0.01). The levels of serum PAPP-A2, PIGF and Adipokine SFRP5 in the well-controlled diabetes group were greater than those in the poorly controlled diabetes group and the high-risk group (P<0.01). However, the urine mAlb level was lower than in the poorly managed diabetes group and the high-risk group (P<0.01). Compared to the group with good pregnancy outcomes, the group with poor pregnancy outcomes had significantly lower serum levels of Adipokine SFRP5, PIGF, and PAPP-A2 (P<0.01), while HbA1c, fasting blood glucose, and urinary mAlb levels were significantly higher in the poor pregnancy outcome group than in the good pregnancy outcome group. However, there was no statistically significant difference between the two groups in terms of body mass index, number of pregnancies, gestational age, or age (P>0.05). Serum PAPP-A2, PIGF, and Adipokine SFRP5 levels were protective factors against unfavourable pregnancy outcomes, according to multivariate logistic regression analysis (P<0.05), whereas urinary mAlb was a risk factor for adverse pregnancy outcomes (P<0.05). The efficacy of serum PAPP-A2, PIGF, and Adipokine SFRP5 detection for the diagnosis of adverse pregnancy outcomes was significantly greater than that of urinary mAlb detection (P<0.05). With a sensitivity of 96.7%, specificity of 90.8%, and an area under the curve (AUC) of 0.967, the combined detection approach outperformed the single-indication PAPP-A2 by a substantial margin (Z=3.088, P<0.01). PIGF (Z=2.615, P<0.01) and Adipokine SFRP5 (Z=3.560, P<0.01) were included, but there was no statistically significant difference in the AUC among the three indicators (P>0.05).

Conclusions: The levels of serum PAPP-A2, PIGF and Adipokine SFRP5 are correlated with the degree of diabetes control in patients with gestational diabetes mellitus (GDM). Combined detection helps improve the diagnostic efficacy for adverse pregnancy outcomes in GDM patients.

Keywords: pregnancy-associated plasma protein A2, placental growth factor, SFRP5, gestational diabetes, adverse pregnancy outcomes

cenjena dijagnostička efikasnost ovih biomarkera za predikciju nepovoljnih ishoda kod pacijentkinja sa GDM.

Rezultati: Nivoi serumskog PAPP-A2, PIGF i adipokina SFRP5 su bili značajno niži u GDM grupi u poređenju sa grupom normalne trudnoće (P<0,01). U grupi dobro kontrolisanog dijabetesa nivoi PAPP-A2, PIGF i SFRP5 bili su viši nego u grupi loše kontrolisanog dijabetesa i grupi visokog rizika (P<0,01), dok je nivo urinarne mAlb bio niži (P<0,01). Kod pacijentkinja sa nepovoljnim ishodom trudnoće zabeleženi su značajno niži nivoi PAPP-A2, PIGF i SFRP5 (P<0,01), uz značajno više vrednosti HbA1c, glukoze natašte i urinarne mAlb (P<0,01), dok razlika u BMI-u, paritetu, gestacionoj starosti i godinama nije bila statistički značajna (P>0,05). Multivarijantna logistička regresija je pokazala da su PAPP-A2, PIGF i SFRP5 zaštitni faktori, dok je povišena mAlb nezavisan faktor rizika za nepovoljan ishod trudnoće (P<0,05). Kombinovana dijagnostika PAPP-A2, PIGF i SFRP5 je imala značajno veću efikasnost od mAlb (P<0,05) i pokazala je visoku senzitivnost (96,7%), specifičnost (90,8%) i površinu ispod krive (AUC=0,967). U poređenju između pojedinačnih markera (PAPP-A2, PIGF, SFRP5) nije bilo statistički značajne razlike u AUC vrednostima (P>0,05).

Zaključak: Nivoi serumskog PAPP-A2, PIGF i adipokina SFRP5 su povezani sa stepenom kontrole glikemije kod pacijentkinja sa gestacijskim dijabetesom mellitus (GDM). Kombinovana analiza ovih biomarkera poboljšava dijagnostičku efikasnost u predikciji nepovoljnih ishoda trudnoće kod GDM pacijentkinja.

Ključne reči: PAPP-A2, placentni faktor rasta (PlGF), adipokin SFRP5, gestacijski dijabetes, nepovoljni ishodi trudnoće

Introduction

A condition affecting glucose metabolism in pregnant women is called gestational diabetes mellitus (GDM) (1). It is a complication of pregnancy, with an incidence rate of approximately 10%, and there is an increasing trend annually. The pathogenesis of GDM is mainly due to insulin resistance and β-cell functional defects, which ultimately lead to disturbances in glucose metabolism. GDM often affects the health of both mothers and infants, resulting in rising rates of unfavourable pregnancy outcomes, like foetal discomfort in utero, premature birth and macrosomia (2–4). However, to date, there are no objective indicators that can predict pregnancy outcomes (5–7). Consequently, a study hotspot for academics is investigating objective markers for forecasting unfavourable pregnancy outcomes in people with gestational diabetes mellitus (GDM) (8). Pregnancy-Associated Plasma Protein A2 (PAPP-A2) is a member of the galactinin family. A decrease in its expression impairs placental oxygenation (9). Some studies (10–12) have reported that the GDM group's serum PAPP-A2 levels are notably lower. PAPP-A2 is involved in the pathophysiology of pregnancy, but its association with pregnancy outcome remains unclear. The vascular endothelial growth factor family includes vascular placental growth factor (PlGF). Its expression level is significantly decreased in gestational diabetes mellitus (GDM), and it is related to adverse pregnancy outcomes (13). Secretory coil-associated protein 5 (SFRP5) is an adipokine that regulates both inflammation and insulin resistance (14). Its level is closely related to gestational diabetes mellitus (GDM) and renal function impairment, but its relationship with pregnancy outcomes remains unclear (15–17).

In this study, the levels of serum PAPP-A2, PIGF, and SFRP5 in patients with gestational diabetes mellitus (GDM) were jointly assessed to evaluate their diagnostic efficacy for adverse pregnancy outcomes.

Materials and Methods

General information

For the GDM group, 242 patients diagnosed with gestational diabetes mellitus (GDM) at our hospital between January 2023 and December 2024 were included. The patients had an average age of 27.36±3.45 years, ranging from 22 to 35 years. The mean gestational age was 25.80±1.34 weeks, with a range of 23 to 29 weeks. The average prepregnancy body mass index (BMI) was 20.36±1.68 kg/m[. Among them, 150 were primiparas, and 92 were multiparas.

The control group consisted of 156 healthy pregnant women who underwent prenatal examinations at our hospital. Their ages ranged from 22 to 35 years, with an average of 27.15±3.10 years. The mean gestational age was 25.62±1.32 weeks (range, 23–29 weeks), and the prepregnancy BMI was 20.47±1.52 kg/m^2. This group included 49 primiparas and 58 multiparas.

All participants provided written informed consent. This study was reviewed and approved by the hospital ethics committee.

Inclusion criteria: (1) Meeting the diagnostic criteria for GDM, ① fasting blood glucose (FBG) 5.1 mmol/L; ② postprandial blood glucose 10.0 mmol/L 1 hour; if the blood glucose level 2 hours after a meal is 8.5 mmol/L and any one of the three conditions is met, a diagnosis can be made. (2) All were singleton pregnancies. (3) There was no history of diabetes, hypertension or other conditions before pregnancy.

Exclusion criteria: (1) Multiple pregnancies; metabolic diseases such as hypertension and thyroid dysfunction; (2) Haematological and immune diseases; infectious diseases; (3) Malignant tumours, intellectual disability or mental illness; insufficiency of functions such as the heart, lungs and liver; (4) Cervical insufficiency, hormone therapy, and insulin resistance before pregnancy.

Collection and testing of blood samples

When the patient was admitted to the hospital, and during the prenatal check-ups of healthy pregnant women at the outpatient department, approximately 5 mL of venous blood from the elbow and approximately 5 mL of midmorning urine were collected. These samples were placed at room temperature and centrifuged, and the supernatant was stored at -80 °C for testing. The levels of glycated haemoglobin (HbA1c) and FBG were determined by using an automatic chemiluminescence immunoassay analyser. The level of microalbumin (mAlb) in the urine was determined via immunoturbidimetry. The levels of serum PAPP-A2, PIGF and SFRP5 were detected via enzyme-linked immunosorbent assay. All reagent kits were produced by Beijing Bell Bioengineering Co., Ltd., and were used in strict accordance with the instructions provided with each kit.

Group study

Patients in the GDM group were divided into two groups according to their HbA1c level: the well-controlled diabetes group (HbA1c<7.0%), the poorly controlled diabetes group (7.0% HbA1c<9.0%), and the high-risk group (HbA1c 9.0%). Preterm birth, foetal distress in utero, foetal growth restriction, neonatal asphyxia, and other conditions were categorised as bad pregnancy outcomes for the GDM group, whereas the remaining patients were classified as favourable pregnancy outcomes.

Observation indicators

Serum PAPP-A2, PIGF, SFRP5, and urine mAlb levels differed between the GDM and normal pregnancy groups. Univariate and multivariate analyses of factors influencing pregnancy outcomes were conducted, and the relationships between serum PAPP-A2, PIGF, SFRP5, and urine mAlb levels and the degree of blood glucose control and adverse pregnancy outcomes were analysed. In addition, it has diagnostic efficacy for adverse pregnancy outcomes in GDM patients.

Statistical processing and analysis

SPSS 22.0 was used for the processing and statistical analysis. The measurement data are normally distributed and reported as $\bar{x}\pm s$. Using the t-test, comparisons between two groups were made. Several groups were compared using analysis of variance, and the SNK-q approach was utilised for further pairwise comparisons. The χ^2 test was used to compare groups, and count results are presented as percentages or as counts. The influencing factors of unfavourable pregnancy outcomes were examined using logistic regression, and the diagnostic effectiveness of each index for unfavourable pregnancy outcomes in GDM patients was assessed using receiver operating characteristic (ROC) curves.

Results

Comparison of the serum PAPP-A2, PIGF, SFRP5 and urine mAlb levels among the groups

Urinary mAlb levels were considerably higher in the GDM group than in the normal pregnancy group, but serum PAPP-A2, PIGF, and SFRP5 levels were significantly lower in the GDM group. Differences were statistically significant (P<0.01), see *Table I*.

Relationships between the levels of serum PAPP-A2, PIGF, and SFRP5 and urinary mAlb and the degree of control of GDM-related diabetes

According to HbA1c levels, the patients in the GDM group were divided into 82 patients in the well-controlled diabetes group, 90 in the poorly controlled diabetes group, and 70 in the high-risk group. The levels of serum PAPP-A2, PIGF and SFRP5 in the high-risk group were significantly lower than those in the poorly controlled diabetes group and the well-controlled diabetes group (P<0.01), and the levels in the poorly controlled diabetes group were significantly lower than those in the well-controlled diabetes group (P<0.01). The urinary mAlb level in the high-risk group was considerably higher than in the poorly controlled diabetes group and the well-controlled diabetes group (P<0.01), and was also considerably higher in the poorly managed diabetes group than in the well-managed diabetes group (P<0.01; see *Table II*).

Univariate analysis of pregnancy outcomes for women with gestational diabetes mellitus (GDM)

The follow-up results of the GDM patients were as follows: 18 cases of foetal growth restriction, 2 cases of neonatal asphyxia, 30 cases of preterm birth and 6 cases of foetal distress in utero. The remaining patients (186 patients) were placed in the good pregnancy result group, while these patients (56 patients) were placed in the bad pregnancy outcome group. Serum PAPP-A2, PIGF, and SFRP5 levels were considerably lower than those in the excellent pregnancy result group (P<0.01), whereas the group with a poor pregnancy outcome had significantly higher levels of urine mAlb, FBG, and HbA1c (P<0.01). Age, gestational age, BMI, and number of pregnancies did not show statistically significant differences between the two groups (P>0.05; see *Table III*).

Multivariate analysis of factors influencing pregnancy outcomes in women with gestational diabetes mellitus (GDM)

Included were variables whose differences in the univariate analysis were statistically significant. The study employed binary logistic regression to determine whether unfavourable pregnancy outcomes occurred. Serum PAPP-A2, PIGF and SFRP5 were found to be protective factors for adverse pregnancy outcomes (P<0.05), whereas urine mAlb was a risk factor for adverse pregnancy outcomes (P<0.05), see *Table IV*.

Table I Comparison of serum PAPP-A2, PIGF, SFRP5, and urine mAlb levels among different groups ($\bar{x}\pm s$).

Group	n	PAPP-A2 (pg/mL)	PIGF (pg/mL)	SFRP5 (ng/mL)	Urine mAlb (mg/L)
GDM group	242	93.59±10.02	55.25±9.89	13.01±3.74	16.00±4.76
Normal pregnancy group	156	126.75±23.21	98.31±21.31	18.29±4.20	14.54±3.20
t		139.776	316.398	95.506	33.108
P		<0.001	<0.001	<0.001	<0.001

Table II The relationship between the levels of serum PAPP-A2, PIGF, SFRP5 and urinary mAlb and the degree of control of GDM diabetes ($\bar{x}\pm s$).

Group	n	PAPP-A2 (pg/mL)	PIGF (pg/mL)	SFRP5 (ng/mL)	Urine mAlb (mg/L)
Well-controlled diabetes group	82	114.54±8.99	65.81±5.39	17.13±2.23	11.56±2.10
Poorly controlled diabetes group	90	90.20±8.38	53.71±4.14	12.39±1.54	17.26±1.86
High-risk group	70	73.26±11.53	44.63±5.52	9.22±2.25	19.80±5.28
F		180.294	173.788	152.026	65.275
P		<0.001	<0.001	<0.001	<0.001

Table III Univariate relationship between clinical indicators and pregnancy outcomes in GDM patients analysis ($\bar{x}\pm s$).

Item	Good pregnancy outcome (n=93)	Adverse pregnancy outcomes group (n=28)	t	P
Age (years)	27.16±3.54	28.03±3.09	1.187	0.232
Gestational age (week)	25.84±1.20	26.00±1.47	0.931	0.353
BMI (kg/m^2)	20.47±1.60	19.99±1.51	1.359	0.171
Pregnancy times (times)	2.18±0.32	2.24±0.45	0.741	0.459
HbAlc (%)	5.45±1.02	6.69±1.07	3.237	0.005
FBG (mmol/L)	5.69±0.87	6.40±1.38	2.235	0.006
PAPP-A2 (pg/mL)	99.20±16.99	74.59±12.39	7.154	<0.001
PIGF (pg/mL)	58.00±9.13	45.71±5.45	8.833	<0.001
SFRP5 (ng/mL)	14.02±3.53	9.77±2.02	8.090	<0.001
Urine mAlb (mg/L)	15.28±4.21	18.72±5.24	3.655	<0.001

Table IV Multivariate analysis of factors affecting pregnancy outcomes in GDM patients.

Indicator	β	Standard deviation	Wald	P	OR	95%CI
HbAlc	0.753	0.444	2.896	0.082	2.110	0.895~5.028
FBG	0.560	0.378	2.293	0.133	1.767	0.849~3.671
PAPP-A2	-0.095	0.035	8.029	0.008	0.915	0.859~0.975
PIGF	-0.164	0.065	6.809	0.002	0.854	0.757~0.964
SFRP5	-483	0.198	6.025	0.017	0.612	0.425~0.901
Urine mAlb	0.234	0.095	6.256	0.015	1.263	1.054~1.502

Table V The efficacy of single and combined detection of serum PAPP-A2, PIGF, and SFRP5 in diagnosing adverse pregnancy outcomes.

Item	Truncation value	Sensitivity (%)	Specificity (%)	AUC	95% CI
PAPP-A2	93.06 pg/mL	98.7	66.0	0.877	0.804~0.920
PIGF	50.02 pg/mL	85.0	82.1	0.884	0.802~0.935
SFRP5	11.87 ng/mL	89.6	80.9	0.860	0.796~0.925
Urine mAlb	17.15 mg/L	75.3	73.4	0.738	0.640~0.814
PAPP-A2+PIGF+SFRP5	–	96.7	90.7	0.967	0.916~0.982

Efficacy of serum PAPP-A2, PIGF and SFRP5 detection in the diagnosis of adverse pregnancy outcomes

Detection of serum PAPP-A2, PIGF, and SFRP5 was substantially more effective than urinary mAlb in diagnosing unfavourable pregnancy outcomes ($P<0.05$). Logistic regression was used for fitting based on the pregnancy outcome to obtain the equation $Y=-0.08\times XPAPP\text{-}A2-0.17\times XPIGF-0.47\times XSFRP5+20.13$, and the combined detection index was obtained. The combined detection method's specificity was 90.3%. Its sensitivity was 96.4%, and the area under the curve (AUC) was 0.967, which was

significantly greater than those of the individual indicators PAPP-A2 ($Z=3.086$, $P<0.01$), PIGF ($Z=2.605$, $P<0.01$), and SFRP5 ($Z=3.562$, $P<0.01$). In contrast, the AUCs of the three indicators were not significantly different ($P>0.05$; see *Table V*).

Discussion

Patients with gestational diabetes mellitus (GDM) experience disorders in glucose and lipid metabolism during pregnancy, which leads to a reduction in the body's utilisation of glucose and an increase in fat oxidation and decomposition, thereby causing spontaneous abortion, macrosomia, polyhydramnios and ketosis, etc., seriously threatening the safety of both the mother and the baby (18–20). Pregnancy outcomes are closely related to gestational diabetes mellitus (GDM), and GDM may raise the risk of unfavourable pregnancy outcomes (21). Therefore, reducing the occurrence of adverse pregnancy outcomes and exploring the predictive factors of adverse pregnancy outcomes are the keys to improving the pregnancy outcomes of pregnant women (22). The serum PAPP-A2, PIGF, and SFRP5 levels were protective factors against adverse pregnancy outcomes, whereas the urinary mAlb level was a risk factor. The level of mAlb in urine is mainly determined by the permeability of the glomerular basement membrane and kidney hemodynamics (23). GDM can cause changes in the glomerular filtration membrane, leading to a loss of charge selectivity and increased permeability, thereby increasing the level of mAlb in urine. Previous studies (24–26) have shown that in patients with gestational hypertension, the level of mAlb in the urine is strongly associated with both the severity of the condition and unfavourable pregnancy outcomes. Whether it is linked to worse pregnancy outcomes in people with gestational diabetes mellitus (GDM) is yet unknown, though. This study showed that serum PAPP-A2, PIGF, and SFRP5 were considerably more effective than urinary mAlb in diagnosing unfavourable pregnancy outcomes in individuals with gestational diabetes mellitus (GDM) (27). Therefore, this study evaluated the diagnostic efficacy of serum PAPP-A2, PIGF, and SFRP5 levels in detecting adverse pregnancy outcomes in patients with GDM.

PAPP-A2 is a pregnancy-related protein secreted by placental trophoblast cells that affects the microenvironment of the foetus and placenta. PAPP-A2 can bind to galactinin and plays important roles in cell proliferation, inflammation and the immune response (28–30). It also has a vital role in the pathophysiological process of GDM. PAPP-A2 can regulate the immune system through anti-inflammatory effects. Pregnancy-related placental inflammation caused by PAPP-A2 downregulation influences the onset and progression of gestational diabetes mellitus (GDM). These findings indicate that serum PAPP-A2 levels are an important indicator of blood glucose control in GDM patients. When the serum PAPP-A2 level fell below the cut-off value, the serum PAPP-A2 level in the group with bad pregnancy outcomes was considerably lower than that in the group with favourable pregnancy outcomes, the sensitivity for diagnosing adverse pregnancy outcomes was 98.4%, the specificity was 66.7%, and the AUC was 0.874, showing that in patients with GDM, the serum PAPP-A2 level has a high diagnostic efficacy for unfavourable pregnancy outcomes.

PIGF, a vascular endothelial growth factor, aids in the proliferation and differentiation of trophoblast cells and plays a role in the formation of placental blood vessels (31). Serum PIGF is an indicator that can reflect the development of a foetus in a pregnant woman's body. A decrease in the PIGF can affect the normal function and hemodynamics of the placenta, leading to a reduction in or interruption of the mother's supply of nutrients to the foetus (32). In severe cases, it can cause premature birth, asphyxia, and even death of the foetus. Therefore, a decrease in serum PIGF levels may be an important factor in adverse pregnancy outcomes (33). According to this study, the GDM group's serum PIGF levels were much lower than those of the normal pregnancy group, and they rose as GDM patients' blood glucose control improved. Additionally, serum PIGF levels are protective against unfavourable pregnancy outcomes and correlate with glycaemic control in GDM patients. With a sensitivity of 85.0%, a specificity of 82.1%, and an AUC of 0.884, serum PIGF shows good diagnostic efficacy for unfavourable pregnancy outcomes in individuals with gestational diabetes mellitus (GDM) when its level is below the threshold.

SFRP5 is a cytokine derived from fat that regulates glucose metabolism and is closely related to insulin resistance. The mechanism by which it regulates blood sugar is that a decrease in SFRP5 levels activates the JNK signalling pathway, stimulates the inflammatory response, and inhibits insulin secretion, thereby affecting pregnancy outcomes (34, 35). Serum SFRP5 levels in GDM patients were significantly lower than those in the normal pregnancy group and increased as blood glucose control improved. This suggests that serum SFRP5 levels are linked to the development and incidence of GDM (36). When the serum SFRP5 level was below the cut-off value, the sensitivity for diagnosing adverse pregnancy outcomes in GDM patients was 89.6%, the specificity was 80.9%, and the AUC was 0.860, indicating that the serum SFRP5 level has high diagnostic value. According to this study, the detection of PAPP-A2, PIGF, and SFRP5 together has a higher diagnostic efficacy for gestational diabetes mellitus (GDM) and unfavourable pregnancy outcomes, with a sensitivity of 96.7%, a specificity of 90.6%, and an AUC of 0.967, which is significantly greater than that of single indicator detection. This indicates some complementarity among the three indicators, and the specific mechanism warrants further study.

Conclusion

The degree of glycaemic control in individuals with gestational diabetes mellitus (GDM) is associated with levels of blood PAPP-A2, PIGF, and SFRP5. Combined detection helps improve the diagnostic efficacy for adverse pregnancy outcomes in GDM patients.

Authors' contribution

Mengjie Gao and Xiaomei Sheng have made equal contributions to the research work of this project.

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Ethical approval

This study was approved by the Medical Research Ethics Committee of our hospital (No. HKYS-2025-A0247).

Conflict of interest statement

All the authors declare that they have no conflict of interest in this work.

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