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Advances in Obstetrics and Gynecology Research

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Observation on the Therapeutic Effect of Lymphocyte Immunotherapy for Repeated Biochemical Pregnancy Loss

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Abstract: *Objective:* To investigate the clinical effect of lymphocyte immunotherapy for women with repeated biochemical pregnancy loss. *Methods:* A retrospective study was conducted from January 2015 to January 2016, involving 100 patients with repeated biochemical pregnancy loss as observation subjects. After enrollment, patients were divided into two groups (50 patients in each group) according to different treatment regimens. The observation group received conventional tocolysis combined with lymphocyte immunotherapy, while the control group only received conventional tocolysis treatment. The pregnancy outcome, improvement of serum factor levels, and treatment safety were evaluated to compare the clinical effects of different treatment regimens. *Results:* The pregnancy success rate was 82.00% in the observation group and 48.00% in the control group ($\chi^2 = 12.7033$, $P < 0.05$). After treatment, the interferon- γ (IFN- γ) level in the observation group was higher than that in the control group, while the interleukin-8 (IL-8) and regulated upon activation, normal T-cell expressed and secreted (RANTES) levels were lower than those in the control group ($P < 0.05$). There was no significant difference in treatment safety between the two groups ($P > 0.05$). *Conclusion:* The introduction of lymphocyte immunotherapy in patients with repeated biochemical pregnancy loss can improve the success rate of pregnancy and has a significant therapeutic effect, which is worthy of application.

Keywords: Lymphocyte; Immunotherapy; Repeated biochemical pregnancy loss; Efficacy

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1. Introduction

Repeated pregnancy loss, also known as “recurrent pregnancy loss,” is a type of pregnancy loss that occurs with a certain incidence in obstetrics and gynecology. The pathological mechanism of this disease is complex and associated with multiple factors, including infection, endocrine abnormalities, and genetics. Modern pathological research has clarified that nearly half of recurrent pregnancy losses are essentially linked to immune factors^[1]. In the past, clinical interventions for pregnancy loss mainly focused on tocolysis, achieving

the desired tocolytic effect through drug control, regulating the body's embryonic response, reducing local sensitivity, and providing favorable conditions for normal fertilization^[2]. However, for patients with recurrent pregnancy loss, due to the specificity of their pathological factors, symptomatic treatment targeting immune factors is needed based on basic tocolysis to improve clinical efficacy^[3]. To further explore treatment options and help patients control their condition, the study analyzed the effects of conventional tocolysis and lymphocyte immunotherapy, focusing on the separate and combined application of these two strategies. 100 subjects were included in the controlled study, and the results are reported below.

2. Materials and methods

2.1. General information

In this retrospective study, a total of 100 patients with recurrent biochemical pregnancy losses were selected as observation subjects. All patients were admitted between January 2015 and January 2016. Based on differences in treatment measures, they were divided into two groups, with 50 cases in each group, and different treatment measures were implemented: conventional fetal protection + lymphocyte immunotherapy (observation group) and conventional fetal protection therapy (control group). In the observation group, the age ranged from 22 to 42 years old, with an average age of (30.24 ± 2.36) years old; the number of miscarriages (2 times/3 times/4 times and above) was 26/8/16. In the control group, the age ranged from 22 to 45 years old, with an average age of (30.33 ± 2.28) years old; the number of miscarriages (2 times/3 times/4 times and above) was 20/12/18. The above data were collated and analyzed using SPSS 22.0 system, with $P > 0.05$ indicating clear comparability. The research process was sorted out, archived, and submitted to the ethics committee for approval before conducting the study. Patients and their families were informed of the project, and consent documents were obtained.

Inclusion criteria: (1) Complete medical history and treatment records; (2) History of spontaneous miscarriage with a frequency of ≥ 2 times; (3) No reproductive tract deformities; (4) Husband's cooperation in physical examination with normal sperm quality; (5) Normal/regular menstruation at the time of enrollment; (6) Normal chromosome screening results; and (7) The patient is aware of the research project and has a certain degree of participation compliance.

Exclusion criteria: (1) Presence of endocrine or autoimmune system disorders/abnormalities; (2) Combined with reproductive system diseases, such as reproductive tract infections, abnormalities, chromosome abnormalities, etc.; (3) Other fetal protection measures have been taken before entering the project; (4) Allergic or contraindicated reactions to medications involved in this project; and (5) Accompanied by psychiatric symptoms, cognitive impairments, and other manifestations.

2.2. Methods

For the control group, only conventional fetal protection measures were intervened. Progesterone (Tongyong Pharmaceutical; National Medicine Approval Number: H31021401; Specification: 1 mL: 20 mg) was administered at a dose of 20 mg via intramuscular injection once a day until 12 weeks of gestation.

On this basis, patients in the observation group were treated with lymphocyte immunotherapy. With the cooperation of their husbands, 20 mL of venous blood (from the upper arm elbow) was collected and anti-coagulant was added. Under a sterile environment, the lymphocyte suspension was washed with 0.9% normal

saline for 3 times. The lymphocytes were then diluted to maintain a concentration of $(2-3) \times 10^7/\text{mL}$ and injected into the patients' anterior thigh medially in a radial pattern. Each injection was followed by another injection 2 weeks later, for a total of 4 consecutive times until 12 weeks of gestation.

2.3. Observation indicators

- (1) Pregnancy outcome: The follow-up time was set for 12 months, and the pregnancy outcomes of patients after the end of treatment were recorded. Successful pregnancy^[4]: The duration is not less than 20 weeks, and the fetal heart is confirmed to be alive by prenatal examination (ultrasonography).
- (2) Serum factor levels: According to the research design requirements, two detection time points were defined to measure patients' serum factor levels, which is before treatment (last prenatal examination) and after treatment (first follow-up examination). Measurement items included IFN- γ , IL-8, and BANTES.
- (3) Treatment safety: During the study period, the responsible nurse followed up on the treatment process and recorded the types and number of adverse events, mainly including nausea, vomiting, bleeding, breast pain, etc.

2.4. Statistical Analysis

Data analysis was performed using SPSS 26.00 statistical software. Enumeration data (including pregnancy outcome items, treatment safety items, etc.) were expressed as the number of cases (n) and percentage (%), and a chi-square test was conducted. Measurement data conforming to a normal distribution (including serum factor level items, etc.) were represented by mean \pm standard deviation (SD), and an LSD- t test was used for comparison between groups. A student's t -test was used for comparison within groups. Statistical differences were considered significant when $P < 0.05$.

3. Results

3.1. Pregnancy outcomes

After treatment, the pregnancy outcome items were evaluated. The statistical value of successful pregnancy rates in the observation group was higher than that in the control group, while the statistical value of miscarriage rates in the observation group was lower than that in the control group ($P < 0.05$) (Table 1).

Table 1. Comparison of pregnancy outcomes (cases, %)

Group	Successful pregnancy	Miscarriage
Observation group ($n = 50$)	41 (82.00)	9 (18.00)
Control group ($n = 50$)	24 (48.00)	26 (52.00)
χ^2	12.7033	12.7033
P	0.0003	0.0003

3.2. Serum factor levels

After treatment, a comparison of serum factor items showed that the measured values of IFN- γ in the observation group were lower than those in the control group, while the measured values of IL-8 and BANTES

were higher than those in the control group ($P < 0.05$) (Table 2).

Table 2. Evaluation of serum factor levels

Group	IFN- γ (ng/L)		IL-8 (pg/L)		BANTES (ng/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group ($n = 50$)	358.45 \pm 58.56	248.42 \pm 32.18*	310.24 \pm 51.58	589.54 \pm 82.27*	220.23 \pm 64.15	435.17 \pm 54.91*
Control group ($n = 50$)	354.37 \pm 57.74	298.24 \pm 35.86*	307.37 \pm 50.55	497.66 \pm 74.72*	223.35 \pm 63.91	362.04 \pm 52.16*
t	0.3508	7.3114	0.2810	5.8458	0.2436	6.8278
P	0.7262	< 0.01	0.7799	< 0.01	0.8080	< 0.01

Note: Compared with before treatment in this group, * $P < 0.05$.

3.3. Treatment safety

In terms of treatment safety items, there was no statistically significant difference in the total incidence of adverse events between the observation group and the control group ($P > 0.05$) (Table 3).

Table 3. Evaluation of treatment safety (cases, %)

Group	Nausea	Vomiting	Bleeding	Breast Tenderness	Total Incidence(%)
Observation group ($n = 50$)	3 (6.00)	3 (6.00)	1 (2.00)	2 (4.00)	18.00
Control group ($n = 50$)	2 (4.00)	2 (4.00)	1 (2.00)	1 (2.00)	12.00
χ^2	-	-	-	-	0.7059
P	-	-	-	-	0.4008

4. Discussion

The causes of recurrent biochemical pregnancy losses are complex, primarily related to the weakened antigen recognition and decreased antigen reactivity of patients after recurrent miscarriages. Typically, due to insufficient secretion efficiency of blocking antibodies in the mother, the fetal surface antigen stimulation is weakened, and the antibody regulation ability is lacking, ultimately leading to unsuccessful pregnancies. Therefore, immunological factors have become a new direction for the treatment of recurrent biochemical pregnancies [5].

Currently, conventional measures for the treatment of recurrent biochemical pregnancies include hormone supplementation, such as progesterone. This study adopted this drug for treatment. As an endogenous hormone, progesterone can promote the recovery of ovarian function after physiological supplementation, affect the fertilized egg, enabling it to implant normally, and influence the body's immune response, weakening the mother's immune reaction [6]. However, in a monotherapy environment, the efficacy is not satisfactory, and patients with insufficient blocking antibodies cannot achieve the desired treatment effect. Therefore, it is clinically recommended to combine other immunotherapy techniques to improve efficacy [7].

Lymphocyte immunotherapy is a new treatment technique in obstetrics and gynecology. Its basic

mechanism is to extract lymphocytes from the father, prepare them, and then inject them into the mother. Through a series of physiological effects, it promotes the generation of antibodies, thereby influencing the body's immune mechanism and protecting normal embryo formation and development, resisting the negative effects of the immune mechanism^[8]. Among pregnant women, due to the special physiological internal environment during this period, the normal function of lymphocytes is limited. Targeted immunotherapy can achieve immune intervention, protect normal embryos, resist the influence of immune cells, promote normal pregnancy, and improve success rates^[9].

For patients with recurrent pregnancy losses, due to changes in the physiological environment, substances such as interferons will continue to be disordered and exhibit hyperreactivity, thereby affecting the body's normal immune mechanism. The toxic effects of some killer cells will continue to increase, thereby affecting embryonic cells and causing trophoblast casualties. Under normal circumstances, the body's serum inflammatory factors are at a low level, and they are in a balanced state with the body's immune function. When this state is destroyed, it will activate the body's immune function, enhance the activity of mother cells, strengthen their immune tolerance, produce physiological reactions that are contrary to antigen stimulation, and affect the pregnancy state^[10]. Therefore, lymphocyte immunotherapy is selected to strengthen the physiological immune function through immune influence, maintain the corresponding lymphatic function, and keep it in an immune balance state to achieve better efficacy^[11].

In addition, in terms of treatment safety, because lymphocyte immunotherapy does not increase additional medications for patients and does not affect other physiological functions during immune regulation, it has high safety and does not increase patients' toxic and side effects. Patient acceptance is relatively high^[12].

In the study by Yang *et al.*^[13], active immunotherapy was introduced for patients with recurrent miscarriages. The efficacy data showed that the pregnancy success rate of patients under active immunotherapy was 83.30%, while the pregnancy success rate without active immunotherapy was 44.00%. The difference was statistically significant. This illustrates the positive effect of immunotherapy on patients with recurrent miscarriages, which is consistent with the research conclusions of this article.

5. Conclusion

In summary, for patients with recurrent biochemical pregnancies, the introduction of lymphocyte immunotherapy technology under basic fetal protection can effectively improve the success rate of pregnancy, regulate the level of serum-related factors in the body, and the treatment has good safety and high patient acceptance. The value is significant and worthy of clinical practice and application.

Disclosure statement

The authors declare no conflict of interest.

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Research Progress on Blood Pressure Management Strategies for Patients with Hypertensive Disorders in Pregnancy

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Abstract: This article summarizes blood pressure management strategies for patients with hypertensive disorders in pregnancy, including establishing a dynamic blood pressure monitoring system from a clinical perspective, strengthening education to improve patients' self-management abilities, applying portable home instruments to assist in monitoring and guiding medication from a technical perspective, and conducting community screening and graded management of hypertensive disorders in pregnancy from a social perspective. The results indicate that individual differences should be considered in clinical practice, and patient-centered individualized blood pressure management strategies should be established.

Keywords: Gestational hypertension; Blood pressure management; Dynamic blood pressure monitoring system; Self-management

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1. Introduction

Hypertensive disorders of pregnancy (HDP), also known as hypertensive complications during pregnancy, are common yet profound conditions during gestation. These disorders are primarily characterized by persistent hypertension in pregnant women, posing significant risks to both the mother and fetus ^[1]. Although the exact causes remain incompletely understood, it is generally believed that they may arise from interactions between genetic factors, lifestyle choices, and certain environmental factors ^[2]. Over time, global medical research has gradually uncovered a growing trend in the incidence of hypertensive disorders during pregnancy, particularly among older mothers and those with previous childbirth experience, where the condition becomes more prevalent ^[3]. More concerning, hypertensive disorders during pregnancy not only threaten the mother's health but may also lead to issues such as abnormal fetal development and premature birth. Therefore, controlling blood pressure

during pregnancy is crucial as it directly relates to the well-being of both the mother and child. To address this challenge, the American College of Obstetricians and Gynecologists (ACOG) released an important guideline in 2018, aimed at providing obstetricians and gynecologists with direction to improve the management of hypertensive disorders during pregnancy. The guideline clearly states the critical role of preventive measures, early diagnosis and intervention strategies, as well as educational and support services, to ensure favorable pregnancy outcomes. These recommendations reflect the medical community's strong emphasis on improving the quality of hypertension management during pregnancy. To further enhance education and research in this area, experts continuously explore new methods and technologies to better monitor pregnant women's blood pressure levels and take necessary intervention measures on time ^[4]. Through this comprehensive treatment approach, the negative impacts of hypertensive disorders during pregnancy can be significantly reduced, thereby protecting the health and safety of both mother and child. Although the exact causes of hypertensive disorders during pregnancy remain to be further investigated, we are steadily moving towards improving this situation through scientific management and comprehensive health education.

2. Managing patients with hypertensive disorders of pregnancy from a clinical perspective

2.1. Establishing a dynamic monitoring system to understand patients' true blood pressure status

2.1.1. Advantages of dynamic blood pressure monitoring

Currently, clinical methods for measuring blood pressure primarily include office blood pressure monitoring and dynamic blood pressure monitoring. Office blood pressure monitoring is mainly applied to patients with gestational hypertension, while dynamic blood pressure monitoring can be used for the diagnosis and monitoring of other diseases such as hypertension and diabetes.

However, due to various reasons, patients with hypertensive disorders during pregnancy may refuse or be unable to complete office blood pressure monitoring, resulting in inaccurate blood pressure data. Therefore, it is necessary to obtain reliable information through dynamic blood pressure monitoring to better guide treatment decisions. According to a study by Zhang et al. ^[5], compared to office blood pressure, using a dynamic blood pressure monitor for continuous 24-hour blood pressure monitoring resulted in a significant reduction of 6.3 mm Hg (0.28–11.7%) in the mean systolic blood pressure (mSBP) of patients with hypertensive disorders during pregnancy, while the mean diastolic blood pressure (mDBP) showed no significant change. A study by Zhou et al. ^[6] demonstrated that dynamic blood pressure monitoring in late pregnancy can effectively avoid the adverse effects of hypotension on the fetus.

2.1.2. Limitations of dynamic blood pressure monitoring

Despite its many advantages, dynamic blood pressure monitoring also has certain limitations ^[7].

- (1) It can only reflect the blood pressure situation at the time of measurement and cannot provide information on blood pressure trends over a period of time.
- (2) Patients may experience discomfort due to factors such as electrode patches pressing on the skin or improper wearing methods, affecting patient compliance.
- (3) Even with qualified monitoring equipment, its results may not meet expected ideals due to equipment performance limitations.

These factors may lead to discrepancies between actual and target blood pressure, thereby increasing hypertension risk.

2.2. Strengthen education during pregnancy to improve patients' self-management ability and compliance

Currently, most nursing staff in primary hospitals in China lack standardized clinical training in the management of hypertensive disorders of pregnancy. Therefore, it is particularly important to strengthen patient education.

- (1) According to Zhu et al. ^[8], efforts should be made from three aspects: doctors, nurses, and family members to improve healthcare workers' knowledge and understanding of HDP. Lectures, education, discussions, and other methods should be used to deepen the impression of relevant knowledge among patients and their family members, helping them understand the characteristics of the disease and how to respond.
- (2) Li et al. ^[9] showed that healthcare workers should actively explain to patients and their family members the pathogenesis, early symptoms, diagnostic criteria, treatment options, drug selection, pregnancy risk assessment, and preventive measures of hypertension during pregnancy. This allows patients to have a full understanding and psychological preparation for the disease, thereby reducing fear and anxiety, enhancing self-confidence and self-protection awareness, and increasing treatment compliance.
- (3) Given that many patients with hypertensive disorders during pregnancy often have comorbidities such as diabetes, nephrotic syndrome, hypothyroidism, and liver or kidney dysfunction, Gang et al. ^[10] revealed that healthcare workers should inform patients of various possible complications during pregnancy, including placental abruption, fetal growth restriction, preterm birth, and low birth weight infants. They should also introduce treatment methods and the prognosis of these complications to eliminate patients' concerns and worries, allowing them to receive treatment with peace of mind.
- (4) Fan et al. ^[11] proposed personalized education content for different populations, such as providing prenatal guidance to pregnant women in early, mid, and late stages of pregnancy, or integrating education throughout the entire pregnancy. This not only helps improve patients' self-management abilities but also facilitates comprehensive management.

3. Management of patients with hypertensive disorders of pregnancy from a technical perspective

3.1. Advantages and disadvantages of using home blood pressure monitors

Since patients may be unable or unwilling to undergo blood pressure monitoring in hospitals, the development of portable home blood pressure monitors (such as wrist and finger clip monitors, electronic blood pressure monitors, etc.) is crucial for managing blood pressure in pregnant women. These devices are easy to operate and use, allowing women to monitor their blood pressure at home, which is beneficial for developing good habits, self-management awareness, timely adjustment of antihypertensive medication dosages, and improving compliance. However, home blood pressure monitors also have some disadvantages ^[12]: (1) They may produce inaccurate measurements without medical supervision; (2) They are not suitable for emergency patients; (3) Due to the lack of standardized data, it is difficult to scientifically analyze relevant factors and determine the best treatment plan.

3.2. Blood pressure measurement methods at home and abroad

Currently, various home blood pressure monitors with certain measurement accuracy and stability have been

developed both domestically and internationally. According to the latest guidelines for the management of hypertensive disorders during pregnancy, it is recommended that all pregnant women undergo regular monitoring using office blood pressure monitoring methods. For pregnant women with hypertension, daily blood pressure monitoring at home can help better control blood pressure levels. It is important to note that to ensure the accuracy of measurements, a relatively fixed time point should be selected for measurement. Additionally, it is advisable to have a family member assist in the measurement to reduce errors caused by human factors. Different measurement methods can be chosen based on the stage of pregnancy, such as the sitting position method recommended for early pregnancy and the supine position method for mid to late pregnancy ^[13]. It is worth mentioning that continuous measurement of blood pressure in the same area for a long time should be avoided to prevent excessive vasoconstriction reaction, which may lead to lower blood pressure values.

3.3. Using home portable devices to assist blood pressure monitoring and medication guidance

When measuring blood pressure, it is crucial to ensure that the selected equipment has undergone strict quality control. Upper arm electronic blood pressure monitors are generally recommended due to their high accuracy. However, before purchasing, it should be ensured that the device has been certified by international authoritative organizations such as the European Society of Hypertension (ESH), the Association for the Advancement of Medical Instrumentation (AAMI), or the British Hypertension Society (BHS). Additionally, selecting the appropriate cuff size based on individual upper arm circumference is important, as oversized or undersized cuffs can affect measurement results.

The correct steps for measuring blood pressure include ^[14]: sitting quietly for at least 5 minutes before measurement to avoid interference from movement and anxiety; maintaining an upright sitting position with feet flat on the ground, arms naturally hanging down, and aligned with the heart; ensuring that the cuff is tightly fitted to the skin, not too loose or tight, to avoid affecting measurement accuracy. Follow the instructions provided in the blood pressure monitor manual, take 2 to 3 consecutive measurements with a 1-minute interval, and calculate the average value as the final blood pressure reading.

Recording blood pressure data plays a significant role in monitoring disease progression and adjusting treatment plans. After each measurement, detailed records should be kept, including the date, specific time, blood pressure readings, and heart rate information. Regularly reviewing these data can help identify abnormal fluctuations. This information will assist doctors in better understanding your health status and adjusting medication regimens promptly ^[15]. To ensure regular medication adherence, patients should strictly follow the prescriptions provided by doctors and avoid unauthorized adjustments to dosages or stopping medications. Doctors will evaluate the need for medication adjustments based on blood pressure data and provide timely feedback to patients, setting reminders to ensure that patients take their medications as scheduled, thus effectively managing their blood pressure conditions ^[16].

4. Management of patients with hypertensive disorders of pregnancy from a social perspective

4.1. Conducting community screening and implementing tiered management

In China, due to the lack of professional management personnel, many pregnant women with hypertensive disorders during pregnancy are not timely identified. Therefore, it is essential to carry out community screening

targeted at patients with hypertensive disorders during pregnancy. Wang^[17] screened 1718 pregnant women who established mother-child health manuals and found that only 12% of them received adequate blood pressure monitoring and health education. Moreover, 45.8% of pregnant women had no understanding of hypertension during pregnancy, indicating that China has not established a comprehensive community screening system for hypertensive disorders during pregnancy.

In the United States, some communities have established standardized tiered management systems for hypertensive disorders during pregnancy. For example, the “Healthy Pregnancy” program has reduced the incidence of hypertensive disorders during pregnancy through multiple free blood pressure checks and lifestyle guidance for pregnant women^[18]. These research results suggest that strengthening social advocacy, raising public awareness of the dangers of hypertensive disorders during pregnancy, and incorporating hypertension classification management into national health policies can effectively prevent the occurrence of hypertensive disorders during pregnancy. China should learn from international experience, consider its national conditions, and establish a sustainable community screening and tiered management model for hypertensive disorders during pregnancy that is tailored to its specific context.

4.2. Develop individualized treatment plans and take comprehensive measures to control blood pressure

For patients whose blood pressure is not at the target level, oral or intravenous antihypertensive medications can be used for control^[19]. Additionally, attention should be paid to other risk factors such as obesity, hyperglycemia, and diabetes. In the early stages of pregnancy, if patients have comorbidities such as diabetes, hypertension, and hyperlipidemia, these conditions should be treated simultaneously to achieve better blood pressure control^[20]. In the later stages of pregnancy, apart from taking antihypertensive medications, appropriate drugs should be administered for antiplatelet aggregation therapy^[21].

However, due to the complex physiological changes during pregnancy, there is currently no standard treatment plan that is suitable for all patients with hypertensive disorders during pregnancy. Therefore, when developing individualized medication plans, doctors must comprehensively evaluate patients, understand the severity and tolerance of their conditions, and consider their unique characteristics. After weighing the pros and cons, doctors should select appropriate medication plans. For instance, Wang’s results showed that pregnant women with a bleeding tendency can be preferentially treated with drugs such as beta-blockers and calcium channel blockers^[22]. For pregnant women at risk of severe preeclampsia, medications such as diuretics, angiotensin-converting enzyme inhibitors (ACEI), and angiotensin II receptor antagonists (ARB) can be administered^[23]. For older pregnant women, drugs such as alpha-blockers or cerebrovascular dilators should be selected based on their conditions, thereby effectively controlling blood pressure levels and reducing the occurrence of maternal and fetal complications^[24].

5. Conclusion

Hypertensive disorders during pregnancy are a global public health issue, and there is still a lack of effective prevention and treatment methods. This article summarizes recent research progress in blood pressure management for patients with hypertensive disorders during pregnancy by domestic and foreign scholars. More high-quality research is needed in the future to clarify whether hypertension increases the risk of preeclampsia, gestational

diabetes, and fetal growth restriction, as well as how to improve the quality of life for pregnant women with hypertension. Furthermore, individual differences should be considered in clinical practice, and patient-centered individualized blood pressure management strategies should be established. Simultaneously, blood pressure monitoring and education for patients and their families should be strengthened, and a community-based tiered management model should be implemented. The roles of home visits and telephone follow-ups should be fully utilized to comprehensively protect the health of mothers and babies, shifting from mere disease management to integrated health management, thereby improving adverse outcomes for mothers and babies in China.

Disclosure statement

The author declares no conflict of interest.

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An Analysis of the Use of Ultrasonography in the Assessment of the Effects of Rectus Abdominis Muscle Separation and Rehabilitation Therapy in Postpartum Women

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Abstract: *Objective:* To explore the effect of ultrasonography in assessing the effect of rectus abdominis muscle separation and rehabilitation in postpartum women. *Methods:* 254 cases of postpartum women admitted to the hospital from January 2022 to July 2023 were selected as the study group, and 63 cases of women with rectus abdominis muscle not separated during the same period were selected as the control group, and all of them used GEDiscoveryE9 ultrasonic diagnostic instrument to compare the separation distance of rectus abdominis muscle of 3 cm above the umbilicus of the women in the two groups; and to compare the separation distance of rectus abdominis muscle of the women in the study group after treatment. *Results:* The rectus abdominis muscle separation distance of 3 cm above the umbilicus was (4.36 ± 0.87) cm in the study group and (1.88 ± 0.07) cm in the control group, and the difference between the study group and the control group was significant ($P < 0.05$); the rectus abdominis muscle separation of the study group was (3.78 ± 0.69) cm, (3.01 ± 0.69) cm and (3.01 ± 0.69) cm respectively in the 1st, 2nd, 3rd, 4th, 5th, and 6th post treatment; and the rectus abdominis muscle separation of the study group was (3.78 ± 0.69) cm, (3.01 ± 0.58) cm, (2.75 ± 0.57) cm, (2.31 ± 0.48) cm, (1.97 ± 0.36) cm, and (1.95 ± 0.44) cm, respectively, with a significant difference compared to the pre-treatment ($P < 0.05$). *Conclusion:* The optimal section for ultrasonographic detection of rectus abdominis muscle separation in the postpartum period was 3.5 cm below the umbilicus, and this section was able to effectively assess the degree of rectus abdominis muscle separation in patients.

Keywords: Ultrasonography; Rectus abdominis separation; Rehabilitation

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1. Introduction

During pregnancy, the pressure on the abdominal wall gradually increases as the foetus grows and the size of the uterus increases. In order to maintain the stability of the body's centre of gravity and protect the internal organs, muscle groups such as the abdominal muscles and diaphragm relax and decrease in contractility during pregnancy,

resulting in the abdominal organs protruding from the anterior superior part of the abdomen into the pelvic cavity; coupled with hormonal effects, adaptive changes occur in the muscles, the white line of the abdomen is stretched and thinned, and the rectus abdominis muscle spacing is increased. After caesarean section, the above phenomena can be rapidly relieved due to faster tissue repair ^[1]. However, some women still have diastasis recti abdominis separation 3–6 months or more after delivery, causing a series of problems such as low back pain, pelvic organ prolapse, scoliosis, and changes in physiological curvature in patients ^[2]. At present, the diagnostic criteria for rectus abdominis muscle separation at home and abroad are mainly to segment the midline of the abdomen with the index and middle fingers, and the distance between the two sides is ≥ 2 cm to confirm the diagnosis, which is easily affected by the subjective judgement of the doctor, and the operation is cumbersome and time-consuming, so it is difficult to promote the use of this method. In addition, the commonly used clinical ultrasonography cannot directly show the separation status and can only be used as an auxiliary means. With the development of ultrasound technology, in recent years, scholars at home and abroad have mostly used two-dimensional ultrasound, three-dimensional ultrasound or colour Doppler ultrasound to assess and diagnose maternal rectus abdominis muscle separation, and have achieved good results ^[3]. In this paper, a combined treatment of ultrasound with pelvic floor muscle trainer was used to evaluate 254 cases of postpartum rectus abdominis muscle separation and analyze the treatment effect, aiming at exploring the feasibility and accuracy of ultrasound evaluation of rectus abdominis muscle separation, and providing reference for clinical diagnosis and treatment.

2. Information and methodology

2.1. General information

254 cases of postpartum women admitted to the hospital from January 2022 to July 2023 were selected as the study group, and all the women were eligible for natural delivery. The ages ranged from 23 to 40 years old, with a mean of 31.24 ± 1.36 years old; the gestational weeks were 37 to 40 weeks, with a mean of 39.51 ± 1.09 weeks; 110 cases had a bodymass index (BMI) ≥ 25 kg/m², and 144 cases had a body mass index (BMI) < 25 kg/m². In the same period, 63 cases of women with an undivided rectus abdominis muscle were used as the control group, with ages ranging from 22 to 40 years old, with a mean of 31.14 ± 1.44 years old, and gestational weeks ranging from 37 to 40 weeks, with a mean of 39.21 ± 1.01 weeks.

Inclusion criteria: (1) age between 20–40 years old; (2) singleton, full-term, vaginal delivery or cesarean section; (3) rectus abdominis muscle separation diagnosed by ultrasound with a separation distance of ≥ 2 cm; (4) subjects were aware of the purpose of the study, the methodology, and the possible risks; and (5) signed an informed consent form.

Exclusion criteria: (1) patients with pregnancy complications and co-morbidities; (2) patients with psychiatric diseases and mental disorders such as mental retardation; (3) patients who have recently undergone abdominal surgery or abdominoplasty; and (4) those suffering from severe organic lesions of the heart, liver, kidneys and lungs.

2.2. Methodology

(1) Ultrasound detection method

The GEDiscoveryE9 ultrasound diagnostic instrument was used, with a probe frequency of 3.5 MHz. Before the detection, the patient was asked to relax the muscles of the abdominal wall and lie on the examination bed in a supine position; the inspector held the probe in his right hand on the abdominal

wall and lifted it immediately after a few seconds of pressure, and at the same time, the patient was asked to cooperate with the head-up and abdominal movements to ensure that the abdomen was filled up and full. Observe whether the rectus abdominis muscle is separated, record the separation distance if there is obvious separation, and mark the location and size of the separation in the two-dimensional image, which is divided into six levels: no separation; type I separation ($1\text{ cm} \leq \text{separation} < 3\text{ cm}$); type II separation ($3\text{ cm} \leq \text{separation} < 6\text{ cm}$); type III separation ($6\text{ cm} \leq \text{separation} < 8\text{ cm}$); type IV separation ($8\text{ cm} \leq \text{separation} < 10\text{ cm}$); Type V separation ($\geq 10\text{ cm}$). Starting from the 10th postpartum day to the end of the 6th postpartum month, a total of 6 times, each with an interval of more than 7 days. All ultrasound results were done by the same doctor in the same time period to ensure data consistency.

(2) Treatment

Firstly, maintain correct standing, sitting and lying postures, avoid bending and increasing abdominal pressure; if an umbilical hernia occurs, you can use air mattress bed or lumbar support. Secondly, eat more high-quality protein food, reduce high-calorie food intake, eat more vegetables and fruits and coarse grains to increase intestinal peristalsis to promote defecation; it is recommended to take the principle of eating less and more frequent meals, while paying attention to nutritional balance, eating less and more frequent meals, and supplementing high-quality protein, vitamins, dietary fibre and other nutrients appropriately, on top of ensuring the energy required by the body, to promote wound healing and recovery. Then, sufficient rest, especially 1 week after delivery, should be bed rest. Then, start walking exercise till the next day, when there is no obvious pain in the abdomen can carry out some simple abdominal muscle exercise, step by step.

(A) Pelvic floor muscle training: Take the supine position, legs bent at the knees and separated from the hip the same width, hands behind the head to support the trunk and buttocks, eyes flat at the ceiling, slowly contract the buttocks and inner thigh muscles upward to lift the anus, lasting 5–6 seconds, and then relax for 5 to 6 seconds. Do 10 times in a row for a group, do 3–5 groups per day, and the interval between each group is not less than 2 minutes.

(B) Abdominal breathing: Inhalation when the abdomen is inflated, exhalation of the abdominal wall ring jump point down to the pubic bone joint, each time to adhere to 15–30 seconds, every day to practice 2–3 times.

(3) Herbal medicine external treatment

Chinese medicines (astragalus, angelica, chuanxiong) with the effect of activating blood circulation and removing blood stasis, tonifying the liver and kidney can be selected and made into medicinal powder, and cotton swabs dipped in the medicinal powder can be applied to the umbilicus and the painful parts of the abdomen twice a day.

2.3. Observation indicators

To compare the rectus abdominis muscle separation distance of 3 cm above the umbilicus between the two groups, and to compare the rectus abdominis muscle separation distance after treatment in the study group.

2.4. Statistical methods

SPSS 23.0 software was applied for statistical analysis, the measurement information was expressed as mean \pm standard deviation (SD), and *t*-test was used for comparison, and the count information was expressed as rate (%), and χ^2 test was used for comparison, and $P < 0.05$ was considered as statistically significant difference.

3. Results

3.1. Distance of rectus abdominis muscle separation 3 cm above the umbilicus in both groups

The separation distance of rectus abdominis muscle 3 cm above the umbilicus was (4.36 ± 0.87) cm in the study group of women and (1.88 ± 0.07) cm in the control group of women, and the difference between the study group and the control group was significant ($P < 0.05$), as shown in **Table 1**.

Table 1. The separation distance of the rectus abdominis muscle 3 cm above the umbilicus in both groups of women

Groups	Number of examples	Rectus abdominis muscle separation distance (cm)
Study group	254	4.36 ± 0.87
Control group	63	1.88 ± 0.07
<i>t</i>		22.581
<i>P</i>		0.000

3.2. Distance of rectus abdominis muscle separation in the study group after maternal treatment

The 1st, 2nd, 3rd, 4th, 5th and 6th rectus abdominis muscle separations of the study mothers after treatment were (3.78 ± 0.69) cm, (3.01 ± 0.58) cm, (2.75 ± 0.57) cm, (2.31 ± 0.48) cm, (1.97 ± 0.36) cm, (1.95 ± 0.44) cm, respectively, which were compared with those before treatment. The difference was significant ($P < 0.05$), as shown in **Table 2**.

Table 2. Distance of rectus abdominis muscle separation in the study group after maternal treatment

Groups	1 st	2 nd	3 rd	4 th	5 th	6 th
Before treatment ($n = 254$)	4.36 ± 0.87	4.36 ± 0.87	4.36 ± 0.87	4.36 ± 0.87	4.36 ± 0.87	4.36 ± 0.87
Post-treatment ($n = 254$)	3.78 ± 0.69	3.01 ± 0.58	2.75 ± 0.57	2.31 ± 0.48	1.97 ± 0.36	1.95 ± 0.44
<i>t</i>	8.325	20.577	24.670	32.881	40.455	39.397
<i>P</i>	0.000	0.000	0.000	0.000	0.000	0.000

4. Discussion

Separation of the rectus abdominis muscle refers to the separation of the rectus abdominis muscle due to the gradual enlargement of the uterus during pregnancy, which forces the rectus abdominis muscle on both sides of the abdominal wall to shift towards the midline. In recent years, with the improvement of social living standards and the influence of factors such as the delay in the age of women's childbearing, the phenomenon of rectus abdominis muscle separation after childbirth has been increasing. Relevant studies have shown that the incidence of rectus abdominis muscle separation in postpartum women is 45–80% and increases with the number of deliveries (9.6%), and one-third of these separated patients require surgical treatment [4]. In addition, some scholars have found that the degree of rectus abdominis muscle separation is closely related to low back pain and fatigue symptoms, which can affect daily activities and even induce psychological problems such as depression and anxiety in severe cases in Chinese mothers [5]. At present, clinicians' diagnosis of postpartum rectus abdominis separation is mainly judged by asking about medical history, physical examination and imaging examination. Before the popularity of

ultrasound instruments, there was a “gold standard” in traditional medicine-rectal manometry to assess the degree of diastasis recti, which calculates the change in the volume of abdominal organs by measuring the difference in abdominal pressure to estimate the degree of diastasis recti. However, this method is complicated and prone to errors, which is not conducive to the timely judgment of maternal condition. Ultrasound, as a non-invasive, rapid and accurate medical imaging technology, has been widely used in the diagnosis of abdominal diseases. Studies have shown that ultrasonography can not only accurately display the contours of abdominal organs and their movements, but also observe the dynamic changes of the uterus, ovaries and other pelvic organs in real time ^[5]. Therefore, ultrasound technology also plays an important role in the diagnosis of postpartum rectus abdominis separation. Rectus abdominis muscle separation refers to the phenomenon in which the tissue between the rectus abdominis muscles separates from the abdominal white line to the sides. Normally, women will gradually recover on their own within 6 months after delivery, but some women still have diastasis recti abdominis separation 3 years or even more than 10 years after delivery, which has a greater impact on the patient’s daily life ^[6,7].

The results of the study showed that the separation distance of the rectus abdominis muscle at 3 cm above the umbilicus was significantly greater in the study group than in the control group ($P < 0.05$), which is consistent with the results of related studies at home and abroad ^[8,9]. Ultrasonography can clearly show the morphology, thickness and separation distance of the rectus abdominis muscle, providing an objective and accurate basis for clinical diagnosis. Secondly, this study confirms the effectiveness of rehabilitation therapy on postpartum rectus abdominis muscle separation. In the study group, the separation distance of the rectus abdominis muscle was gradually reduced after the rehabilitation treatment, and the difference was significant compared with that before the treatment ($P < 0.05$), which indicated that the rehabilitation treatment could effectively improve the symptoms of the separation of the rectus abdominis muscle, and promote the recovery of the function of the abdominal wall.

Separation of the rectus abdominis muscle refers to an increase in the distance between the anterior sheath of the rectus abdominis muscle and the white line of the abdomen, which can cause changes in the morphology of the abdominal muscles and result in some degree of dysfunction. The occurrence of rectus abdominis muscle separation is mainly related to the gestational week, the size of the foetus and the mother’s factors. In late pregnancy, as the uterus gradually increases in size, the abdominal muscles are stretched and lengthened; in late pregnancy, under the pressure of the uterus, the abdominal muscles show passive relaxation. When a woman gives birth, the abdominal muscles have not yet returned to their original position, which leads to widening of the rectus abdominis muscle, increasing the distance between the rectus abdominis muscles. In addition, due to the heavier weight of the newborn, it also puts pressure on the abdomen, which leads to separation of the rectus abdominis muscles. Studies have shown that 25–40% of women develop diastasis recti abdominis separation postpartum and the prevalence increases with age ^[10]. Most scholars believe that rehabilitation within 6 weeks postpartum can help prevent or reduce the degree of diastasis recti separation ^[11]. In addition, the degree of diastasis recti abdominis separation may be exacerbated if the mother suffers from diabetes mellitus or hypertension.

Currently, the commonly used clinical diagnostic criteria is the method developed by the American College of Obstetricians and Gynecologists: place a finger on the navel, move it along the midline of the rectus abdominis muscle from left to right, and then observe the maximum distance between the finger and the skin surface, with a measurement interval of about 2.5 cm; if it is less than this range, it indicates the presence of rectus abdominis muscle separation; if it is greater than 2.5 cm, a further CT scan is required to confirm the diagnosis ^[12]. This method is simple to perform, but it cannot distinguish whether it is a separation of the external abdominal oblique muscle or not, and is prone to misdiagnosis.

Some scholars suggested other diagnostic methods. For example, the thickness of the abdominal wall is calculated based on maternal height, body fat percentage and abdominal circumference, and then the degree of rectus abdominis muscle separation is deduced based on the above formula ^[12]. In addition, other scholars have found by comparing the ultrasound images that there is a large difference in rectus abdominis muscle separation in mothers of different ages, and the older the woman is, the more serious the degree of rectus abdominis muscle separation is ^[13], both methods can effectively distinguish the type of rectus abdominis muscle separation, but the Due to the more complicated calculation process, it is not favourable for generalization.

In recent years, ultrasound technology has been widely used in the diagnosis of rectus abdominis separation. Among them, the three-point, five-point, and seven-point methods are currently the most common clinical measurements ^[14,15]. The three-point method uses the hand placed on the upper edge of the umbilicus, the index and middle fingers placed on the lower edge of the umbilicus, and the two fingers separated horizontally around the umbilicus for one week, obtaining three intersections, and then measuring the vertical distances of these three intersections, respectively, and calculating the degree of rectus abdominis separation according to the formula. The five-point method is to take the navel as the centre, respectively, 3 cm above and below the navel by touching with the fingers, looking for five checkpoints, measuring the vertical distance between these points, and calculating the degree of rectus abdominis separation according to the formula ^[16].

5. Conclusion

In conclusion, the optimal view for ultrasound detection of rectus abdominis muscle separation in the postpartum period is 3.5 cm below the umbilicus, and this view is effective in assessing the degree of rectus abdominis muscle separation in patients. When self-testing the presence of abdominal wall muscle separation, it should be noted that the thumb is placed above the umbilicus (about 2–3 cm above the pubic symphysis), and the index, middle and ring fingers are pressed below the umbilicus and pushed in the direction of the spine, and the width of their contact with the skin surface is observed, which is the degree of abdominal wall muscle separation. After delivery, due to pelvic congestion, uterine contraction, and breastfeeding, some mothers will experience different degrees of rectus abdominis muscle separation, but with the extension of time, most of the mothers can gradually recover. If the separation of the rectus abdominis muscle is still obvious within 6 months after delivery, it is recommended to go to the hospital for timely consultation and professional and systematic rehabilitation treatment to reduce or avoid the adverse consequences. For the multilayer spiral CT and MRI examination methods commonly used in clinical work, there are certain limitations due to the need for multiple scans. Ultrasound, as a simple and easy non-invasive means of examination, has the advantages of easy operation and low cost, and is of great significance to clinical diagnosis and treatment.

Disclosure statement

The authors declare no conflict of interest.

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Exploration of High-Risk HPV Genotyping Test as an Initial Screening Method for Cervical Cancer

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Abstract: *Objective:* The purpose of this study was to evaluate the clinical value of high-risk HPV typing as a primary screening method for cervical cancer. *Methods:* From July 2023 to June 2024, 871 women, aged 23 to 77 years old, with an average age of (42.5 ± 3.45) years old, were selected for initial screening of cervical cancer in the health examination center and gynecological clinic of the hospital. All patients underwent HPV-DNA typing and cervical fluid-based thin-layer cytology (TCT). Colposcopic cervical biopsy was performed in women with high-risk HPV single or multiple infection or with TCT \geq ASC-US. The diagnostic efficacy of HPV-DNA typing, TCT and HPV + TCT combined detection was calculated using the pathological results of biopsy as the gold standard. *Results:* Compared with TCT alone, HPV-DNA typing was significantly more sensitive in the diagnosis of cervical lesions ($P < 0.05$), and the rate of missed diagnosis was significantly reduced ($P < 0.05$). At the same time, the efficacy of the HPV-DNA typing test is similar to that of HPV + TCT combined screening. In terms of misdiagnosis rate and specificity, there was no statistical difference among the three screening strategies ($P > 0.05$). *Conclusion:* HPV-DNA typing alone has the same effect as TCT + HPV combined screening for cervical cancer.

Keywords: Cervical cancer; Screening; HPV-DNA; TCT; Pathological examination

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1. Introduction

Cervical cancer, as one of the most common malignancies among women, poses a serious threat to the physical and mental health of a wide range of females. According to 2022 statistics, there were up to 150,700 new cases of cervical cancer in China, accounting for 22.7% of the total global incidence, and close to 56,000 deaths, representing 16% of the global mortality rate ^[1]. Given the severity of cervical cancer incidence, effective screening and treatment are particularly important. With in-depth research on the risk factors of cervical cancer, persistent infection with high-risk human papillomavirus has been identified as the definite cause of cervical cancer. On July 6, 2021, the World Health Organization (WHO) released the latest guidelines for the screening

and treatment of precancerous cervical lesions, which recommend HPV-DNA testing as the preferred method for cervical cancer screening. This study conducted an in-depth analysis of HPV, TCT, and colposcopy biopsy results from 871 women.

2. Materials and methods

2.1. General information

In this study, 871 women who voluntarily underwent initial cervical cancer screening at our hospital's health examination center and gynecology clinic from July 2023 to June 2024 were selected as the research subjects. Their ages ranged from 23 to 77 years old, with an average age of (42.5 ± 3.45) years old. All participants had a history of sexual activity and were currently not pregnant. To ensure the accuracy of the study, women with a history of cervical surgery or hysterectomy, as well as a history of pelvic radiotherapy and chemotherapy, were excluded. HPV-DNA typing and cervical liquid-based thin-layer cytology (TCT) were performed simultaneously or sequentially. Colposcopy biopsy and pathological examination were performed on those with positive HPV or TCT test results. Using pathological diagnosis as the gold standard, the diagnostic efficacy of HPV, TCT, and combined HPV + TCT detection was calculated separately. The optimal effects of the three screening methods were evaluated.

2.2. Methods

2.2.1. HPV genotyping and TCT cytology testing

Samples were collected during non-menstrual periods, ensuring no vaginal douching or medication history within 72 hours before sampling and no sexual activity within 24 hours. During sampling, the vulva was first lubricated with normal saline, the cervix was exposed through a vaginal speculum, and then the cervical mucus was wiped off with a cotton swab. The sampling order was to collect the TCT sample first, followed by the HPV sample. A specialized cervical sampling brush was placed at the external of the cervix and rotated clockwise for 3 to 5 weeks to fully collect cervical exfoliated cells, which were immediately placed in a specialized specimen tube for testing. HPV-DNA genotyping was performed using the PCR-based fluorescence probe method, which can simultaneously detect 18 high-risk HPV types (16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82). If any one or more high-risk HPV subtypes tested positive, it was judged as HPV positive. The diagnostic criteria for TCT followed the new TBS grading evaluation standard recommended by the National Cancer Institute (NCI) in 2001^[1]. A TCT test result \geq ASC-US (Atypical Squamous Cells of Undetermined Significance) was used as the positive criterion.

2.2.2. Colposcopy and cervical tissue biopsy for pathological examination

Multiple biopsies were performed on suspicious lesions of the cervix under colposcopy. For those without visible lesions, biopsies were taken at 3, 6, 9, and 12 o'clock positions. For type III transformation zones, cervical canal curettage was also performed. The biopsy sites were labeled, and the specimens were fixed with formaldehyde before sending for pathological examination. Pathological examination results \geq CIN2+ (Cervical Intraepithelial Neoplasia grade 2 and above) were considered positive for cervical lesions.

2.3. Criteria

In this study, histopathological examination was used as the "gold standard" for diagnosis.

2.4. Statistical analysis

SPSS 26.0 statistics was used to process and analyze the data. Measurement data were expressed as mean \pm standard deviation (SD), and count data were expressed as a percentage (%). The chi-square test was used to compare rates between groups. A statistically significant difference was considered when $P < 0.05$. Diagnostic efficiency was calculated based on the following formulas: sensitivity = true positive / (true positive + false negative), specificity = true negative / (true negative + false positive), misdiagnosis rate = false positive / (false positive + true negative), missed diagnosis rate = false negative / (false negative + true positive), negative predictive value = true negative / (true negative + false negative), and positive predictive value = true positive / (true positive + false positive).

3. Results

3.1. Pathological results using TCT as the primary screening indicator for cervical cancer screening

Using TCT as a screening strategy, 271 positive cases were screened among the 871 women participating in this study. Of these, 28 were judged as high-grade or higher lesions (i.e., true positives), while 243 were diagnosed as normal cervix or low-grade lesions (i.e., false positives). Of the 600 negative screening cases, 22 were false negatives (i.e., missed diagnosis cases), and 578 were true negatives. See **Table 1**.

Table 1. Pathological results using TCT as the primary screening indicator for cervical cancer screening

TCT test results	Pathological biopsy (Gold standard)	
	High-grade cervical and cervical cancer	Normal cervix and low-grade
Positive	28 (true positive)	243 (false positive)
Negative	22 (false negative)	578 (true negative)

3.2. Pathological results using HPV as the primary screening indicator for cervical cancer screening

Among the 871 women included in this study, using HPV as a screening strategy, 376 positive cases were identified. Pathological diagnosis revealed 64 cases of high-grade or higher lesions (i.e., true positives) and 312 cases diagnosed as normal cervix or low-grade lesions (i.e., false positives). Among the 495 negative screening cases, 7 were false negatives (i.e., missed diagnosis cases), and 488 were true negatives. See **Table 2**.

Table 2. Pathological results using HR + HPV as the primary screening indicator for cervical cancer screening

HR + HPV test results	Pathological biopsy (Gold standard)	
	High-grade cervical and cervical cancer	Normal cervix and low-grade
Positive	64 (true positive)	312 (false positive)
Negative	7 (false negative)	488 (true negative)

3.3. Analysis of pathological results using combined TCT + HPV screening as the primary screening strategy for cervical cancer screening

In this cervical cancer screening study involving 871 women, a total of 359 positive cases were identified using

combined TCT + HPV screening as the screening strategy. Pathological diagnosis revealed 67 cases of high-grade or higher lesions (i.e., true positives) and 292 cases diagnosed as normal cervix or low-grade lesions (i.e., false positives). Among the 512 negative screening cases, 6 were false negatives (i.e., missed diagnosis cases), and 506 were true negatives. See **Table 3**.

Table 3. Pathological results of HPV + TCT combined screening as the primary screening indicator for cervical cancer screening

HPV + TCT test results	Pathological biopsy (Gold standard)	
	High-grade cervical and cervical cancer	Normal cervix and low-grade
Positive	67 (true positive)	292 (false positive)
Negative	6 (false negative)	506 (true negative)

3.4. Screening efficacy of three screening strategies

To comprehensively and accurately compare the efficacy of TCT, HPV, and TCT + HPV screening strategies in the primary screening of cervical cancer, we calculated the diagnostic efficacy indicators for TCT, HPV, and TCT + HPV screening strategies based on established formulas (**Table 4**). When evaluating the screening efficacy of the three strategies, the results showed similar performance in terms of misdiagnosis rate and specificity, with no statistically significant difference ($P > 0.05$).

Table 4. Screening efficacy of three screening strategies

Primary screening indicator	<i>n</i>	Sensitivity (%)	Missed diagnosis rate (%)	Specificity (%)	Misdiagnosis rate (%)	Negative predictive value	Positive predictive value
TCT	871	56	44	70.4	29.60	96.33	10.33
HPV	871	90.14	9.85	61.0	39.00	98.58	17.02
TCT+HPV	871	91.78	8.22	63.41	36.59	98.83	18.66
χ^2 -value		49.932	49.932	1.955	1.955		
<i>P</i> -value		< 0.05	< 0.05	> 0.05	> 0.05		

4. Discussion

Cervical cancer, as a preventable and treatable disease, has undergone intensive research on its pathogenesis, which has confirmed that persistent infection with high-risk human papillomavirus (HPV) is the main inducer of cervical lesions ^[2,3]. The invasion of this virus into cervical epithelial cells is a long process from quantitative to qualitative change, taking 8 to 10 years, providing us with a sufficient time window for early screening and intervention ^[4,5].

Liquid-based cytology (TCT) testing has been a traditional means of cervical cancer screening and has played an important role in the past 50 years. However, the limitations of its morphological detection, such as the high demand for pathological doctors' professional skills, have led to high rates of missed diagnosis and false positives, especially in primary medical institutions ^[6].

With the rapid development of molecular biology, cervical lesion screening has shifted from traditional cytological morphology examination to HPV-based molecular screening. Compared with cytological examination,

HPV detection technology exhibits higher screening efficiency^[7,8]. Domestic and foreign studies have shown that HR-HPV detection has higher sensitivity for detecting cervical intraepithelial neoplasia grade 2 and more severe lesions (CIN2+) ^[9,10]. This study also confirms this point, with the sensitivity of HPV screening being similar to that of TCT + HPV combined screening and higher than that of TCT screening. In terms of specificity, although the specificity of HPV screening (61.0%) is slightly lower than that of TCT (70.4%) and combined screening (63.41%), the differences between the three are not statistically significant ($P > 0.05$). However, it is worth noting that the misdiagnosis rate (39.0%) and missed diagnosis rate (9.85%) of HPV screening are both maintained at relatively low levels, especially the missed diagnosis rate, which is significantly lower than that of TCT screening (44%). This is important for reducing missed detections and missed diagnoses of cervical cancer. Additionally, the negative predictive values of HPV screening and combined screening (98.58% and 98.83%, respectively) are higher than that of TCT screening (96.33%), indicating that these two screening strategies have higher accuracy in identifying truly disease-free individuals. Meanwhile, the positive predictive values of HPV screening and combined screening (17.02% and 18.66%, respectively) are also significantly higher than that of TCT screening (10.33%), which helps reduce unnecessary further examination and treatment.

5. Conclusion

In summary, the use of HPV-DNA detection as a primary screening tool for cervical cancer has high diagnostic value, with high sensitivity, low missed diagnosis rate, and high negative and positive predictive values. This screening strategy is not only feasible but also effective in reducing missed detections and missed diagnoses, as well as lowering the incidence and mortality of cervical cancer. Promoting HPV screening in primary hospitals can not only improve the early diagnosis rate of cervical cancer but also effectively protect women's health and safety. Therefore, HPV screening should be regarded as an important tool for cervical cancer screening.

Although this study has achieved certain results in exploring the effectiveness of TCT, HPV, and TCT + HPV screening strategies in primary cervical cancer screening, there are still some limitations. The sample size of this study is limited, with only 871 women included in the screening, which may affect the universality and representativeness of the results to some extent. A larger sample size would help to more accurately evaluate the effectiveness of different screening strategies and reduce the impact of random errors on the results.

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Clinical Study on the Treatment of Cold-Dampness Stagnation Type of Dysmenorrhea with Shaofu Zhuyu Decoction Combined with Thunder-Fire Moxibustion

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Abstract: *Objective:* To investigate the therapeutic effect of Shaofu Zhuyu Decoction combined with Thunder-Fire Moxibustion on patients with cold-dampness stagnation type of dysmenorrhea. *Methods:* A total of 40 patients with cold-dampness stagnation type of dysmenorrhea who visited the hospital from January 2023 to December 2024 were selected as samples and randomly divided into two groups using the lottery method. The observation group received Shaofu Zhuyu Decoction combined with Thunder-Fire Moxibustion, while the control group received Shaofu Zhuyu Decoction only. The efficacy, pain score, menstrual volume, menstrual duration, symptom score, and adverse reactions were compared between the two groups. *Results:* The efficacy of dysmenorrhea treatment in the observation group was higher than that in the control group ($P < 0.05$). After treatment, the Visual Analog Scale (VAS) score in the observation group was lower than that in the control group, the menstrual volume was lower, and the menstrual duration was shorter ($P < 0.05$). The scores for menstrual flow obstruction, menstrual volume reduction, abdominal distension and pain, and menstrual blood clots with purple and dark color were lower in the observation group compared to the control group ($P < 0.05$). There was no significant difference in the adverse reaction rate between the observation group and the control group ($P > 0.05$). *Conclusion:* The combination of Shaofu Zhuyu Decoction and Thunder-Fire Moxibustion is effective in reducing pain and improving related symptoms of cold-dampness stagnation type of dysmenorrhea, and it is safe and efficient.

Keywords: Dysmenorrhea; Cold-dampness stagnation type; Thunder-Fire Moxibustion; Shaofu Zhuyu Decoction; Efficacy

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1. Introduction

Dysmenorrhea patients often suffer from lumbosacral pain and abdominal pain, which can significantly affect

women's physical and mental health. Some women experience severe dysmenorrhea that requires active treatment to avoid disrupting their daily work and life. Based on etiology analysis, primary dysmenorrhea is associated with the release of prostaglandins stimulated by menstruation, while secondary dysmenorrhea is related to organic diseases such as endometriosis and adenomyosis. Although symptomatic intervention with Western medication can alleviate pain, it cannot achieve a complete cure. Traditional Chinese medicine scholars classify dysmenorrhea as “abdominal pain during menstruation” and believe that it is mostly caused by cold-dampness stagnation. Typical symptoms include internal cold, cold intolerance, and abdominal cold pain. Treatment principles include pain relief, Qi regulation, and blood nourishment, with Shaofu Zhuyu Decoction being a commonly used prescription ^[1]. However, single herbal therapy has a slow onset time, prolonged duration of symptoms, and limited pain relief in the initial stages of medication. Therefore, combination therapy with Thunder-Fire Moxibustion is necessary to achieve pain relief, cold dispersal, meridian activation, and menstrual regulation. This article explores the efficacy of Shaofu Zhuyu Decoction combined with Thunder-Fire Moxibustion in the treatment of 40 patients with cold-dampness stagnation type of dysmenorrhea.

2. Materials and methods

2.1. Materials

Forty patients with cold-dampness stagnation type dysmenorrhea who visited the clinic from January 2023 to December 2024 were selected as samples and grouped by drawing lottery. The observation group consisted of patients aged 17–36 (25.11 ± 2.43) years old, with a disease duration of 6 months to 10 (3.52 ± 1.06) years, and a menstrual cycle of 22–34 (26.81 ± 2.43) days. The control group consisted of patients aged 17–37 (25.09 ± 2.41) years old, with a disease duration of 6 months to 9 (3.48 ± 1.02) years, and a menstrual cycle of 21–34 (26.78 ± 2.41) days. The baseline data of the observation group were compared with those of the control group, with $P > 0.05$.

2.2. Inclusion and exclusion criteria

- (1) Inclusion criteria: (1) Meet the criteria for menstrual pain in “Obstetrics and Gynecology” ^[2]; (2) Conform to the dampness-cold stagnation type in “Clinical Research on Gynecology of Traditional Chinese Medicine” ^[3]; (3) Provide informed consent; (4) Experience lower abdominal pain with regular menstrual cycles.
- (2) Exclusion criteria: (1) Have allergic constitution; (2) Have audio-visual impairments; (3) Have gynecological cancer; (4) Are lost to follow-up.

2.3. Treatment methods

- (1) Control group: Shaofu Zhuyu Decoction Treatment: 6 g each of red peony root, Sichuan lovage rhizome, myrrh, fennel, dried ginger, and Wulingzhi; 3 g each of *cinnamon cassia* bark and *corydalis rhizome*; 9 g each of typhae pollen and Chinese angelica. The medicines are made into granules and taken orally with 150 mL of boiling water 7 days before menstruation, 1 dose per day, taken warm in the morning and evening. The medication is suspended during menstruation. Each menstrual cycle counts as one course of treatment, and medication is administered for 3 courses.
- (2) Observation group: Combined with Thunder-Fire Moxibustion Treatment: Using a 2.5 cm × 10.0 cm moxibustion stick, apply moxibustion to points such as Diji, bilateral Zigong, Zhongji, Guanyuan,

and Shuidao. Then, ignite one end of the Thunder-Fire Moxibustion stick and place it in a special moxibustion tool, maintaining a distance of 3–5 cm between the moxa stick and the skin. Thunder-Fire Moxibustion is performed once a day, 7 days before menstruation, with each session lasting 20 minutes. Thunder-fire moxibustion is suspended during menstruation. Treatment is given for 3 menstrual cycles.

2.4. Observation indicators

- (1) Efficacy: Complete disappearance of menstrual pain symptoms with a symptom score reduction of $\geq 70\%$ is considered markedly effective; relief of menstrual pain symptoms with a symptom score reduction of $\geq 30\%$ is considered effective; failure to meet the above criteria is considered ineffective.
- (2) Menstrual indicators: VAS score is positively correlated with the degree of menstrual pain, ranging from 0–10; menstrual volume, menstrual duration, and menstrual cycle indicators are recorded.
- (3) Symptom score: The degree of menstrual discomfort, menstrual scarcity, lower abdominal pain, and menstrual blood clots with purple-dark color are evaluated based on the principles of none, mild, moderate, and severe, with scores ranging from 0–3. The score is positively correlated with the severity of the condition.
- (4) Adverse reactions: Skin allergies, gastrointestinal reactions, menstrual abnormalities, and other situations are recorded.

2.5. Statistical analysis

SPSS 23.0 is used to process the data. Count data is described using percentages (%) and analyzed using the chi-square test (χ^2 test). Measurement data is described using mean \pm standard deviation (SD) and analyzed using the *t*-test. Statistical significance is indicated by $P < 0.05$.

3. Results

3.1. Efficacy

The efficacy of menstrual pain treatment in the observation group is higher than that in the control group, with $P < 0.05$. See **Table 1**.

Table 1. Comparison of efficacy in patients with menstrual pain (*n*, %)

Group	Effective markedly	Effective somewhat	Ineffective	Effective rate
Observation group (<i>n</i> = 20)	11 (55.00)	8 (40.00)	1 (5.00)	19 (95.00)
Control group (<i>n</i> = 20)	4 (20.00)	10 (50.00)	6 (30.00)	14 (70.00)
χ^2	-	-	-	4.3290
<i>P</i>	-	-	-	0.0375

3.2. Menstrual indicators

After treatment, the VAS score, menstrual volume, and duration of menstruation in the observation group were lower than those in the control group, with $P < 0.05$. See **Table 2**.

Table 2. Comparison of menstrual indicators in patients with dysmenorrhea (mean \pm SD)

Group	VAS score before treatment (points)	VAS score after treatment (points)	Menstrual volume (mL)	Menstrual duration (days)	Menstrual cycle (days)
Observation group ($n = 20$)	4.71 \pm 1.25	2.39 \pm 0.33	51.22 \pm 2.29	4.31 \pm 0.48	28.68 \pm 1.84
Control group ($n = 20$)	4.73 \pm 1.28	3.71 \pm 0.42	66.26 \pm 3.14	5.92 \pm 0.69	28.11 \pm 1.62
t	0.0500	11.0519	17.3070	8.5661	1.0398
P	0.9604	0.0000	0.0000	0.0000	0.3050

3.3. Symptom scores

After treatment, the scores for menstrual discomfort, low menstrual volume, abdominal pain, and dark menstrual blood with clots in the observation group were lower than those in the control group, with $P < 0.05$. See **Table 3**.

Table 3. Analysis of symptom scores in patients with dysmenorrhea (mean \pm SD)

Group	Menstrual flow obstruction (score)		Scanty menstruation (score)		Abdominal distension and pain (score)		Dark purple menstrual blood with clots (score)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group ($n = 20$)	2.41 \pm 0.25	0.69 \pm 0.14	2.36 \pm 0.33	0.67 \pm 0.18	2.42 \pm 0.26	0.68 \pm 0.14	2.45 \pm 0.29	0.69 \pm 0.15
Control group ($n = 20$)	2.43 \pm 0.27	1.35 \pm 0.19	2.38 \pm 0.35	1.39 \pm 0.21	2.44 \pm 0.28	1.42 \pm 0.23	2.46 \pm 0.31	1.44 \pm 0.26
t	0.2431	12.5064	0.1859	11.6417	0.2341	12.2907	0.1054	11.1741
P	0.8093	0.0000	0.8535	0.0000	0.8162	0.0000	0.9167	0.0000

3.4. Adverse reactions

There was no difference in the rate of adverse reactions between the observation group and the control group, with $P > 0.05$. See **Table 4**.

Table 4. Analysis of adverse reactions (Score, mean \pm SD)

Group	Skin allergy	Gastrointestinal reaction	Abnormal menstruation	Incidence rate
Observation group ($n = 20$)	0 (0.00)	1 (5.00)	0 (0.00)	0 (0.00)
Control group ($n = 20$)	1 (5.00)	1 (5.00)	1 (5.00)	3 (15.00)
χ^2	-	-	-	3.2432
P	-	-	-	0.0717

4. Discussion

Dysmenorrhea is a highly prevalent disease among women, with individual differences in pain severity. Clinically, contraceptives, anti-inflammatory drugs, and analgesics are often used to treat dysmenorrhea. Although they can quickly relieve pain, they cannot cure the condition, and long-term use may cause gastrointestinal adverse reactions. Traditional Chinese medicine believes that female dysmenorrhea is related to various factors such as daily life habits, emotions, and congenital deficiencies. The disease is located in the

uterus and Chong and Ren meridians, and the common syndrome type is cold-dampness stagnation. Treatment should follow the principles of pain relief, removing blood stasis, and promoting blood circulation. Shaofu Zhuyu Decoction originates from “Corrections in Medical Classics.” It can warm the meridians, relieve pain, and promote blood circulation. In the prescription, *Radix paeoniae rubra* can relieve pain, remove blood stasis, cool the blood, and clear heat; *Rhizoma chuanxiong* can relieve pain, promote Qi circulation, remove blood stasis, and promote blood circulation; Myrrh can relieve pain and disperse blood stasis; *Fructus foeniculi* can warm and disperse cold, warm the middle jiao, promote pulse circulation, restore Yang, and also warm and tonify the liver and kidney; *Rhizoma zingiberis* can warm and disperse cold, and warm the middle jiao; *Troglodytes dung* can relieve pain and remove blood stasis; *Cortex cinnamomi* can promote menstruation, activate blood circulation, relieve pain, and warm and disperse cold; *Rhizoma corydalis* can relieve pain and promote qi circulation; *Pollen typhae* can remove blood stasis and stop bleeding; *Radix angelicae sinensis* can regulate menstruation and promote blood circulation. These herbs work together to remove blood stasis, promote blood circulation, eliminate dampness, and warm and disperse cold. Thunder-Fire Moxibustion treatment follows the principles of meridian theory in traditional Chinese medicine to select acupoints. The heat generated during the burning of moxa sticks promotes the penetration of medicinal factors into the acupoints, which can regulate Qi, relieve pain, remove blood stasis, and promote blood circulation. It is suitable for the treatment of deficiency and cold syndromes ^[4]. Additionally, the infrared rays generated during thunder-fire moxibustion create a high-concentration medicinal area at specific acupoints, which can penetrate deep into the acupoints under the influence of heat, regulating body functions.

Based on the data analysis in this article, the efficacy of dysmenorrhea treatment in the observation group was higher than that in the control group, with $P < 0.05$. The reason for this is that most patients with dysmenorrhea have the cold-dampness stagnation type, which is related to the obstruction of Qi and blood circulation caused by cold pathogens entering the body. The selection of Shaofu Zhuyu Decoction can harmonize the Qi and blood of the uterus and Chong and Ren meridians, achieving the effects of pain relief, removing blood stasis, warming and dispersing cold, and warming the meridians, thereby improving patients’ physical signs and relieving pain. Thunder-Fire Moxibustion is an external treatment method that places burning moxa sticks at specific acupoints to stimulate the acupoints with warming effects, enhancing the efficacy of traditional Chinese medicine decoctions in removing blood stasis, promoting blood circulation, relieving pain, and promoting Qi circulation ^[5]. Another set of data shows that after treatment, the VAS score, menstrual volume, and duration of menstruation in the observation group were lower than those in the control group, with $P < 0.05$. Based on modern pharmacological analysis, tetrahydropalmatine in *Rhizoma corydalis* from Shaofu Zhuyu Decoction can effectively relieve pain; total flavonoids of *Pollen typhae* can dredge Qi and blood and promote blood circulation in the affected area ^[6]. Combined with thunder-fire moxibustion, the thermal stimulation on the local skin can improve uterine artery blood flow and promote pelvic blood circulation, thereby improving menstrual indicators and relieving pain ^[7]. Another set of data indicates that the symptom scores in the observation group were lower than those in the control group, with $P < 0.05$. The reason for this is that although Shaofu Zhuyu Decoction monotherapy can remove blood stasis, promote blood circulation, and relieve symptoms, its onset is slow. Combining it with Thunder-Fire Moxibustion stimulates the penetration of medicinal factors into the acupoints, rapidly reducing pain and improving physical signs ^[8]. The final set of data shows no difference in the rate of adverse reactions between the observation group and the control group, with $P > 0.05$. This is because traditional Chinese medicine is administered based on syndrome differentiation, with

scientific adjustment of dosages to ensure high safety. Additionally, thunder-fire moxibustion is performed by professional physicians with standardized operations, avoiding damage to patients' skin and ensuring treatment safety.

5. Conclusion

In summary, the combination of Shaofu Zhuyu Decoction and thunder-fire moxibustion for the treatment of dysmenorrhea can reduce related symptoms, enhance the efficacy of dysmenorrhea management, and reduce adverse reactions related to dysmenorrhea. This treatment approach can be widely promoted.

Disclosure statement

The author declares no conflict of interest.

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Study on the Correlation between Pregnancy Anemia and Serum Ferritin Levels in Jinan Area and Prevention of Iron Deficiency

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Abstract: *Objective:* To analyze the correlation between pregnancy anemia and serum ferritin (SF) levels in Jinan area and explore methods for preventing iron deficiency. *Methods:* A total of 1000 pregnant women who underwent prenatal check-ups and gave birth in the hospital from January 2020 to July 2022 were selected as samples. Routine blood tests and SF detection were performed, and the number of patients with iron deficiency anemia (IDA) in the second and third trimesters, blood routine data, and SF level data were recorded. *Results:* There were 160 cases (16.00%) of IDA in the second trimester and 200 cases (20.00%) in the third trimester. The erythrocyte parameters and SF levels of IDA pregnant women in the second trimester were lower than those of healthy pregnant women ($P < 0.05$). The incidence of IDA was higher in pregnant women with SF < 10 ng/mL than in those with SF 10–19.9 ng/mL, SF 20–29.9 ng/mL, and SF ≥ 30 ng/mL, and the lower the SF level, the higher the incidence of IDA ($P < 0.05$). There was no statistical difference in adverse pregnancy outcomes between anemic and non-anemic pregnant women among different levels of SF ($P > 0.05$). *Conclusion:* Pregnant women with low SF levels in the second and third trimesters are more prone to IDA. Active intervention can reduce adverse pregnancy outcomes and ensure the safety of mothers and babies.

Keywords: Pregnancy anemia; Serum ferritin level; Correlation; Prevention of anemia

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1. Introduction

IDA is a type of nutritional disorder during pregnancy, which is related to the reduction of the body's iron storage capacity during pregnancy and the inability to produce red blood cells. It is a common type of anemia during pregnancy. In addition, due to the special physiological state during pregnancy and the increase in blood volume, pregnant women's demand for iron increases. Coupled with the growth and development of the fetus, which also requires iron, inadequate intake and absorption of iron by pregnant women can induce IDA. After the occurrence of IDA, the blood cell's oxygen-carrying capacity of pregnant women is further reduced, which

can easily lead to adverse events such as low birth weight infants, premature infants, and fetal death in utero. The fetus's congenital deficiency can affect brain development and reduce immunity. Therefore, it is extremely important to carry out iron supplementation therapy for IDA patients in combination with relevant guidelines. SF is a glycoprotein substance with strong iron storage capacity, which can regulate the distribution of iron elements in the human body. The fluctuation of SF levels is not affected by recent iron intake levels and can objectively reflect the iron storage situation of pregnant women. It is sensitive in evaluating iron deficiency diseases ^[1]. Based on this, this article explores the correlation between SF levels and IDA in pregnant women using 1000 pregnant women who underwent prenatal check-ups and gave birth in our hospital from January 2020 to July 2022 as samples and discusses methods for preventing iron deficiency.

2. Materials and methods

2.1. Materials

A total of 1000 pregnant women who underwent prenatal check-ups and gave birth in our hospital from January 2020 to July 2022 were selected as samples, aged 21–39 years old, with an average age of (28.43 ± 1.58) years old. The number of pregnancies ranged from 1 to 4, with an average of (1.89 ± 0.42) times. The pre-pregnancy BMI ranged from 18 to 29 kg/m², with an average of (25.74 ± 1.58) kg/m². Inclusion criteria: (1) Singleton pregnancy; (2) Regular prenatal check-ups; (3) Blood routine and SF tests ≥ 2 times in the second and third trimesters. Exclusion criteria: (1) Prenatal bleeding; (2) Immune system diseases; (3) History of hypertension.

2.2. Methods

In the second and third trimesters of pregnancy, 3–4 mL of blood samples were collected from the median cubital vein of the enrolled pregnant women. Routine blood tests were performed using a BC6800-Plus full blood cell analyzer. Platelet and red blood cell results were obtained using the sheath flow impedance method, hemoglobin results were obtained using the colorimetric method, and cell classification and counting were obtained using flow cytometry. Serum ferritin (SF) was detected using an automatic electrochemiluminescence immunoassay analyzer. After collecting 5 mL of peripheral venous blood samples, they were stored in a vacuum blood collection tube without anticoagulant. After resting for 60 minutes, the samples were centrifuged at 3000 revolutions per minute for 10 minutes. The supernatant serum was stored in a refrigerator at -20 °C, and the examination was completed according to the kit. Based on the “Guidelines for the Diagnosis and Treatment of Iron Deficiency and Iron Deficiency Anemia During Pregnancy” ^[2] criteria, SF < 20 mg/L was considered as iron deficiency, hemoglobin < 110 g/L was considered as anemia, and meeting both criteria was considered as IDA (iron deficiency anemia). Pregnant women diagnosed with IDA were treated with iron supplementation based on their physiological status.

2.3. Statistical analysis

Data were processed using SPSS 23.0. Count data were recorded as percentages (%) and tested using the chi-square test (χ^2 test). Measurement data were recorded as mean \pm standard deviation (SD) and tested using the *t*-test. Statistical differences were considered significant at $P < 0.05$.

3. Results

3.1. Occurrence of IDA in the second and third trimesters of pregnancy

There were 160 cases (16.00%) of IDA in the second trimester and 200 cases (20.00%) in the third trimester.

3.2. Red blood cell parameters and SF levels in healthy and IDA pregnant women

The red blood cell parameters and SF levels in IDA pregnant women were lower than those in healthy pregnant women during the second trimester ($P < 0.05$). See **Table 1** for details.

Table 1. Analysis of red blood cell parameters and SF levels in healthy and IDA pregnant women (mean \pm SD)

Group	SF (ng/mL)	Red blood cell count ($\times 10^{12}/L$)	Hemoglobin (g/L)	Mean corpuscular volume (fl)	Mean corpuscular hemoglobin (pg)
IDA pregnant women ($n = 160$)	9.98 \pm 1.21	3.52 \pm 0.58	101.25 \pm 3.26	26.81 \pm 1.85	26.33 \pm 1.25
Healthy pregnant women ($n = 840$)	47.26 \pm 8.69	4.01 \pm 0.69	120.48 \pm 4.11	30.39 \pm 1.96	30.11 \pm 1.69
<i>t</i>	54.1432	8.4322	55.9193	21.3616	26.9196
<i>P</i>	0.0000	0.0000	0.0000	0.0000	0.0000

3.3. Correlation analysis between SF level and IDA

Pregnant women with SF levels < 10 ng/mL have a higher incidence of IDA compared to those with SF levels of 10–19.9 ng/mL, 20–29.9 ng/mL, and ≥ 30 ng/mL. Moreover, the lower the SF level, the higher the incidence of IDA ($P < 0.05$). See **Table 2**.

Table 2. Correlation analysis table between SF level and IDA (n , %)

SF level	Second trimester ($n = 160$)		Third trimester ($n = 200$)	
	Mild anemia	Moderate anemia	Unresolved anemia from second trimester	Newly developed anemia in third trimester
< 10 ng/mL	73 (45.63)	12 (7.50)	36 (18.00)	70 (35.00)
10–19.9 ng/mL	32 (20.00)	4 (2.50)	14 (7.00)	34 (17.00)
20–29.9 ng/mL	25 (15.63)	4 (2.50)	12 (6.00)	22 (11.00)
≥ 30 ng/mL	6 (3.75)	4 (2.50)	6 (3.00)	6 (3.00)
χ^2/P (1 and 2)	31.9083/0.0000		35.5190/0.0000	
χ^2/P (1 and 3)	42.7321/0.0000		56.9670/0.0000	
χ^2/P (1 and 4)	84.2105/0.0000		106.2147/0.0000	
χ^2/P (2 and 3)	0.9460/0.3307		3.0066/0.0829	
χ^2/P (2 and 4)	17.1628/0.0000		25.4118/0.0000	
χ^2/P (3 and 4)	10.5411/0.0012		11.8890/0.0006	

3.4. Analysis of adverse pregnancy outcomes

Among pregnant women with different levels of SF, there was no statistical difference in adverse pregnancy outcomes between anemic and non-anemic pregnant women ($P > 0.05$). See **Table 3**.

Table 3. Analysis table of adverse pregnancy outcomes (*n*, %)

	SF level	Postpartum hemorrhage	Premature rupture of membranes	Low birth weight infant	Fetal distress	Total	χ^2	<i>P</i>
< 10 ng/mL	Anemia (<i>n</i> = 103)	2 (1.94)	2 (1.94)	1 (0.97)	1 (0.97)	6 (5.83)	0.0092	0.9237
	Normal (<i>n</i> = 55)	1 (1.82)	1 (1.82)	1 (1.82)	0 (0.00)	3 (5.45)		
10–19.9 ng/mL	Anemia (<i>n</i> = 41)	1 (2.44)	1 (2.44)	0 (0.00)	0 (0.00)	2 (4.88)	0.1601	0.6890
	Normal (<i>n</i> = 115)	2 (1.74)	2 (1.74)	1 (0.87)	0 (0.87)	4 (3.48)		
20–29.9 ng/mL	Anemia (<i>n</i> = 33)	0 (0.00)	1 (3.03)	0 (0.00)	0 (0.00)	1 (3.03)	0.0030	0.9565
	Normal (<i>n</i> = 175)	1 (0.57)	2 (1.74)	0 (0.00)	2 (1.74)	5 (2.86)		
≥ 30 ng/mL	Anemia (<i>n</i> = 23)	1 (4.35)	1 (4.35)	0 (0.00)	0 (0.00)	2 (8.70)	0.2930	0.5883
	Normal (<i>n</i> = 455)	8 (1.76)	8 (1.76)	8 (1.76)	3 (0.66)	27 (5.93)		

4. Discussion

Iron is an essential trace element for maintaining the normal functioning of bodily organs. It regulates the oxygen transport of myoglobin and hemoglobin. Inadequate intake or absorption of iron can induce anemia, especially during pregnancy, where the incidence of IDA is relatively high, making it a common type of anemia pathology. IDA can cause malnutrition in pregnant women, leading to various pregnancy complications^[3]. Additionally, insufficient nutrient intake can restrict fetal growth and development, indicating that IDA poses a significant hazard to the health of both mother and child. Furthermore, different degrees of anemia in pregnant women manifest as various symptoms. Pregnant women with mild IDA may experience weakness, fatigue, tiredness, dizziness, blurred vision, paleness, inability to concentrate, and memory decline. Those with moderate IDA may suffer from shortness of breath, palpitations, and abdominal distension. In severe IDA, the blood's oxygen-carrying capacity decreases, which can lead to placental hypoxia, resulting in placental villus necrosis and degeneration, thereby increasing the risk of intrauterine distress^[4]. According to the data presented in this paper, there were 160 cases (16.00%) of IDA in the second trimester and 200 cases (20.00%) in the third trimester, indicating a relatively high incidence of IDA during pregnancy.

SF is an iron-containing protein belonging to macromolecules that can store iron and control its intracellular distribution. When the level of free iron in the human body rises, SF plays a storage role, reducing cytotoxic reactions. When iron levels decrease, SF releases iron to meet the body's daily needs. Based on the different proportions of SF light subunit (L) and heavy subunit (H), it can be divided into acidic ferritin (dominated by the H subunit) and basic ferritin (dominated by the L subunit), which play roles in areas such as the myocardium, placenta, liver, and spleen tissues^[5]. During pregnancy, SF levels undergo changes. This paper monitored blood routine indicators and SF indicators during pregnancy. The results showed that the erythrocyte parameters and SF levels of pregnant women with IDA in the second trimester were lower than those of healthy pregnant women ($P < 0.05$). This indicates abnormalities in both SF and erythrocyte parameters in pregnant women with IDA. Clinically, blood routine results are often used to evaluate anemia, but the sensitivity and accuracy of IDA assessment are insufficient, requiring a comprehensive analysis of anemia status based on other laboratory results^[6]. The SF indicator can accurately reflect the body's iron storage state, enabling precise prediction of IDA during pregnancy. Specifically, individuals with lower SF concentrations are more prone to IDA. Additionally, hemoglobin is a primary indicator for screening anemia. Obtaining hemoglobin levels

in pregnant women can assist physicians in initially assessing anemia risk. However, numerous factors can influence hemoglobin, such as acute or chronic blood loss, nutritional deficiencies, and lack of hematopoietic materials, which can cause hemoglobin levels to fluctuate. Iron is a crucial component of hemoglobin, and iron deficiency can affect the body's hemoglobin synthesis, leading to decreased hemoglobin concentration and even inducing symptoms like memory loss and tinnitus, posing significant hazards to the physical and mental health of pregnant women ^[7]. Another set of data presented in this paper demonstrates that pregnant women with SF levels < 10 ng/mL have a higher IDA incidence compared to those with SF levels of 10–19.9 ng/mL, 20–29.9 ng/mL, and ≥ 30 ng/mL. Moreover, the lower the SF level, the higher the IDA incidence ($P < 0.05$). This suggests a certain relationship between SF levels and IDA incidence, making it possible to evaluate the IDA incidence during pregnancy by monitoring SF indicators.

Pregnant women in a healthy state should provide 3–7 mg of iron daily to the fetus, transported via the placenta. However, as the gestational period increases, the pregnant woman's demand for iron increases. Some pregnant women develop IDA (Iron Deficiency Anemia) due to long-term iron deficiency, which can affect placental nutrition supply, restrict normal fetal growth and development, and increase the risk of premature birth and fetal death ^[8]. Based on the data analysis in this article, there was no statistical difference in adverse pregnancy outcomes between anemic and non-anemic pregnant women among different levels of SF (serum ferritin), with $P > 0.05$. The reason for this is that most of the IDA pregnant women in this study had mild anemia, and all received active treatment after being monitored for anemia, leading to rapid correction of the anemia. Only a few anemia patients remained untreated in the late pregnancy. Additionally, a few patients developed new anemia in the late pregnancy, but as they were close to delivery, the harm of anemia to the fetus was reduced, so anemia did not affect fetal growth and development. In this study, there were no serious adverse pregnancy outcomes among pregnant women with different SF levels, regardless of whether they developed anemia ^[9].

However, it should be noted that after a pregnant woman is diagnosed with IDA, she should adjust her diet, increase intake of iron-rich foods such as mutton, beef, blood products, and animal liver, and pay attention to vitamin C supplementation to improve the body's iron intake. Pregnant women should also avoid coffee and strong tea, as the calcium and tannic acid in these foods can form insoluble complexes with iron, inhibiting the body's absorption of iron. They should also avoid strenuous activities, excessive fatigue, correct poor sleep habits, and increase daily sleep time to reduce anemia symptoms. If dietary adjustments cannot meet the iron supplementation needs, pregnant women can take iron element such as ferrous gluconate and ferrous sulfate orally as prescribed by a doctor, starting with a small dose and gradually increasing the dose to reduce gastrointestinal irritation. When taking iron supplements, tetracyclines and antacids should be avoided to prevent adverse effects on iron absorption. Some pregnant women who are not tolerant of oral iron supplements can be prescribed iron supplements such as iron sorbitol and iron dextran injections ^[10]. Additionally, pregnant women should regularly monitor blood routine tests to evaluate changes in red blood cells, hemoglobin SF, and analyze the correction of IDA. They should also periodically review indicators such as transferrin saturation to analyze the storage and utilization of iron elements in pregnant women.

5. Conclusion

In summary, the lower the SF level in the second and third trimesters of pregnancy, the higher the incidence of

IDA. Active management and control after IDA diagnosis can reduce adverse pregnancy outcomes and ensure the health of both mother and baby. However, the number of pregnant women in the second and third trimesters included in this study for blood routine and SF testing was relatively small, and there may be some chance in the evaluation of the correlation between SF and IDA. In the future, the number of pregnant women samples should be increased to further analyze the correlation between SF and IDA, and summarize iron deficiency prevention strategies in clinical practice.

Disclosure statement

The authors declare no conflict of interest.

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Association between *FcγRIIB* Gene Polymorphism, Periodontitis and Pregnancy-induced Hypertension in Chinese Pregnancy Women

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Abstract: *Objective:* Research suggests a link between maternal periodontitis and pregnancy-induced hypertension (PIH). As an immunoglobulin G (IgG) receptor, *FcγRIIB* delivers inhibitory signals to B lymphocytes. Previous studies have demonstrated that *FcγRIIB*-232I/T polymorphism is associated with periodontitis, and the link between 232T allele carriers and periodontitis may stem from their reduced IgG antibody responses to *P. gingivalis*. The role of *FcγRIIB*-232I/T polymorphism in predisposing Chinese pregnant women to periodontitis and PIH was explored in this investigation. *Methods:* Clinical periodontal parameters and obstetric records were retrospectively analyzed in 87 Chinese pregnant women. *FcγRIIB*-232I/T genotyping was performed using genomic DNA isolated from peripheral blood samples from each participant. The expression levels of *FcγRIIB* on peripheral B lymphocytes from 10 women were measured by flow cytometry. *Results:* The *FcγRIIB*-232T allele was associated with elevated third-trimester blood pressure, with compounded effects observed in carriers concurrently affected by periodontitis. Periodontitis and PIH exhibited a shared genetic predisposition through the *FcγRIIB*-232I/T polymorphic locus. Among individuals carrying the *FcγRIIB*-232T allele, periodontitis was significantly associated with PIH. *Conclusion:* *FcγRIIB*-232T allele carriers of Chinese pregnancy women are more susceptible to periodontitis and PIH, and those with periodontitis are more susceptible to PIH.

Keywords: *FcγRIIB* gene polymorphism; Periodontitis; Pregnancy-induced hypertension

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1. Introduction

The ITIM-containing cytoplasmic architecture of *FcγRIIB* establishes its unique position as the sole inhibitory

member of the Fc receptor family ^[1]. Functional studies reveal that IgG complex-mediated co-ligation of *FcγRIIb* and BCR triggers ITIM-dependent tyrosine phosphorylation events that negatively regulate BCR signaling amplitude ^[2,3]. Pathophysiological observations in *FcγRIIb*-knockout mice, characterized by severe immune complex-induced inflammatory syndromes, validate its critical role in maintaining immunological equilibrium ^[4,5].

Systemic maternal infections may increase risks of placental infection, preterm birth and premature rupture of membranes through inflammatory cytokines and prostaglandin release ^[6,7]. Periodontitis, a chronic inflammatory oral condition, is involved in the pathogenesis of gestational hypertensive disorders, particularly PIH and preeclampsia ^[8–11].

11 single-nucleotide polymorphisms (SNPs) have been confirmed to be *FcγRIIB*-specific of which to be associated with periodontitis. Yasuda et al. ^[12] demonstrated distinct associations between *FcγRIIB* genetic variations and periodontitis subtypes through case-control analysis. Their investigation revealed a statistically significant variation in the allelic distribution of the *FcγRIIB* gene polymorphism at exon5 (nt232I/T) when comparing subjects with aggressive periodontitis to healthy individuals, where the 232T allele exhibited higher prevalence in the disease cohort. Additionally, the study identified differential patterns in the intronic region (nt646-184A/G) of this gene, with the 646-184A variant showing increased frequency in chronic periodontitis patients relative to non-diseased controls. These findings suggest subtype-specific genetic predispositions involving distinct regulatory domains of the *FcγRIIB* receptor in periodontal pathogenesis. Prior investigations have identified associations between the *FcγRIIB*-nt645+25A/G polymorphism and multiple gestational complications, including periodontal disease, preterm delivery accompanied by low birth weight, as well as PIH and preeclampsia in maternal populations ^[11,13]. However, the mechanism of these associations remains unclear.

Emerging evidence suggests a potential mechanistic link between periodontal pathogenesis and pregnancy complications. Subgingival microbial colonization induces systemic inflammation through elevated circulating proinflammatory mediators, which may propagate to the chorioamniotic membranes, potentially contributing to gestational disorders. Particularly, imbalanced Th1/Th2 cytokine profiles characterized by elevated interleukin-1β and IL-6 concentrations have been significantly associated with preterm deliveries occurring before 35 weeks' gestation and histologically confirmed chorioamnionitis ^[14]. Of clinical relevance, genetic variations in *FcγRIIB* (specifically nt232I/T and nt645+25A/G loci) have been implicated in periodontal disease pathogenesis. Functional analyses reveal that the 232T/nt645+25AA haplotype correlates with attenuated IgG-mediated responses to *Porphyromonas gingivalis* antigens ^[15,16], concomitant with enhanced *FcγRIIB* receptor expression on B-lymphocytes in AA genotype carriers relative to GG individuals ^[15]. This immunogenetic profile suggests a biological plausibility for *FcγRIIB* polymorphisms modulating host-inflammatory responses to periodontal pathogens, potentially establishing a proinflammatory milieu that could adversely affect pregnancy maintenance through cytokine-mediated pathways.

This study aims to investigate whether the *FcγRIIB*-nt232I/T polymorphism is associated with periodontitis and/or PIH in Chinese pregnant women, and to further explore the potential mechanisms involved.

2. Materials and methods

2.1. Subjects

This study enrolled 200 pregnant women (mean age: 37.89 years old) who were referred to the Department of Obstetrics and Gynecology, HMU4 (Fourth Affiliated Hospital, Harbin Medical University), and delivered live

infants (Oct 2015–Oct 2019). This study implemented rigorous exclusion criteria to minimize confounding: (1) Pre-existing medical conditions (hypertension, hepatitis B, anemia, diabetes, psychiatric disorders, renal/genetic diseases); (2) Obstetric risks (multifetal gestation, cervical insufficiency, placental anomalies)^[13]; (3) Substance exposure (active smoking post-conception, alcohol/drug abuse); (4) Nutritional compromise. The inclusion criteria were selected based on documented confounding variables and established risk predictors for obstetric complications, as delineated in prior epidemiological studies^[11]. Following rigorous screening protocols, the analytical cohort ultimately included 87 eligible participants. All enrolled subjects provided written informed consent through standardized documentation prior to parturition. This consent procedure underwent ethical review and received formal certification from the Institutional Review Board of Harbin Medical University, ensuring compliance with the Declaration of Helsinki guidelines.

2.2. Clinical assessment

Perinatal records were retrospectively abstracted from the obstetrical database of HMU4. PIH diagnosis adhered to China's gestational hypertension management guidelines (CSOG-2020), requiring sustained blood pressure elevation (SBP \geq 140 mmHg and/or DBP \geq 90 mmHg) on two consecutive readings post-20 gestational weeks. Embryonic age determination utilized the Naegele formula, with gestational dating anchored to the initial day of the last confirmed menstrual cycle.

2.3. Periodontal examination

Periodontal evaluations were systematically conducted during gestational weeks 16–24 by three trained clinicians blinded to maternal health status. Standardized oral assessments included multilevel diagnostic parameters: (1) Probing depth measurements quantifying connective tissue detachment (recorded at six anatomical locations per dental unit), reflecting cumulative periodontal destruction; (2) Gingival bleeding index documentation as an inflammatory activity indicator; (3) Microbial accumulation quantification through visible plaque index scoring. Case definition followed established epidemiological criteria, requiring \geq 60% of examined sites to demonstrate \geq 3 mm clinical attachment loss, a threshold indicative of significant periodontal breakdown^[17].

2.4. *FcγRIIB*-nt232I/T genotyping protocol

Genetic material extraction from venous blood samples was conducted using commercial isolation reagents (Easy-DNA system, Invitrogen, San Diego, CA). Purified nucleic acid aliquots were cryopreserved at 4 °C pending molecular analysis. Target gene amplification employed a nested PCR strategy adapted from established protocols¹². Initial amplification targeted the *FcgRIIB* locus using intronic primers (spanning introns 3–6), designed to circumvent sequence homology between *FcgRIIB* and the homologous *FcgRIIC* locus. Amplimers underwent restriction enzyme digestion and purification before serving as templates for secondary amplification focusing on exon5 sequences. The exon-specific reaction utilized a 25 μ L amplification system containing 1.25 U ExTaq polymerase, with 30 ng template DNA subjected to initial denaturation (95 °C \times 5 min), followed by 35 cycles of three-step amplification (94 °C \times 30 s, 60 °C \times 30 s, 72 °C \times 30 s), concluding with terminal extension (72 °C \times 5 min).

2.5. *FcγRIIB* expression levels on peripheral B lymphocytes

The expression levels of *FcgRIIB* on peripheral B lymphocytes were compared among *FcgRIIB*-232I/T genotypes in 10 Chinese pregnancy women volunteers. Present smokers were excluded. Five millilitres of

EDTA-anticoagulated peripheral blood was obtained from each subject. Erythrocytes were lysed by incubation with ammonium chloride. Following three PBS rinsing cycles ($300\text{ g} \times 5\text{ min}$), cellular suspensions underwent sequential immunolabeling procedures. Primary incubation utilized monoclonal antibody clone 41H.16 (mouse origin) paired with species-matched FITC-conjugated F(ab')_2 secondary reagents (1:200 dilution, 30 min RT). Subsequent pre-blocking with homologous serum (10% v/v, 15 min) preceded counterstaining with PE-labeled anti-CD19 lineage markers (clone HIB19, 20 $\mu\text{L}/\text{test}$). Viable cell populations were discriminated through 7-AAD viability dye exclusion (5 $\mu\text{L}/\text{test}$, 10 min incubation). Processed samples were vortex-mixed in staining buffer and subjected to flow cytometric analysis (BD FACSCanto II), with *FcγRIIB* expression quantitation determined by median fluorescence intensity (MFI) of CD19⁺lymphocyte subsets.

2.6. Statistical analysis

The correlation between pregnancy-induced hypertension (PIH) and periodontitis was analyzed using nonparametric Mann-Whitney U tests. Categorical analyses of *FcγRIIB*-nt232I/T genotypic distributions versus PIH status employed chi-square tests, with Fisher's exact substitution applied when expected cell frequencies fell below 5. For quantitative comparisons of *FcγRIIB* receptor density on B lymphocytes, nonparametric comparative analyses were implemented based on data distribution characteristics. Statistical analyses were conducted using Stat View with significance threshold at $P < 0.05$.

3. Results

Based on determination of *FcγRIIB*-232I/T genotypes, the 87 Chinese pregnancy women were separated into *FcγRIIB*-232T carriers group ($n = 61$) and T non-carriers group ($n = 26$) in **Table 1**. 232-T carriers exhibited: Higher periodontitis prevalence ($P = 0.041$); Elevated third-trimester blood pressure (Systolic blood pressure, SBP, $P = 0.031$; Diastolic blood pressure, DBP, $P = 0.021$). No significant intergroup differences emerged in postpartum blood pressure or clinical periodontal parameters (**Table 1**).

Table 1. Clinical characteristics between *FcγRIIB*-nt232T carriers and non-carriers

	<i>FcγRIIB</i> -nt232T carriers ($n = 61$)	<i>FcγRIIB</i> -nt232T non-carriers ($n = 26$)	<i>P</i> -value
Periodontitis (+)	13 (21%)	1 (4%)	0.0411*
CAL (mm)	2.5 ± 0.5	2.5 ± 0.4	0.3624
Bleeding on probing (%)	12.4 ± 15.8	14.0 ± 16.7	0.7883
Plaque control record (%)	35.7 ± 22.5	30.1 ± 20.8	0.3252
Gestational age at delivery (weeks)	36.68 ± 3.56	40.12 ± 4.73	0.1767
SBP at the third trimester	134.35 ± 8.75	115.67 ± 13.22	0.0314*
DBP at the third trimester	83.34 ± 5.04	72.15 ± 9.75	0.0211*
SBP after delivery	129.08 ± 9.97	120.89 ± 16.12	0.1040
DBP after delivery	80.63 ± 5.75	74.67 ± 9.34	0.1441

Based on periodontal and obstetric records, the *FcγRIIB*-232T carriers of Chinese pregnant women were

separated into periodontitis group ($n = 13$) and non-periodontitis ($n = 48$) in **Table 2**. The level of SBP ($P = 0.0106$) and DBP ($P = 0.0193$) at the third trimester were significantly higher in the periodontitis of *FcgRIIB*-232T carriers group compared with the non-periodontitis of *FcgRIIB*-232T carriers group, however, the level of SBP and DBP after delivery were not significantly higher in the periodontitis of *FcgRIIB*-232T carriers group compared with the non-periodontitis of *FcgRIIB*-232T carriers group.

Table 2. Characteristics of T carries with/without periodontitis

	<i>FcgRIIB</i> -nt232T		
	Periodontitis ($n = 13$)	Non-periodontitis ($n = 48$)	P-value
Gestational age at delivery (weeks)	36.68 \pm 3.56	40.12 \pm 4.73	0.5442
Maternal age (years)	42.18 \pm 4.03	39.35 \pm 4.15	0.1081
SBP at the third trimester	136.12 \pm 8.07	119.71 \pm 14.55	0.0106*
DBP at the third trimester	82.44 \pm 4.98	73.89 \pm 11.07	0.0193*
SBP after delivery	132.31 \pm 14.54	127.90 \pm 12.86	0.4657
DBP after delivery	81.50 \pm 10.70	76.97 \pm 9.64	0.2547

The *FcgRIIB*-nt232I/T polymorphism was associated with periodontitis ($P = 0.0319$) and PIH ($P = 0.414$) in Chinese pregnancy women. In the *FcgRIIB*-232T carriers group, periodontitis was significantly associated with PIH ($P = 0.0052$). The percentage of periodontitis with *FcgRIIB*-232T carriers (T/I+TT) group was significantly higher than non-periodontitis with *FcgRIIB*-232T carriers (T/I+TT) group, periodontitis with *FcgRIIB*-232T non-carriers (II) group, non-periodontitis with *FcgRIIB*-232T non-carriers (II) group in **Table 3**. The significant higher percentage in PIH with *FcgRIIB*-232T carriers (T/I+TT) group was observed compared with T non-carriers group ($P = 0.0414$) in **Table 3**. The percentage of periodontitis with PIH in the *FcgRIIB*-232T carriers (T/I+TT) group was the highest in all the groups ($P = 0.0052$) in **Table 4**. The expression of level of *FcgRIIB* on peripheral B lymphocytes with *FcgRIIB*-232T carriers of Chinese pregnant women were significantly higher than in non-carriers, as shown in **Figure 1**.

Table 3. Association between *FcgRIIB*-nt232-I/T genotypes and status(periodontitis/PIH)

	T/I ($n = 11$)	TT ($n = 50$)	II ($n = 26$)	χ^2	P-value
Periodontitis	3 (21%)	10 (72%)	1 (7%)	6.890	0.0319*
Non-Periodontitis	8 (12%)	40 (55%)	25 (33%)		
PIH	5 (29%)	11 (65%)	1 (6%)	21.672	0.0414*
Non-PIH	6 (8%)	39 (56%)	25 (36%)		

* P -value < 0.05 .

Table 4. Periodontitis-PIH comorbidity in *FcgRIIB*-232T carries

	Periodontitis ($n = 13$)	Non-periodontitis ($n = 48$)	χ^2	P-value
PIH	12 (86%)	2 (14%)	18.471	0.0052*
Non-PIH	1 (2%)	46 (98%)		

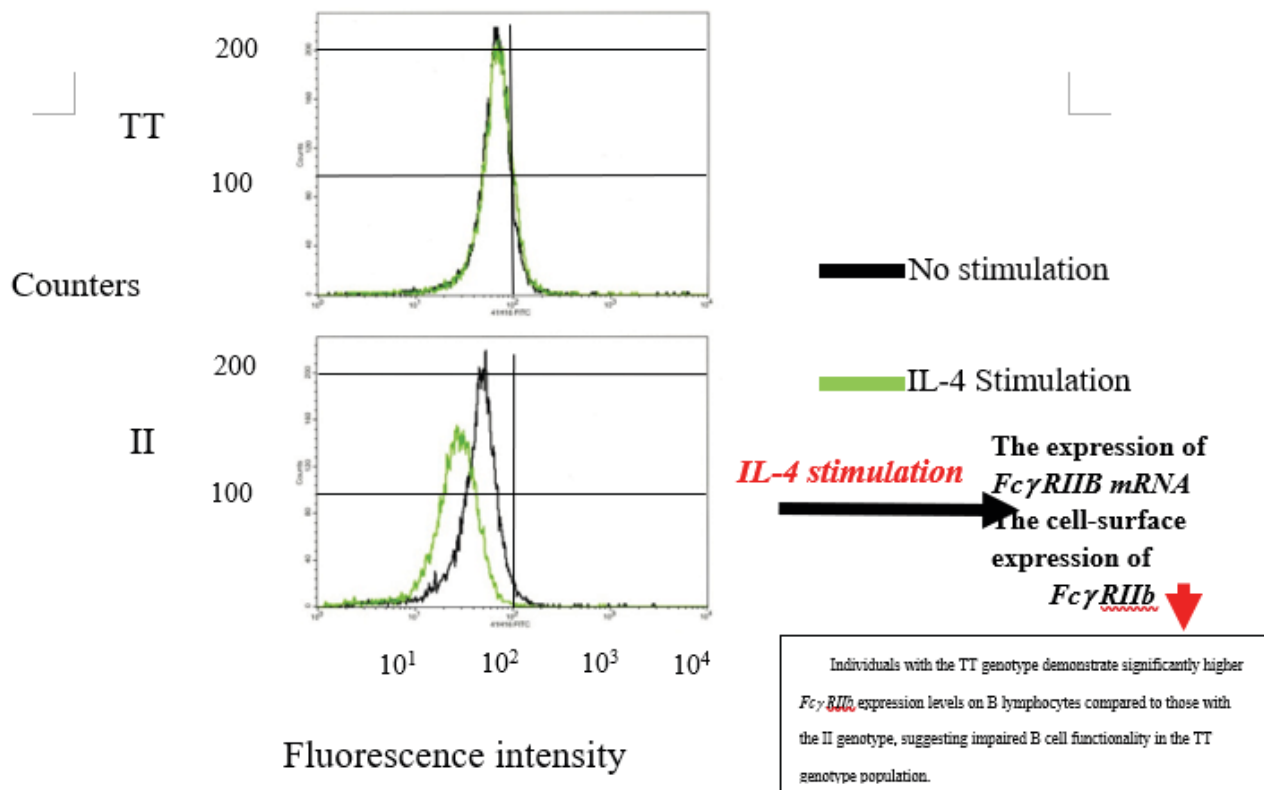


Figure 1. FcγRIIB expression levels on B lymphocytes across FcγRIIB-232I / T genotypes.

4. Discussion

Emerging evidence highlights the immunomodulatory effects of periodontal pathogens, particularly *Porphyromonas gingivalis*, on host immune regulation^[18–20]. Clinical investigations demonstrate enhanced humoral immune responses in periodontitis-affected individuals, manifested by elevated serum IgG titers targeting the 40-kDa outer membrane antigen of *P. gingivalis* compared to healthy counterparts. Central to this immunological interplay *FcγRIIB*, a critical inhibitory receptor governing B-cell activation thresholds through its co-ligation with antigen-specific B-cell receptors via immune complexes, thereby modulating antibody-mediated feedback regulation^[16]. Murine models of autoimmune disorders reveal that allelic variants of this receptor correlating with diminished surface expression predispose to pathogenic autoantibody production through impaired immune complex clearance^[21]. The study extends these mechanistic insights to human periodontal disease pathogenesis. The observed enrichment of the *FcγRIIB*-232T allele (exon5) in aggressive periodontitis cohorts suggests a genotype-phenotype correlation, potentially mediated through attenuated IgG responsiveness to periodontal pathogens. Specifically, this allelic variant demonstrates reduced opsonophagocytic capacity against *P. gingivalis* antigens in chronic periodontitis patients. The study proposes that *FcγRIIB* polymorphisms may establish a proinflammatory microenvironment through two synergistic pathways: (1) Compromised pathogen clearance due to suboptimal IgG-mediated bacterial neutralization; (2) Dysregulated B-cell activation thresholds resulting in amplified inflammatory cytokine cascades^[16]. However, the objects of these studies were not pregnant women. In this paper, the study first finds that there is a higher

prevalence of periodontitis in the *FcgRIIB*-232T carriers group compared with the T non-carriers group in Chinese pregnant women in **Table 1**, and the percentage of periodontitis with *FcgRIIB*-232T carriers (T/I+TT) group was significantly highest in all groups in **Table 3**. These results suggest that the *FcgRIIB*-232T allele of Chinese pregnant women is more susceptible to periodontitis than *FcgRIIB*-232I allele of Chinese pregnant women.

Infections play a significant role in spontaneous preterm labor and birth as well as in related neonatal complications ^[22]. The study's prior work established that the association of the 232T allele and the nt645+25AA genotype carriers with periodontitis might be related to the lower levels of IgG antibody response to *P. gingivalis* ^[15,16]. Our longitudinal investigations revealed a significant pathophysiological association between attenuated humoral responses to periodontal pathogens during first-trimester gestation and subsequent gestational complications. Specifically, diminished pathogen-specific immunoglobulin G (IgG) titers targeting *Porphyromonas gingivalis* in early pregnancy correlated with increased incidence of fetal growth restriction and spontaneous preterm delivery. Complementing these findings, functional genomics analyses have established the *FcgRIIB*-nt645+25A/G allelic variant as a predisposing factor for obstetric complications, demonstrating significant associations with premature rupture of membranes, early-onset preeclampsia, and preterm labor in maternal cohorts with periodontal infections ^[11,13]. In this paper, the *FcgRIIB*-232T allele of Chinese pregnant women is more susceptible to higher levels of SBP and DBP at the third trimester compared with the *FcgRIIB*-232I allele of Chinese pregnant women in **Table 1**, meanwhile, the significant higher percentage in PIH with *FcgRIIB*-232T carriers (T/I+TT) group was observed compared with T non-carriers group in **Table 3** also have been found. However, the significantly higher level of SBP and DBP after delivery has not been observed in this paper. Therefore, pregnancy is the main cause of these different results.

One limitation of this study is that the number of women with periodontitis and PIH with *FcgRIIB*-232T non-carriers is too less to difficult to statistical analysis; therefore, the study only analyzed the relationship between periodontitis and PIH in the *FcgRIIB*-232T carriers group in **Table 2** and **Table 4**. The study also finds that periodontitis in Chinese pregnant women is more susceptible to levels of SBP and DBP at the third trimester compared with non-periodontitis, and the percentage of periodontitis with PIH is the highest in all of the *FcgRIIB*-232T carriers groups. These results suggest that *FcgRIIB*-232T allele carriers of Chinese pregnant women are more susceptible to periodontitis and PIH, and periodontitis with *FcgRIIB*-232T allele carriers of Chinese pregnant women are more susceptible to PIH. However, the clinical periodontal parameters have not been found to associate with *FcgRIIB*-232I/T polymorphism. The observed inter-study variations likely stem from population heterogeneity in obstetric history profiles and differential gradients of periodontal disease progression, parameters that were systematically quantified in our longitudinal cohort analyses ^[23].

To understand the mechanism of these associations, we get peripheral blood from 3 *FcgRIIB*-232T non-carriers and 7T carriers of Chinese pregnant women, and determine the expression levels of *FcgRIIB* on peripheral B lymphocytes. The higher levels of *FcgRIIB* with T allele carriers are observed compared with the T allele non-carriers, but the result is not significant. This result suggests that the function of B lymphocytes with *FcgRIIB*-232T carriers of Chinese pregnant women may be weaker than non-carriers. This study did not test the IgG level response to periodontal bacteria and the level of maternal proinflammatory cytokines, therefore, it remains unclear whether adverse pregnancy outcomes are caused by *FcgRIIB* gene polymorphism-related inflammation, triggered by periodontal infection via increased proinflammatory cytokine levels. Further studies should validate this etiological hypothesis.

5. Conclusion

FcγRIIB-232T allele carriers of Chinese pregnant women are more susceptible to periodontitis and PIH, and periodontitis with *FcγRIIB*-232T allele carriers of Chinese pregnant women are more susceptible to PIH.

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Authors contribution

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Data analysis: Junqiang Shan and Jiayu Fan

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Combination of Misoprostol and Oxytocin for Effective Control of Postpartum Hemorrhage During Cesarean Section

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Abstract: *Objective:* This study is to analyze the value of combining misoprostol and oxytocin in the prevention and control of postpartum hemorrhage during cesarean section. *Methods:* 82 cesarean section patients from July 2023 to July 2024 were selected as samples and randomly divided into two groups. Group A received misoprostol combined with oxytocin treatment, while Group B received only misoprostol treatment. The amount of postpartum hemorrhage, coagulation indicators, postpartum recovery indicators, and adverse reactions were compared between the two groups. *Results:* The intraoperative, 2-hour postpartum, 2-24-hour postpartum, and total blood loss in Group A were all lower than those in Group B ($P < 0.05$). The activated partial thromboplastin time (APTT), plasma prothrombin time (PT), fibrinogen (FIB), and thrombin time (TT) in Group A were all lower than those in Group B ($P < 0.05$). The first exhaust time, first time out of bed, and hospital stay after cesarean section in Group A were all shorter than those in Group B ($P < 0.05$). The adverse reaction rate in Group A was lower than that in Group B ($P < 0.05$). *Conclusion:* The application of misoprostol combined with oxytocin during cesarean section can optimize coagulation indicators, reduce blood loss, shorten postpartum recovery time, and is highly effective and feasible.

Keywords: Oxytocin; Misoprostol; Cesarean section; Postoperative bleeding

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1. Introduction

Cesarean section has become a commonly used assisted delivery technique for difficult births, referring to the assisted delivery technique of removing the fetus through the abdomen. However, postpartum bleeding can easily occur, which can increase the risk of maternal death. In recent years, the number of cesarean sections has increased year by year, but how to prevent and control postoperative bleeding remains a hot research topic in clinical practice. There are many inducements for postoperative bleeding after cesarean section, such as uterine atony, incision laceration, and placental abruption, which can increase the amount of postoperative bleeding

and prolong the recovery period of the mother. Intramuscular injection of oxytocin is a commonly used method to prevent and control postpartum hemorrhage. The active ingredient stimulates uterine contraction, which can reduce uterine bleeding. However, the risk of side effects of oxytocin alone is high, and combining it with misoprostol can further enhance uterine contraction, resulting in reduced postoperative bleeding ^[1]. Based on this, this article explores the effect of misoprostol combined with oxytocin using 82 cesarean section patients from July 2023 to July 2024 as samples.

2. Materials and methods

2.1. Materials

A sample of 82 pregnant women who underwent cesarean section from July 2023 to July 2024 were selected and randomly divided into groups.

2.2. Inclusion and exclusion criteria

- (1) Inclusion criteria: (a) Meet the cesarean section standards in the “Expert Consensus on Cesarean Section Surgery” ^[2]; (b) Singleton pregnancy; (c) Primiparas.
- (2) Exclusion criteria: (a) Coagulation disorders; (b) Drug intolerance; (c) Mental disorders.

2.3. Treatment methods

Group A received intravenous infusion of oxytocin injection (Shanghai Hefeng Pharmaceutical Co., Ltd.; National Medical Approval Number H31020850; 1 mL 10 units 10 vials) at a dose of 20 IU mixed with 500 mL of sodium chloride solution, administered within 1 hour, once; misoprostol tablets (Wuhan Jiulong Renfu Pharmaceutical Co., Ltd.; National Medical Approval Number H20073696; 0.2 mg × 3 tablets) were inserted into the anus. After observing the completion of delivery, 0.2 mg of misoprostol tablets were pushed into the anus 5 cm area through the rectum, administered once. The oxytocin method for Group B was the same as Group A.

2.4. Observation indicators

- (1) Blood loss: Record the amount of blood loss during surgery, 2 hours postpartum, 2-24 hours postpartum, and total blood loss.
- (2) Coagulation indicators: Detect APTT, PT, FIB, TT and other indicators using the solidification method.
- (3) Postoperative recovery indicators: Record the time of first exhaustion, first time out of bed, and length of hospital stay after cesarean section.
- (4) Adverse reactions: Record vomiting, nausea, and skin itching.

2.5. Statistical analysis

Data was processed using SPSS 21.0. Chi-square (χ^2) test was used to compare counting data (% recorded), and *t*-test was used for measurement indicators (mean ± standard deviation, SD recorded). There was a statistically significant difference with $P < 0.05$.

3. Results

3.1. Baseline data

Comparing the data of Group A with Group B, $P > 0.05$. As shown in **Table 1**.

Table 1. Baseline data analysis table (n , mean \pm SD)

Group	Age (years)	Gestational weeks	Body mass index (kg/m ²)
Group A ($n = 41$)	29.11 \pm 0.81	38.11 \pm 1.05	23.74 \pm 1.61
Group B ($n = 41$)	29.09 \pm 0.79	38.09 \pm 1.06	23.71 \pm 1.63
t	0.1132	0.0858	0.0838
P	0.9102	0.9318	0.9334

3.2. Blood loss

The blood loss during surgery, 2 hours postpartum, 2-24 hours postpartum, and total blood loss in Group A were all lower than those in Group B, with $P < 0.05$. As shown in **Table 2**.

Table 2. Blood loss (mL, mean \pm SD)

Group	Intraoperative blood loss	2h postpartum blood loss	2-24h postpartum blood loss	Total blood loss
Group A ($n = 41$)	207.44 \pm 8.09	150.44 \pm 3.82	147.41 \pm 2.89	451.44 \pm 10.25
Group B ($n = 41$)	309.81 \pm 9.44*	190.36 \pm 4.41*	175.44 \pm 4.06*	550.69 \pm 12.19*
t	52.7246	43.8111	36.0145	39.9023
P	0.0000	0.0000	0.0000	0.0000

Note: *Indicates a statistically significant difference compared to Group A with $P < 0.05$.

3.3. Coagulation indicators

At 24 hours postoperatively, APTT, PT, FIB, and TT in Group A were all lower than those in Group B, with $P < 0.05$. As shown in **Table 3**.

Table 3. Coagulation indicators (mean \pm SD)

Group	APTT(s)		PT(s)		FIB(g/L)		TT(s)	
	Pre-operation	24h Post-operation	Pre-operation	24h Post-operation	Pre-operation	24h Post-operation	Pre-operation	24h Post-operation
Group A ($n = 41$)	41.29 \pm 1.42	27.49 \pm 1.06	13.18 \pm 1.12	7.21 \pm 0.48	5.39 \pm 1.02	2.61 \pm 0.46	16.41 \pm 1.21	11.25 \pm 0.48
Group B ($n = 41$)	41.31 \pm 1.38	30.21 \pm 1.15*	13.19 \pm 1.11	8.52 \pm 0.69*	5.41 \pm 1.04	3.62 \pm 0.57*	16.39 \pm 1.19	12.62 \pm 0.57*
t	0.0647	11.1359	0.0406	9.9795	0.0879	8.8293	0.0755	11.7720
P	0.9486	0.0000	0.9677	0.0000	0.9302	0.0000	0.9400	0.0000

Note: *Indicates a statistically significant difference compared to Group A with $P < 0.05$.

3.4. Postoperative recovery indicators

The time of first exhaust, first time out of bed, and length of hospital stay after cesarean section in Group A

were all shorter than those in Group B, with $P < 0.05$. As shown in **Table 4**.

Table 4. Postoperative recovery indicators (mean \pm SD)

Group	First exhaust time after surgery (h)	First time out of bed after surgery (d)	Hospital stay (d)
Group A ($n = 41$)	17.15 \pm 0.49	1.79 \pm 0.42	5.05 \pm 0.46
Group B ($n = 41$)	21.79 \pm 0.68*	2.96 \pm 0.51*	7.06 \pm 0.69*
t	35.4476	11.3393	15.5199
P	0.0000	0.0000	0.0000

Note: *Indicates a statistically significant difference compared to Group A with $P < 0.05$.

3.5. Adverse reaction indicators

The adverse reaction rate in Group A was lower than that in Group B, with $P < 0.05$. As shown in **Table 5**.

Table 5. Adverse reaction indicators (n , %)

Group	Vomiting	Nausea	Skin Itching	Incidence Rate
Group A ($n = 41$)	0 (0.00)	1 (2.44)	0 (0.00)	1 (2.44)
Group B ($n = 41$)	2 (4.88)	2 (4.88)	2 (4.88)	6 (14.63)*
χ^2	-	-	-	3.9048
P	-	-	-	0.0481

Note: *Indicates a statistically significant difference compared to Group A with $P < 0.05$.

4. Discussion

Cesarean section is often used in emergencies such as transverse or breech delivery, multiple pregnancy delivery, fetal distress delivery, preeclampsia, cephalopelvic disproportion, and labor stagnation. Additionally, a few women request a cesarean section due to fear of pain during childbirth. However, with the increasing number of cesarean sections, the incidence of postpartum hemorrhage, a common complication of cesarean section, has also increased, which can lead to increased blood loss and risk of maternal death. The causes of postpartum hemorrhage after cesarean section are related to the mother's factors. For example, excessive fear and anxiety of the mother can lead to endocrine disorders and uterine atony. During childbirth, long-term violent contraction of uterine muscles consumes a lot of physical strength, making it more prone to uterine muscle fatigue. Factors such as oversized fetuses or multiple pregnancies can cause excessive stretching of uterine muscle fibers during childbirth, reducing the uterus's ability to contract. Additionally, having too many births or preeclampsia can increase the risk of postpartum hemorrhage after cesarean section. The pathological feature of postpartum hemorrhage after cesarean section is a large amount of vaginal bleeding in a short period, which can cause symptoms such as tachycardia, hypotension, and paleness in the mother. As the amount of bleeding increases, it can also induce symptoms such as thirst, fatigue, and dizziness.

Currently, postpartum hemorrhage after cesarean section is treated with physical methods, medication, or surgical intervention in severe cases to ensure the mother's health and safety. Uterotonic agents are commonly used drugs to prevent post-cesarean bleeding, and oxytocin is often used to reduce the amount of bleeding after cesarean section and shorten the recovery time. However, due to individual differences among mothers, the

hemostatic effect of oxytocin is limited, and it should be combined with other drugs to enhance the hemostatic effect ^[3]. Additionally, oxytocin has a dose-dependent characteristic, and high-dose administration can increase the risk of uterine tetanic contraction and hypotension. Moreover, oxytocin can only prevent and control bleeding caused by uterine atony and has a poor effect on preventing postpartum hemorrhage caused by birth canal injury. Misoprostol is derived from prostaglandin E. After administration, it can excite the uterine muscle layer, accelerate uterine contraction, increase the contraction amplitude of the muscle layer, repair cervical damage caused by childbirth, increase intrauterine pressure, and enhance the hemostatic effect ^[4]. Compared with single oxytocin treatment, combined use with misoprostol can accelerate drug absorption and optimize the mother's coagulation function.

The data presented in this article indicates that Group A had lower blood loss compared to Group B, with $P < 0.05$. This difference can be attributed to the intravenous infusion of oxytocin injection, a polypeptide hormone drug that stimulates rhythmic uterine contractions in the mother, increasing the frequency and intensity of contractions, thereby achieving excellent hemostatic effects. However, it's important to note that the active ingredient of oxytocin only acts on the upper segment of the uterus, and oxytocinase in the mother's body can dilute the concentration of oxytocin, while intestinal activity can deactivate it, limiting the hemostatic effect of oxytocin alone ^[5]. Additionally, due to the short half-life and duration of oxytocin, it should be combined with misoprostol for synergistic hemostatic treatment. This combination can regulate intrauterine pressure, increase uterine tension, restore rhythmicity of smooth muscle, soften the cervix, and stimulate uterine contractions. Administered through the anus, misoprostol takes effect within 2.5–20 minutes, and its half-life is up to 90 minutes, making the combined administration more effective in controlling postpartum hemorrhage ^[6]. Another set of data shows that 24 hours after surgery, Group A had lower APTT, PT, FIB, and TT compared to Group B, with $P < 0.05$. This can be explained by the use of oxytocin treatment, which stimulates smooth muscle contraction to stop bleeding, slowing blood loss and maintaining blood concentration. This reduces the adverse effects of blood loss on coagulation factor function, helping to stabilize coagulation indicators. However, long-term or excessive use of oxytocin can affect uterine smooth muscle function, leading to poor uterine contraction and even indirectly damaging coagulation function. Combination therapy with misoprostol enhances the uterus's sensitivity to oxytocin, improves hemostatic efficacy, protects vascular endothelial cells and platelet function, and indirectly improves coagulation indicators ^[7,8].

Another set of data indicates that Group A had shorter times for first exhaust, first ambulation, and hospital stay after cesarean section compared to Group B, with $P < 0.05$. This is because during pregnancy, the expression of uterine receptors for contractions gradually increases in the myometrial region, reaching a peak during childbirth, enhancing the effect of oxytocin on stimulating uterine contractions. Therefore, injecting oxytocin before childbirth can effectively prevent and control bleeding. The active ingredient of misoprostol can bind to prostaglandin receptors in smooth muscle, activating calcium ion channels in cells and stimulating uterine contractions. It can also soften and dilate the cervix, reducing cervical resistance during childbirth ^[9,10]. Combined administration during cesarean section surgery results in synergistic effects, increasing uterine contractility and reducing blood loss in the myometrium. The complementary advantages of combined administration, with misoprostol's long-lasting and slow-acting properties, can compensate for the fast-acting and short-duration limitations of oxytocin alone. This combination can effectively relieve symptoms such as dizziness and fatigue, improve postoperative recovery, shorten early ambulation time, accelerate gastrointestinal motility, reduce the risk of deep vein thrombosis in the lower extremities after cesarean section, and help reduce cesarean section complications and

hospital stay^[11,12].

Finally, data shows that the adverse reaction rate in Group A was lower than that in Group B, with $P < 0.05$. This is because misoprostol administered through the anus results in a high local blood drug concentration, reducing systemic side effects of the drug. Additionally, misoprostol does not induce hypertension and has minimal damage to the cardiovascular system^[13,14]. Furthermore, oxytocin can continuously exert its effect for 1.5–2 hours, with a drug half-life of 10–15 minutes. Combining it with misoprostol enhances hemostatic effects and ensures high safety. However, it's essential to prioritize wound care after cesarean section, maintaining dryness and cleanliness of the wound, observing for any fluid leakage or redness, and actively preventing postoperative wound infection. Encouraging early ambulation once the mother's vital signs are stable can help shorten the postoperative recovery period and prevent venous thrombosis in the lower extremities. Initially, strenuous or vigorous activities should be avoided. Providing a scientific diet for the mother, increasing vitamin and protein intake, and encouraging her to drink more water are also crucial. Breastfeeding should be arranged as soon as possible after cesarean section to stimulate uterine contractions and shorten the time for uterine involution^[15].

5. Conclusion

In summary, the combination of oxytocin and misoprostol for the prevention and control of postpartum hemorrhage after cesarean section can reduce drug side effects, improve coagulation indicators, shorten postoperative recovery time, and reduce perioperative blood loss. This approach has significant promotional value.

Disclosure statement

The author declares no conflict of interest.

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