

Advances in Obstetrics and Gynecology Research

Editors-in-Chief

K. Matsuo

University of Southern California, USA

Qionghua Chen

The First Affiliated Hospital of Xiamen University, China

BIO-BYWORD SCIENTIFIC PUBLISHING PTY LTD

(619 649 400)

Level 10

50 Clarence Street

SYDNEY NSW 2000

Copyright © 2026. Bio-Byword Scientific Publishing Pty Ltd.

Complimentary Copy



Advances in Obstetrics and Gynecology Research

Focus and Scope

Advances in Obstetrics and Gynecology Research is a peer-reviewed, open access journal that aims to provide a forum for scientists and clinical professionals working in obstetrics and gynecology. Then as is now, the goal of the journal is to promote excellence in the

The journal publishes original research articles and review articles related to the latest progress in obstetrics and gynecology domestic and foreign. Academic papers at all levels such as clinical, scientific research, surgical innovation, experience exchange, and difficult case discussion are published.

About Publisher

Bio-Byword Scientific Publishing is a fast-growing, peer-reviewed and open access journal publisher, which is located in Sydney, Australia. As a dependable and credible corporation, it promotes and serves a broad range of subject areas for the benefit of humanity. By informing and educating a global community of scholars, practitioners, researchers and students, it endeavors to be the world's leading independent academic and professional publisher. To realize it, it keeps creative and innovative to meet the range of the authors' needs and publish the best of their work.

By cooperating with University of Sydney, University of New South Wales and other world-famous universities, Bio-Byword Scientific Publishing has established a huge publishing system based on hundreds of academic programs, and with a variety of journals in the subjects of medicine, construction, education and electronics.

Publisher Headquarter

BIO-BYWORD SCIENTIFIC PUBLISHING PTY LTD

Level 10

50 Clarence Street

Sydney NSW 2000

Website: www.bbwpublisher.com

Email: info@bbwpublisher.com

Table of Contents

- 1 Research and Application of Continuous Inverted U-shaped Suture Technique in Skin Suture of Cesarean Section**
Lixiang Dun, Jing Qu
- 5 Joint Trajectories of Depression, Anxiety, and Sleep Quality During Pregnancy and Their Risk Factors: A Prospective Longitudinal Study**
Meng Zhao, Zhixiong Li, Zhiyue Zhang, Qiqi Yang, Jiaying Tao
- 19 Analysis of Etiological Distribution and Clinical Therapeutic Effects in Children with Respiratory Tract Infections in Pediatric Outpatient Departments of Primary Hospitals**
Rui Gao
- 26 Clinical Study on the Integrated Treatment of Adenomyosis without Fertility Requirements Using High-Intensity Focused Ultrasound Combined with Sequential Drug Therapy and Long-Term Standardized Management**
Xiaoli Zhang, Zhongfang Qin, Wenting Li
- 32 Clinical Analysis of Cervical HSIL with Poorly Differentiated Squamous Cell Carcinoma Metastatic to the Ovary**
Ziyu Qi, Jingna Xing, Wenling Fan
- 38 Evaluation of the Initiation Effect of QLB Combined with General Anesthesia in the “Painless Mode” during Gynecological Laparoscopic Surgery**
Yu Jiao
- 45 Research on Establishing a Prediction Model for Pregnancy Outcomes Based on Retrospective Analysis of 1,131 Cases of Frozen-Thawed Single Embryo Transfer**
Lijun Lou, Zhengfang Zhang
- 56 Case Analysis of Cervical Cancer Complicated with Von Hippel-Lindau Syndrome**
Xiaojing Sun, Li Li, Hongyun Shi

- 62 **A Phenomenological Study on Ovarian Reserve Health Risk Experiences, Fertility Difficulties, and Support Needs among Obstetric, Gynecologic, and Pediatric Nurses**
Ruizhi Huang, Shuang Zhang, Jialin Ye
- 69 **Study on the Association Between Maternal Cognitive Emotion Regulation Strategies and Their Coping Styles and Mental Health in High-risk Pregnancies**
Yeqing Su, Jinjin Qin, Jiejie Xing
- 77 **Research Progress in Clinical Treatment of Polycystic Ovary Syndrome from the Perspective of Evidence-Based Medicine: A Comprehensive Evaluation of Hormonal Therapy and Traditional Chinese Medicine Regimens**
Zhao Wang, Nan Li
- 85 **Meta-analysis of Preterm Premature Rupture of Membranes and Fetal Inflammatory Response Syndrome**
Xiuyan Huang, Chen Jiang, Cuiyan Yan, Jing Yang

Research and Application of Continuous Inverted U-shaped Suture Technique in Skin Suture of Cesarean Section

Lixiang Dun, Jing Qu

Department of Obstetrics, Xiangtan Maternal and Child Health Hospital, Xiangtan 411100, Hunan, China

Copyright: © 2026 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To explore the clinical effect of the continuous inverted U-shaped suture technique in skin wound suture during cesarean section. *Methods:* A total of 600 pregnant women who underwent cesarean section in our hospital from June 2024 to March 2026 were selected and randomly divided into a control group ($n = 300$) and a modified group ($n = 300$). The control group received an interrupted subcutaneous fat suture with 2/0 absorbable suture and a continuous intradermal suture with 4/0 synthetic absorbable suture; the modified group received an interrupted subcutaneous fat suture with 2/0 absorbable suture and a continuous inverted U-shaped suture with 4/0 synthetic absorbable suture. The postoperative incision evenness, Vancouver Scar Scale (VSS) score, incidence of subcutaneous nodules, complications, and maternal satisfaction were compared between the two groups. *Results:* The excellent and good rate of postoperative incision evenness in the modified group (98.0%) was significantly higher than that in the control group (85.3%). The VSS score [(1.2 ± 0.4) points vs (2.8 ± 0.7) points] and the incidence of subcutaneous nodules (0.7% vs 8.3%) in the modified group were significantly lower than those in the control group, with statistically significant differences ($P < 0.05$). There were no significant differences in the incidence of complications such as incision infection and fat liquefaction between the two groups ($P > 0.05$). Maternal satisfaction in the modified group (98.7%) was significantly higher than that in the control group (89.0%). *Conclusion:* The continuous inverted U-shaped suture technique can effectively improve the alignment and evenness of skin incisions in cesarean section, reduce scar hyperplasia and subcutaneous nodule formation, and offer better cosmetic results and patient satisfaction, making it worthy of clinical promotion and application.

Keywords: Cesarean section; Skin suture; Continuous inverted U-shaped suture; Scar; Cosmetics CLC number R719.8 Document code A

Online publication: May 31, 2026

1. Introduction

With the adjustment of the national fertility policy and the increasing demand for postpartum rehabilitation among women, the cosmetic outcome of incisions following cesarean section has garnered increasing

attention. Although traditional continuous intradermal sutures can achieve a seamless appearance without exposed sutures, they are prone to causing misalignment of the skin edges and uneven tension at the upper and lower margins of the incision, leading to depression, keloid formation, or subcutaneous nodules after healing, which affect aesthetics and increase wound traction and discomfort. The continuous inverted U-shaped suture is a modified suture technique that evenly distributes suture tension across the deeper subcutaneous layers through an inverted U-shaped needle path. By utilizing the elastic lifting effect of the suture itself, it enables precise alignment of the skin edges at the upper and lower margins of the incision under tension-free conditions. This study aims to systematically evaluate the clinical application value of the continuous inverted U-shaped suture in skin suturing during cesarean section through a large-sample randomized controlled trial.

2. Materials and methods

2.1. General information

A total of 600 pregnant women who underwent cesarean section at Xiangtan Maternal and Child Health Hospital from June 2024 to June 2026 were selected. Inclusion criteria: singleton full-term pregnancy; elective or emergency cesarean section; signed informed consent. Exclusion criteria: severe pregnancy complications (e.g., severe preeclampsia, coagulopathy); severe abdominal wall infection; anatomical abnormalities due to previous abdominal wall surgery. The participants were randomly divided into a control group and a modified group using a random number table method, with 300 cases in each group. There were no statistically significant differences in baseline data such as age, gestational age, BMI, parity, and surgical indications between the two groups ($P>0.05$), indicating comparability.

2.2. Methods

Both groups received combined spinal-epidural anesthesia and underwent a Pfannenstiel transverse incision. The suture methods for the uterus and fascial layers were consistent between the two groups.

Control group: The subcutaneous fat layer was sutured intermittently using 2/0 absorbable sutures (Hualikang). Continuous intradermal sutures were performed using 4/0 synthetic absorbable sutures (Hualikang), with a stitch spacing of approximately 0.5 cm.

Modified group: The subcutaneous fat layer was sutured in the same manner as the control group. Skin suturing was performed using 4/0 synthetic absorbable sutures in a continuous inverted U-shaped pattern. Specific procedure: The needle was inserted approximately 0.5 cm from the incision margin, passed vertically through the dermis to the corresponding point on the opposite side, and exited to form an inverted U-shaped trajectory; the stitch spacing was approximately 1.0 cm, and the suture tension was kept moderate to ensure tension-free alignment of the incision.

2.3. Observation indicators

2.3.1. Incision evenness

Assessed at suture removal on postoperative day 7. Excellent: complete alignment of the incision without a step-like appearance; Good: good alignment with a slight step-like appearance; Poor: obvious misalignment of the incision.

2.3.2. Scar assessment

Follow-up at 3 months postoperatively using the Vancouver Scar Scale (VSS) score (0-13 points), with lower scores indicating better outcomes.

2.3.3. Complications

The incidence of postoperative incision infection, fat liquefaction, dehiscence, and subcutaneous nodules (palpable hard nodules with a diameter ≥ 0.5 cm) was recorded.

2.3.4. Satisfaction

A Likert 5-point scale was used to survey maternal satisfaction with the incision appearance at 3 months postoperatively (very satisfied/satisfied/neutral/dissatisfied/very dissatisfied).

2.4. Statistical methods

SPSS 26.0 software was used. Continuous data are expressed as mean \pm standard deviation (SD), and comparisons between groups were performed using *t*-tests. Categorical data are expressed as n (%), and comparisons between groups were performed using χ^2 tests. A *P*-value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of incision healing

The excellent and good rate of incision evenness in the modified group was significantly higher than that in the control group, and the VSS score was significantly lower in the modified group ($P < 0.05$). The incidence of subcutaneous nodules was significantly lower in the modified group than in the control group ($P < 0.05$), with no significant differences in the rates of infection and fat liquefaction between the two groups ($P > 0.05$). See **Table 1**.

Table 1. Comparison of postoperative incision healing and scar conditions between the two groups [n (%), mean \pm SD]

Group	n	Flatness (Excellent/Good)	VSS Score	Subcutaneous Nodules	Infection	Fat Liquefaction
Modified Group	300	294 (98.0)	1.2 \pm 0.4	0 (0.0)	0 (0.0)	0 (0.0)
Control Group	300	256 (85.3)	2.8 \pm 0.7	25 (8.3)	0 (0.0)	4 (1.3)
χ^2/t value	-	25.634	-28.192	16.892	0.342	0.171
<i>P</i> value	-	<0.001	<0.001	<0.001	0.559	0.679

3.2. Comparison of maternal satisfaction

The overall satisfaction rate (very satisfied + satisfied) in the modified group was 98.7%, significantly higher than that in the control group (89.0%) ($\chi^2 = 22.115$, $P < 0.001$).

4. Discussion

The results of this study indicate that the continuous inverted U-shaped suture technique outperforms traditional intradermal suturing in improving incision evenness, reducing VSS scores, and minimizing the formation of subcutaneous nodules. The underlying mechanisms can be analyzed as follows:

- (1) Mechanical advantage: The inverted U-shaped needle path distributes suture tension across the deep dermis and superficial subcutaneous layers, avoiding the “inward rolling” effect caused by simple epidermal alignment in intradermal suturing. This technique is particularly suitable for parturients with thicker abdominal wall fat or misaligned incision margins.
- (2) Vascular protection: The suture forms a mesh-like support beneath the skin, reducing compression on dermal capillaries and eliminating subcutaneous ecchymosis. This reduces excessive proliferation of fibrous tissue due to ischemia, thereby minimizing the formation of subcutaneous hard nodules.
- (3) Cosmetic outcome: This technique achieves tension-free alignment of the skin, resulting in linear scars with coloration closely resembling that of the surrounding skin after healing. This meets the modern demand among women for “invisible” cesarean section incisions.

5. Conclusion

The continuous inverted U-shaped suture technique is a safe and effective method for skin suturing in cesarean sections. It offers significant advantages in promoting aesthetically pleasing incision healing and enhancing patient satisfaction, making it worthy of widespread clinical adoption.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Lu Y, Liao Y, Huang Y, 2021, Clinical Study on Suturing Techniques and Management of Skin Incisions in Cesarean Sections. *Medical Dietetics and Health*, 19(5): 56–57.
- [2] Perinatal Medicine Branch of the Chinese Medical Association, 2018, Expert Consensus on Suturing Techniques and Material Selection for Cesarean Sections (2018). *Chinese Journal of Perinatal Medicine*, 21(5): 289–293.
- [3] Sullivan T, Smith J, Kermode J, et al., 1990, Rating the Burn Scar. *J Burn Care Rehabil*, 11(3): 256–260.

Publisher's note

Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Joint Trajectories of Depression, Anxiety, and Sleep Quality During Pregnancy and Their Risk Factors: A Prospective Longitudinal Study

Meng Zhao^{1,2}, Zhixiong Li³, Zhiyue Zhang⁴, Qiqi Yang², Jiaying Tao^{1,5}

¹Nursing Department of Xinjiang Medical University, Urumqi 830017, Xinjiang Uygur Autonomous Region, China

²Nursing Department of Xinjiang Second Medical College, Karamay 834000, Xinjiang Uygur Autonomous Region, China

³The Third Department of Clinical Psychology, Karamay Integrated Traditional Chinese and Western Medicine Hospital (People's Hospital of Karamay), Karamay 834000, Xinjiang Uygur Autonomous Region, China

⁴Xinjiang Production and Construction Corps Health Committee, Urumqi 830000, Xinjiang Uygur Autonomous Region, China

⁵Health Care Research Center for Xinjiang Regional Population, Urumqi 830000, Xinjiang Uygur Autonomous Region, China

Copyright: © 2026 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* This study aimed to describe the joint trajectories of depression, anxiety, and sleep quality during pregnancy, identify at-risk trajectory populations, and identify their predictable risk factors. *Methods:* The sample consisted of 146 pregnant women who completed the pregnancy follow-up. Data were collected at four gestational time points. Parallel process latent class growth analysis (PP-LCGA) was employed to identify the synchronous trajectory patterns of depression, anxiety, and sleep quality. Multiple logistic regression models determined the risk factors associated with individuals exhibiting these vulnerable trajectories. *Results:* Three trajectories related to changes in depression, anxiety, and sleep quality during pregnancy were identified as follows: the stable asymptomatic group (34.2%), the general health group (43.8%), and the joint symptoms group (21.9%). The predictors of the joint symptoms group trajectory included abortion experience (OR = 2.366, 95% CI [1.153;4.856]), lower back pain during pregnancy (OR = 3.286, 95% CI [1.296;8.331]), and the impact of pregnancy on daily life (OR = 5.619, 95% CI [1.843;17.128]). *Conclusions:* There is heterogeneity in the trajectories of depression, anxiety, and sleep quality during pregnancy. Previous miscarriage, low back pain in the first trimester, and the impact of pregnancy on life were predictors in the combined trajectory group.

Keywords: Gestational depression; Pregnancy-related anxiety; Sleep quality during pregnancy; Prospective longitudinal study; Joint trajectory analysis; PP-LCGM

Online publication: May 31, 2026

1. Introduction

According to the World Health Organization's 2017 report, the global prevalence of depression has reached approximately 300 million individuals. Among pregnant women, the prevalence of depression is increasing, with one Netherlands-based study showing an increase from approximately 7% in 1988-1989 to 14% in 2012-2014. Studies in China have shown that the prevalence of prenatal depression among women in the second trimester significantly increased from 31.82% to 60.59% between 2016 and 2021 ^[1], and the most recent umbrella review and meta-analytic synthesis have revealed that the pooled prevalence of antenatal depression is 29% ^[2]. Depression can be detected early in pregnancy, suggesting that timely interventions can be made during pregnancy to control the risk ^[3]. However, depression and anxiety can co-occur during pregnancy ^[4], and poor sleep quality often co-occurs with both ^[5-9], which complicates the intervention process because anxiety and poor sleep quality are also independent risk factors for depression ^[10,11]. Compared with those without such risk factors, women who present with multiple risk factors, including sleep disturbances, depressive symptoms, and anxiety, are at a significantly greater risk of developing postpartum depression ^[12]. In pregnancy health management, if the complex relationships among depression, anxiety, and sleep quality are not considered, some risk groups may be missed. Moreover, cross-sectional screening for depression, anxiety, and sleep quality does not predict how they will change throughout pregnancy.

Advances in longitudinal research methods have provided new support for current mental health care during pregnancy. Via trajectory model studies, we have found significant population heterogeneity in the trajectory of depression, anxiety, and sleep quality during pregnancy ^[13-15] Bmoderate-stable[^] (42.3%). These independent trajectory studies have revealed changes in depression, anxiety, and sleep quality during pregnancy and their respective risk factors, providing an indispensable basis for identifying risk groups throughout pregnancy. However, these studies did not consider the covariant relationships among depression, anxiety, and sleep quality, which could reduce the ability to identify this at-risk group. Moreover, the discrete modeling method for depression, anxiety, and sleep quality increases the number of potential subgroups (3 depression subgroups \times 3 anxiety subgroups \times 2 sleep subgroups = 18 combinations), significantly reducing clinical operability.

Few studies have examined synchronized trajectories of depression, anxiety, and sleep quality during pregnancy in the same sample. To the best of our knowledge, one study has used the latent growth curve model (LGCM) and the parallel process model to analyze the relationship between depressive symptom trajectory and sleep quality from the second trimester to 3 months postpartum ^[16]. The results indicated that women with poorer sleep quality were more likely to exhibit more severe depressive symptoms ($\beta = 0.73$, $P < 0.001$). The sleep quality trajectory slope interacted with the depression slope ($\beta = 0.33$, $P < 0.05$), with a greater sleep slope associated with a greater depression slope. These findings suggest that depression during pregnancy and poor sleep quality may change together. Unfortunately, owing to the scope of the purpose of the study, it failed to explore the population heterogeneity of depression trajectories or to fit the change trajectories of depression and sleep quality. Another study, examining postpartum women, has identified four bivariate growth targets for postpartum depression and anxiety through a mixed model of potential category growth, including high comorbidity (5.4%), moderate comorbidity (19.4%), low anxiety and depression symptom reduction (18.6%), and low symptoms (56.6%) ^[17]. Multiple logistic regression has revealed that mothers who slept less during pregnancy were more likely to fall into the high comorbidity or moderate symptom categories than into the low symptom category.

This prior study did not focus on the pregnant population. Because pregnancy is the early process of the postpartum stage, we speculate that the combined trajectory of depression, anxiety, and sleep in the pregnant population may be similar to the results of these bivariate trajectories, with the possibility of population heterogeneity and joint changes.

The present study employed a potential growth model to analyze the concurrent trajectories of depression, anxiety, and sleep quality during pregnancy. This approach offers two significant advantages over traditional methods. This approach can effectively identify multidimensional patterns of simultaneous changes in these three dimensions, and subgroup optimization on the basis of the Bayesian information criterion (BIC) allows for appropriate balancing of model complexity while maintaining clinical utility. The present study had two primary objectives. First, parallel-process latent class growth analysis was employed to identify the synchronous trajectory patterns of depression, anxiety, and sleep quality. The characteristics of these trajectories were examined to pinpoint vulnerable trajectories. Second, multiple logistic regression models were subsequently used to determine the risk factors associated with individuals exhibiting these vulnerable trajectories, including sociodemographic factors, obstetrical factors, family factors, personal habits, interpersonal factors, and physiological and life changes after pregnancy. The anticipated findings provide a robust foundation for early investigation and intervention within the pre- and post-birth psychological services system.

2. Method

2.1. Population description

The present study used convenience sampling to sample 203 women in the first trimester of pregnancy who underwent prenatal care at all five community hospitals in a city in western China between June 2023 and December 2023.

The inclusion criteria were as follows: participants who possessed normal expressive and comprehension abilities, and participants who intended to reside in the city throughout their pregnancy. The exclusion criteria included twin or multiple pregnancies, individuals diagnosed with mental or personality disorders, individuals with intellectual disabilities, those with a history of substance or alcohol abuse, and women who experienced severe infections or fetal abnormalities during pregnancy.

2.2. Data collection

Data were obtained via an electronic questionnaire. At 11–13 weeks of gestation (T1), researchers collected basic information and depression, anxiety, and sleep quality data from pregnant women after they completed a pregnancy examination and signed an informed consent form. Follow-up was performed at 20–22 weeks (T2), 30–32 weeks (T3), and 36–38 weeks (T4) of gestation. These specific assessment times were selected to capture the progression of depression, anxiety, and sleep quality throughout pregnancy; these time points are consistent with clinical follow-up visits during pregnancy and can contribute to early detection and ongoing monitoring of depression, anxiety, and sleep quality during pregnancy.

As with any longitudinal study, sample depletion was inevitable. The sample sizes for the four measurements were 203, 177, 167, and 146, respectively. In the present study, the main reason for sample loss was that during pregnancy, such as during teratological examination and predelivery examination, some pregnant women chose a tertiary hospital rather than a community hospital for examination to obtain more

reliable results. To determine whether the missing samples were biased, the differences in depression, anxiety, and sleep quality scores were analyzed between the participating and missing samples, which revealed no statistical significance. Missing data were identified as random missing data.

The basic information covered the following six areas: sociodemographic factors (e.g., age, education, income and expenditure); obstetric factors (e.g., number of births, history of miscarriage, and whether pregnancy was planned); personal habit factors (e.g., time of daily activity, frequency of smoking, frequency of drinking, and frequency of exercise); interpersonal factors (e.g., extroversion, sociability, and relationship); family factors (e.g., number of family members living together, satisfaction with living conditions, and disturbance of sleep by family members); and physical, psychological and life changes after pregnancy (e.g., fatigue, low back pain, leg cramps, abdominal discomfort, the impact of pregnancy on daily life, birth fears, happiness, and other discomforts). All the information was gathered through a structured questionnaire, and the participants selected the most suitable options on the basis of their individual situations.

In this study, depression, anxiety, and sleep quality were evaluated using standardized scales.

The Self-Rating Depression Scale (SDS), developed by William W.K. Zung in 1965^[18], is a standardized self-rating scale used to assess the severity of depressive states and their changes during treatment. The scale contains 20 declarative sentences and corresponding question items. The item scores are summed and multiplied by 1.25 to obtain the standard score. The abnormal threshold of the SDS standard score is set at 53 points according to the results of the Chinese norm. Specifically, a score ranging from 53 to 62 points indicates mild depression, a score ranging from 63 to 72 points suggests moderate depression, and a score of 72 points or more indicates severe depression. In this study, the Cronbach's α coefficients of the SDS at the four measurement time points were 0.877, 0.880, 0.871, and 0.880.

The Self-rating Anxiety Scale (SAS), compiled by William W.K. Zung in 1971^[19], is a standardized self-rating scale that accurately reflects the subjective feelings of patients with anxiety tendencies. The scale consists of 20 declarative sentences and corresponding question items. The scores of the 20 questions are summed and multiplied by 1.25 to obtain a standard score. In accordance with the results of the Chinese norm, we set the cutoff value of the SAS standard score at 50 points. Specifically, a score between 50 and 59 is classified as mild anxiety, a score between 60 and 69 is classified as moderate anxiety, and a score of 70 or above is classified as severe anxiety. In this study, the Cronbach's α coefficients of the SDS at the four measurement time points were 0.880, 0.871, 0.871, and 0.872.

The Pittsburgh Sleep Quality Index (PSQI) was used to assess sleep quality^[20]. The scale is composed of 19 self-rated items and five other rated items. The 18 self-rated items included seven factors, namely, sleep quality, time to fall asleep, sleep duration, sleep efficiency, sleep disorders, use of hypnotic drugs, and daytime function, to assess the subjective sleep quality of individuals in the last month. Each factor in the scale is scored on a scale of 0–3, and the score of each factor is summed to obtain the PSQI total score, which ranges from 0–21 points. The higher the score is, the worse the sleep quality. A score of more than 5 indicates a sleep quality problem. In this study, the Cronbach's α coefficients of the SDS at the four measurement time points were 0.893, 0.893, 0.892, and 0.895.

2.3. Ethical considerations

The study was approved by the Ethics Committee of Xinjiang Medical University, China (2023 Ethics Approval Number XJYKDXR20230303010). All female participants in the study signed informed consent forms and were informed of their right to withdraw at any time. Their personal information was only used for

this study and will remain strictly confidential.

2.4. Statistical analyses

Following the first research objective, Mplus 7.4 software was utilized to investigate the joint trajectory of depression, anxiety, and sleep quality during pregnancy via parallel process latent class growth modeling analysis (PP-LCGM). This method extends traditional single-variable latent class growth modeling (LCGM) by constructing a parallel process model that simultaneously examines multiple growth trajectories. This approach is crucial for studying the co-development trajectories of closely related variables. While it is conceptually similar to the growth mixture model (GMM), the parallel process latent class growth modeling analysis does not account for changes in trajectories within the population. The significant differences in growth factors (intercept and slope) observed in this study suggested distinct subgroup characteristics of depression, anxiety, and sleep quality during pregnancy. To simplify the estimation process, four models containing two to five potential classes were subsequently estimated using Mplus 7.4, with the intragroup variance constrained to zero. To accurately determine the optimal number of trajectory categories, various fit indices, including the Akaike information criterion (AIC), Bayesian information criterion (BIC), and sample-size adjusted Bayesian information criterion (a-BIC), were considered. Generally, models with lower AIC, BIC, and a-BIC values are preferred. The Lo-Mendell-Ubin likelihood ratio test (LMR-LRT) was also employed to compare models with k trajectory classes against those with $k-1$ trajectory classes. A significant p -value from the LMR-LRT indicates that the model with k trajectory classes is superior to that with $k-1$ trajectory classes. Moreover, entropy is used to evaluate the accuracy of the classification. The entropy ranges from 0 to 1.0. The higher the value is, the more accurate the individual classification is. To enhance the universality of the study results, it is also necessary to consider whether each category size accounts for at least 5% of the total sample size. In addition to the above fitting index, the substantial interpretability of trajectory classes cannot be ignored. Thus, we used robust maximum likelihood estimation to process the missing data and complete the model estimation, mapping the covariant trajectories of depression, anxiety, and sleep quality during pregnancy.

The second purpose was analyzed using SPSS 24.0 software. First, we categorized the participants according to the optimal model group information of the covariant trajectories of depression, anxiety, and sleep quality during pregnancy obtained from the first objective. Next, we used a one-way chi-square test to determine whether the baseline variables of different groups were risk factors, setting the significance level at $P < 0.01$. Finally, we incorporated the statistically significant baseline variables into the independent variables for multiple logistic regression analysis. To explore the influencing factors of the common vulnerability trajectory categories of depression, anxiety, and sleep quality during pregnancy, the track grouping category was considered the dependent variable, and the good group category was considered the reference.

2.5. Common method bias test

The common method deviation of the data was tested by the Harman single-factor test. It was found that the first common factor explained 15.29% of the total variance, which was less than the critical value of 40%. Therefore, there is no common method bias problem in the data of this study. It was found that the first common factor explained 15.29% of the total variance, which was less than the critical value of 40%. Therefore, there is no common method bias problem in the data of this study.

3. Results

3.1. General trends in depression, anxiety, and sleep quality during pregnancy

The parallel process latent class growth modeling analysis revealed that the quadratic model fit better than the linear growth model, indicating that depression, anxiety, and sleep quality during pregnancy followed nonlinear growth trends at all four time points. Moreover, the intercepts of the tracks of depression, anxiety, and sleep quality during pregnancy showed significant differences; that is, the initial levels were significantly different ($P < 0.001$). Significant differences were detected only in the second slope of the depression trajectory during pregnancy ($P < 0.001$). However, there was no significant difference in the slopes of anxiety trajectories during pregnancy and sleep quality trajectories ($P = 0.113, 0.528$). These results suggested that parallel processing of LCGMs was necessary.

3.2. Results of parallel process latent class growth modeling analysis

One to six categories were analyzed via process parallel latent class growth modeling to determine the most appropriate number of trajectory categories. The process parallel latent class growth modeling method accounts for multiple growth tracks simultaneously. Parallel process LCGM is particularly useful when joint trajectory fitting is performed on closely related variables, and it has been used in several studies. Because AIC, BIC, and a-BIC gradually increase with the number of categories, selecting the best model according to the information index is challenging. The scree plot of the BIC index revealed that there was an inflection point in the second category, supporting the second category. The entropy value was always higher than 0.8 in classes 1 to 6, indicating high classification accuracy. Classes 2 and 5 were closest to 1, indicating that both categories had higher classification accuracy because the P -value of LMR-LRT was only significant in class 2. The scales of classes 5 and 6 were small ($n < 5\%$). Thus, class 2 was supported, and the class 5 model was not selected. However, compared with the statistical index, interpretability and significance based on each category were more important. After carefully examining each class model, we determined that the new class found in the three-class model was more meaningful than the two-class models. The mean scores of depression, anxiety, and sleep quality during pregnancy in the new class were all higher than the clinical value of the scale, which is more meaningful from the perspective of explanation. The solution was also statistically acceptable. Furthermore, compared with the class 3 model, the class 4 model subdivided a class in the class 3 model into two similar subclasses. Therefore, based on the fit index of the trajectory class and its substantial interpretability, the present study determined the class 3 model as the final model. **Table 1** provides the fit indices of the six categories of models for the combined trajectory of depression, anxiety, and sleep quality during pregnancy.

Table 1. Fit statistics for the parallel process latent class growth modeling analysis

	AIC	BIC	a-BIC	Entropy	LMR-LRT (p)	Class Proportions
Class 1	10902.134	10955.839	10898.879	-	-	1.000
Class 2	10405.899	10480.490	10401.378	0.913	0.0005	0.38/0.62
Class 3	10255.892	10351.367	10250.105	0.892	0.0996	0.23/0.34/0.43
Class 4	10195.548	10311.909	10188.495	0.888	0.5629	0.49/0.25/0.18/0.08
Class 5	10147.596	10284.842	10139.277	0.910	0.7091	0.20/0.02/0.05/0.49/0.24
Class 6	10110.364	10268.477	10100.761	0.889	0.6524	0.19/0.34/0.12/0.02/0.05/0.29

Note: Boldface indicates the selected model. AIC: Akaike information criterion; BIC: Bayesian information criterion; a-BIC: sample-

size-adjusted Bayesian information criterion; LMR-LRT: Lo–Mendell–Rubin adjusted likelihood ratio test. The bold category is the final selection category.

The mean values of the joint trajectory classes (three classes) of depression, anxiety, and sleep quality during pregnancy are shown in **Figure 1**. The first category accounted for 34.2% of the sample ($n = 50$). For pregnant women in this class, the scores of the depression, anxiety, and sleep quality scales were lower than the prescribed thresholds at the beginning of pregnancy and remained stable throughout pregnancy. These findings indicated that the pregnant woman did not have depression or anxiety throughout pregnancy and that the quality of sleep remained good; this group was called the stable asymptomatic group. The second class comprised 43.8% of the total sample ($n = 64$). Women in this class were characterized by relatively high depression, anxiety, and sleep quality scales in early pregnancy, with scores close to the critical value, but the scores remained stable later in pregnancy, with a slight improvement in depression; this group was called the general health group. Class 3 accounted for 21.9% of the total sample ($n = 32$). Compared with women in the first two classes, women in this category had scores above the threshold on the depression, anxiety and sleep quality scales from early cognition, and these scores continued to be above the threshold throughout pregnancy. Considering that depression, anxiety, and sleep quality concurrently affected women in this group throughout pregnancy, this class was named the joint symptoms group.

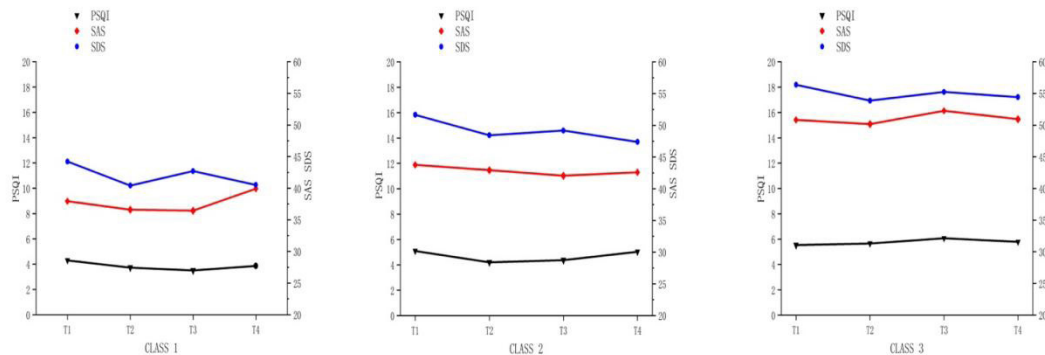


Figure 1. Mean values of the combined trajectories of depression, anxiety, and sleep quality during pregnancy (3 classes). Note: The three figures represent class 1 “stable asymptomatic group”, class 2 “general health group”, and class 3 “joint symptoms group”. The X-axis represents the following four measurement times: T1, 11-13 weeks; T2, 20-22 weeks; T3, 30-32 weeks; and T4, 36-38 weeks. The left Y-axis represents the Pittsburgh Sleep Quality Index Scale (PSQI) score, and the right Y-axis represents the Self-rating Anxiety Scale (SAS) and Self-rating Depression Scale (SDS) scores.

3.4. Predictors of trajectory classes membership

The single-factor test based on demographic factors, sociological factors, obstetrical factors, personal habit factors, interpersonal factors, family factors, and physical and psychological changes after pregnancy is shown in **Table 2**. The trajectory classes were considered as the dependent variables, while demographic and psychosocial factors were considered as the independent variables. χ^2 test analysis was performed, and $P < 0.01$ was considered as the test level. The results revealed statistically significant differences in terms of abortion experience, disturbance of sleep by family members, impact of pregnancy on daily life, and symptoms of low back pain.

Table 2. Univariate analysis of indicators related to depression, anxiety and sleep quality during pregnancy on the basis of joint trajectory categories

Item	Joint trajectories classes			χ^2	<i>P</i>
	Stable asymptomatic group (n = 50)	General health group (n = 64)	Joint symptoms group (n = 32)		
Obstetric factor					
Abortion experience				17.221	0.002
No miscarriage	8	42	31		
One miscarriage	14	13	14		
Two or more miscarriages	10	9	5		
Family-related factors					
Family members interfere with sleep					
Yes	15	14	8	9.847	0.007
No	17	50	42		
Some changes after pregnancy					
The impact of pregnancy on daily life				15.485	0.004
Tremendous	6	9	4		
Normal	24	41	25		
Small	2	14	21		
Lower back pain after pregnancy				10.561	0.005
Present	9	27	31		
Not present	23	37	18		

Note: Given the space constraints, only variables that exhibited statistical significance were included. The threshold for statistical significance was set at $P < 0.01$.

With the above statistically significant single-factor test results as independent variables, the trajectory classes were considered as dependent variables, and the multivariate logistic regression was performed for analysis. In this process, the trajectory order was adjusted to the stable asymptomatic group for reference, and the order of the independent variables was also adjusted according to the same hierarchical law. A likelihood ratio test of $P < 0.001$ indicated that the model was valid. The multivariate logistic regression model results revealed that the three independent risk predictors of the joint symptoms group compared with the stable asymptomatic group were abortion experience (OR = 2.366, 95% CI [1.153;4.856]), the impact of pregnancy on daily life (OR = 3.286, 95% CI [1.296;8.331]), and signs of low back pain after pregnancy (OR = 5.619, 95% CI [1.843;17.128]). Compared with the stable asymptomatic group, two independent risk predictors of the general health group were the impact of pregnancy on daily life (OR = 2.712, 95% CI [1.296;5.674]) and signs of low back pain (OR = 3.183, 95% CI [1.343;7.543]). The detailed statistical results are shown in **Table 3**. This result remained unchanged after removing the single variable, indicating that the regression result was stable.

Table 3. Logistics regression analysis of indicators related to depression, anxiety and sleep quality during pregnancy on the basis of joint trajectory categories

Item	Joint symptoms group			General health group		
	OR	95%CI	P	OR	95%CI	P
Abortion experience	2.366	1.153-4.856	0.019	1.080	0.578-2.020	0.809
The impact of pregnancy on daily life	3.286	1.296-8.331	0.012	2.712	1.296-5.674	0.008
Lower back pain after pregnancy	5.619	1.843-17.128	0.002	3.183	1.343-7.543	0.009
Family members interfere with sleep	3.363	0.995-11.369	0.051	1.309	0.444-3.856	0.625

Note: The threshold for statistical significance was set at $P < 0.05$.

4. Discussion

4.1. The joint trajectory of depression, anxiety, and sleep quality remains stable during pregnancy

The trajectories of depression, anxiety, and sleep quality during pregnancy were heterogeneous and were categorized into the following three distinct classes: the stable asymptomatic group, the general health group, and the joint symptoms group.

Although scores for the depression, anxiety, and sleep quality scales varied with gestational week across classes, the trajectory of each symptom change was relatively stable over time. A previous study ^[21] has used the LCGA model to analyze the trajectories of depression and anxiety throughout pregnancy, revealing that these trajectories remain stable throughout gestation. The present study confirmed this finding using the PP-LCGM method, and the present results suggested that sleep quality during pregnancy was generally stable, which was consistent with the trajectories of depression and anxiety. However, longitudinal studies have revealed several trajectory groups of sleep quality during pregnancy, including high sleep quality throughout pregnancy (21.5%), low sleep quality during pregnancy (59.5%), significantly lower sleep quality during pregnancy (12.3%), and low sleep quality throughout pregnancy (6.7%) ^[15]. The present study adopted a joint trajectory model of sleep, depression, and anxiety, revealing that on the basis of an average sleep value, the sleep quality changed for each class. Sleep quality tended to deteriorate in the third trimester of pregnancy; however, the change in the slope of sleep quality was not statistically significant, indicating that the change trend was not obvious. The group with a significant decline in sleep quality was not fitted. This inconsistency may be due to different statistical models having different assumptions regarding changes in the growth trajectory of the individuals identified in each group, and it may also be due to stable depression and anxiety trajectories during pregnancy, as well as stable sleep quality. Previous studies have shown that poor sleep quality during pregnancy is associated with depressive symptoms ^[21]. Regardless of the cause, the present study revealed that the joint trajectory of depression, anxiety, and sleep quality during pregnancy remained stable throughout pregnancy. These findings suggested that screening for depression, anxiety, and sleep quality in pregnant women and early intervention could theoretically yield better intervention effects, supporting early psychological screening in pregnancy care.

4.2. Comorbidities with depression, anxiety, and sleep quality during pregnancy exist

The joint trajectory results obtained in the present study did not fit the single vulnerable trajectory,

confirming that gestational anxiety, depression, and sleep trajectories are simultaneously correlated and are universal throughout pregnancy^[23]. This result was in line with our expectations, as previous studies have reported associations between depression and anxiety during pregnancy^[21,23,24]. The present study is the first to analyze the common trajectory changes of depression, anxiety, and sleep quality from the perspective of a joint trajectory. In particular, the joint symptoms group class of pregnant women identified in this study had depression, anxiety, and sleep quality scores above the scale threshold throughout pregnancy, indicating that these pregnant women were affected by multiple symptoms from early pregnancy until delivery. As this group accounts for 21.9%, these results cannot be ignored. In mental health care during pregnancy, the depression, anxiety, and sleep quality of pregnant women should receive equal attention; after all, mental health during pregnancy is closely related to postpartum depression, and multiple symptoms may significantly increase the likelihood of postpartum depression^[28].

4.3. Factors influencing the joint trajectory of depression, anxiety, and sleep quality during pregnancy

Through multivariate logistic regression analysis, the present study revealed that the joint trajectory of depression, anxiety, and sleep quality during pregnancy had several significant characteristics. The predictors of the joint symptoms group included previous miscarriage experience and changes in physiological and life factors after pregnancy, such as low back pain symptoms and the impact of pregnancy on life. These results were inconsistent with previous results of separate regression analyses of depression and anxiety trajectories^[13], which identified nation, maternal age, and relationship satisfaction as risk factors for the perinatal depression trajectory, as well as past depression, stress level, and income level as significant risk factors for the anxiety trajectory. However, the present study did not identify maternal age, income, and relationship satisfaction as factors influencing the combined trajectory of depression, anxiety, and sleep quality during pregnancy. The differences may be due to a smaller range of regression results in the vulnerable group of the joint trajectories in our study. It is also possible that the influencing factors differ after adding sleep variables to the measurement.

Women with a history of miscarriage may have worse depression, anxiety, and sleep during pregnancy^[29]. In the present study, we focused on factors that might be modifiable. Women whose self-reported pregnancies had a more significant impact on daily life were more likely to experience more depression symptoms, more anxiety symptoms and poorer sleep quality throughout pregnancy, suggesting the need to focus on postpregnancy life changes in early pregnancy. The impact of pregnancy on daily life may be multifaceted and may have individual differences. Unfortunately, the present study was unable to explore this in depth. In practical work, however, taking this factor into account and conducting targeted analysis and intervention for individuals may improve the symptoms of depression, anxiety, and poor sleep quality during pregnancy.

In addition, we found that physiologic low back pain symptoms were risk factors for the joint symptoms group trajectory of depression, anxiety, and sleep quality during pregnancy. Low back pain is common during pregnancy and has been reported to be associated with depression, anxiety, and sleep quality. A retrospective case-control study has revealed that women who report low back pain have an increased risk of perinatal depression, with differences in the prevalence of depressive symptoms among prenatal, postnatal, and perinatal women with different types of low back pain^[30].

The specific mechanism underlying the relationship between low back pain symptoms and a persistent poor combination of depression, anxiety, and sleep quality during pregnancy is unclear. Studies have shown

that chronic pain can directly affect sleep and anxiety^[31]. Chronic pain has also been reported to correlate with depression^[32]. A recent study on adolescents has also revealed that social anxiety and depressive symptoms are associated with back pain^[33]. Thus, low back pain is closely related to depression and anxiety. In terms of interventions, recent studies^[34] have shown that yoga training can change the lower back pain symptoms, depression, anxiety, and sleep quality of IT practitioners, but further verification is needed to determine if yoga training is effective for pregnant women.

4.4. Limitations and strengths

The present findings should be interpreted with caution, considering multiple limitations. The study samples were obtained from relatively healthy women during pregnancy in urban areas, and they were not collected in rural or low-income areas. Thus, the samples were not representative of pregnant women in rural or low-income areas. Moreover, individuals excluded from the present study may not follow the same depressive symptom trends as those in the present study. According to the regression results of the present study, women who felt that their pregnancy had a significant impact on their lives were more likely to enter the trajectory of depression, anxiety, and a shared vulnerability to sleep quality, which may be caused by higher stress levels resulting from this stressor. Previous studies have reported that a high stress level is a significant risk factor for high depression and anxiety^[13]. Although the present study failed to measure and analyze the stress level, self-assessment of the impact of pregnancy on life early in pregnancy may be simpler than measuring stress scales.

Because few studies have been conducted on sleep quality during pregnancy and during the perinatal period, the present study could not explore risk factors in depth. However, similar studies are expected in the future, which will contribute to the identification and prevention of depression, anxiety, and sleep quality during pregnancy.

The present study also had several advantages. Depression, anxiety, and sleep quality during pregnancy have received extensive attention in the fields of perinatal health care and psychology. However, the process by which they all develop together is unclear. The present study used the parallel process LCGA approach to better describe the developmental relationships among the three factors. In a longitudinal study involving four waves of data, the three co-developmental trajectories of depression, anxiety, and sleep quality presented different degrees of co-development but similar patterns. These findings shed new light on how all three factors develop. In addition, the present study analyzed risk factors for trajectories. Among those with persistent depression, anxiety, and poor sleep quality during pregnancy, the risk factors included a history of prior miscarriage, lower back pain during pregnancy, and a greater impact of pregnancy on daily life. These risk factors, especially the physiological symptoms of low back pain, have guiding significance for mental health care during pregnancy.

4.5. Implications

Perinatal professionals need to identify depression, anxiety, and sleep quality early in pregnancy to allow adequate opportunities for ongoing monitoring and early intervention, and they need to focus on physiological and life changes in early pregnancy, especially symptoms of low back pain and the extent to which pregnancy affects daily life.

5. Conclusion

This prospective longitudinal study used parallel process latent class growth analysis (PP-LCGA) to identify three heterogeneous joint developmental trajectories of depression, anxiety, and sleep quality during pregnancy. It confirmed that the three psychosomatic symptoms showed non-linear stable changes and significant comorbidity during pregnancy, and 21.9% of pregnant women remained in a high-risk state comorbid with depression, anxiety, and sleep disturbance from early pregnancy. Multivariate logistic regression analysis identified abortion experience, low back pain during pregnancy, and the significant impact of pregnancy on daily life as independent predictive factors for pregnant women to enter the high-risk trajectory of joint symptoms. From the perspective of multi-dimensional joint trajectory, this study fills the research gap of the covariate pattern of psychosomatic symptoms during pregnancy, and provides evidence-based support for precise screening and stratified intervention of perinatal mental health. Limited by the sample from the urban community pregnant women in western China, the generalizability of the results is restricted. Future research can expand to rural and low-income populations, further analyze the mechanism of symptom comorbidity and verify early intervention programs. In clinical practice, combined screening of depression, anxiety and sleep quality should be carried out in early pregnancy, with focus on pregnant women with abortion history, low back pain symptoms and strong perception of pregnancy impact on daily life. Early identification and continuous intervention should be adopted to reduce the risk of multiple psychosomatic symptom comorbidity during pregnancy and optimize maternal and fetal health outcomes.

Funding

Natural Science Foundation of Xinjiang Uygur Autonomous Region, China (Project No.: 2022D01F32)

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Zhou C, Li C, Huang Q, et al., 2025, Trends in the Prevalence of Antenatal Depression and Social Support among Pregnant Women in China, 2016–2021: A Repeated Cross-Sectional Study. *Public Health*, 240: 161–166.
- [2] Caffieri A, Gómez-Gómez I, Barquero-Jimenez C, et al., 2024, Global Prevalence of Perinatal Depression and Anxiety during the COVID-19 Pandemic: An Umbrella Review and Meta-Analytic Synthesis. *Acta Obstet Gynecol Scand*, 103(2): 210–224.
- [3] Findik E, Yılmaz Sezer N, Aker MN, et al., 2025, The Effects of the Mindfulness-Based Childbirth and Parenting Program (MBCP) on Prenatal Attachment, Depression, Stress, and Anxiety in Pregnant Women: A Randomized Controlled Trial. *J Affect Disord*, 376: 341–346.
- [4] Hulsbosch LP, Boekhorst MGBM, Lodder P, et al., 2023, Association between High Levels of Comorbid Anxiety and Depressive Symptoms and Decreased Likelihood of Birth without Intervention: A Longitudinal Prospective Cohort Study. *BJOG Int J Obstet Gynaecol*, 130(5): 495–505.
- [5] González-Mesa E, Cuenca-Marín C, Suarez-Arana M, et al., 2019, Poor Sleep Quality Is Associated with Perinatal Depression. A Systematic Review of Last Decade Scientific Literature and Meta-Analysis. *J Perinat Med*, 47(7):

689–703.

- [6] Sedov ID, Tomfohr-Madsen LM, 2021, Trajectories of Insomnia Symptoms and Associations with Mood and Anxiety from Early Pregnancy to the Postpartum. *Behav Sleep Med*, 19(3): 395–406.
- [7] Tomfohr-Madsen L, Rioux C, MacKinnon A, et al., 2022, Sleep and Mental Health in Pregnancy during COVID-19: A Parallel Process Growth Model. *Sleep Health*, 8(5): 484–490.
- [8] Wang Y, Liu H, Zhang C, et al., 2022, Antepartum Sleep Quality, Mental Status, and Postpartum Depressive Symptoms: A Mediation Analysis. *BMC Psychiatry*, 22(1): 521.
- [9] Yu Y, Li M, Pu L, et al., 2017, Sleep Was Associated with Depression and Anxiety Status during Pregnancy: A Prospective Longitudinal Study. *Arch Womens Ment Health*, 20(5): 695–701.
- [10] Maghami M, Shariatpanahi SP, Habibi D, et al., 2021, Sleep Disorders during Pregnancy and Postpartum Depression: A Systematic Review and Meta-Analysis. *Int J Dev Neurosci*, 81(6): 469–478.
- [11] Schafer KM, Mulligan E, Shapiro MO, et al., 2024, Antenatal Anxiety Symptoms Outperform Antenatal Depression Symptoms and Suicidal Ideation as a Risk Factor for Postpartum Suicidal Ideation. *Anxiety Stress Coping*, 37(6): 811–821.
- [12] Pietikäinen JT, Härkänen T, Polo-Kantola P, et al., 2021, Estimating the Cumulative Risk of Postnatal Depressive Symptoms: The Role of Insomnia Symptoms across Pregnancy. *Soc Psychiatry Psychiatr Epidemiol*, 56(12): 2251–2261.
- [13] Ahmed A, Feng C, Bowen A, et al., 2018, Latent Trajectory Groups of Perinatal Depressive and Anxiety Symptoms from Pregnancy to Early Postpartum and Their Antenatal Risk Factors. *Arch Womens Ment Health*, 21(6): 689–698.
- [14] Gao Y, Tang X, Deng R, et al., 2023, Latent Trajectories and Risk Factors of Prenatal Stress, Anxiety, and Depression in Southwestern China—A Longitudinal Study. *Int J Environ Res Public Health*, 20(5): 3818.
- [15] Tomfohr LM, Buliga E, Letourneau NL, et al., 2015, Trajectories of Sleep Quality and Associations with Mood during the Perinatal Period. *Sleep*, 38(8): 1237–1245.
- [16] Wang C, Hou J, Li A, et al., 2023, Trajectory of Perinatal Depressive Symptoms from the Second Trimester to Three Months Postpartum and Its Association with Sleep Quality. *Int J Womens Health*, 15: 711–723.
- [17] Gueron-Sela N, Shahar G, Volkovich E, et al., 2021, Prenatal Maternal Sleep and Trajectories of Postpartum Depression and Anxiety Symptoms. *J Sleep Res*, 30(4): e13258.
- [18] Zung WWK, 1965, A Self-Rating Depression Scale. *Arch Gen Psychiatry*, 12(1): 63.
- [19] Zung WWK, 1967, Factors Influencing the Self-Rating Depression Scale. *Arch Gen Psychiatry*, 16(5): 543.
- [20] Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ, 1989, The Pittsburgh Sleep Quality Index: A New Instrument for Psychiatric Practice and Research. *Psychiatry Res*, 28(2): 193–213.
- [21] Astbury L, Pinnington DM, Milgrom J, et al., 2025, The Longitudinal Trajectory of Depression and Anxiety across the Perinatal Period. *J Affect Disord*, 370: 1–8.
- [22] Pauley AM, Moore GA, Mama SK, et al., 2020, Associations between Prenatal Sleep and Psychological Health: A Systematic Review. *J Clin Sleep Med*, 16(4): 619–630.
- [23] Cheng C-Y, Chou Y-H, Chang C-H, et al., 2021, Trends of Perinatal Stress, Anxiety, and Depression and Their Prediction on Postpartum Depression. *Int J Environ Res Public Health*, 18(17): 9307.
- [24] Lee H, Kim K-E, Kim M-Y, et al., 2021, Trajectories of Depressive Symptoms and Anxiety during Pregnancy and Associations with Pregnancy Stress. *Int J Environ Res Public Health*, 18(5): 2733.
- [25] Basu A, Sarvet A, Chen JT, et al., 2024, An Examination of Sleep as a Protective Factor for Depression and

- Anxiety in the Perinatal Period: Novel Causal Analyses in a Prospective Pregnancy Cohort. *Am J Epidemiol*, 2024: kwae349.
- [26] Lin-Lewry M, Tzeng Y, Li C, et al., 2023, Trajectories of Sleep Quality and Depressive Symptoms in Women from Pregnancy to 3 Months Postpartum: A Prospective Cohort Study. *J Sleep Res*, 32(5): e13918.
 - [27] Poeira AF, Zangão MO, 2022, Construct of the Association between Sleep Quality and Perinatal Depression: A Literature Review. *Healthcare*, 10(7): 1156.
 - [28] Kalmbach DA, Cheng P, Ong JC, et al., 2020, Depression and Suicidal Ideation in Pregnancy: Exploring Relationships with Insomnia, Short Sleep, and Nocturnal Rumination. *Sleep Med*, 65: 62–73.
 - [29] Tsartsara E, Johnson MP, 2006, The Impact of Miscarriage on Women’s Pregnancy-Specific Anxiety and Feelings of Prenatal Maternal–Fetal Attachment during the Course of a Subsequent Pregnancy: An Exploratory Follow-Up Study. *J Psychosom Obstet Gynecol*, 27(3): 173–182.
 - [30] Long G, Yao ZY, Na Y, et al., 2020, Different Types of Low Back Pain in Relation to Pre- and Post-Natal Maternal Depressive Symptoms. *BMC Pregnancy Childbirth*, 20(1): 551.
 - [31] Xu C, Fu Z, Wang J, et al., 2022, Differences and Correlations of Anxiety, Sleep Quality, and Pressure-Pain Threshold between Patients with Chronic Low Back Pain and Asymptomatic People. *Pain Res Manag*, 2022: 1–7.
 - [32] Huang J, Peng D, Wang X, 2024, Estimating the Impact of Metabolic Syndrome on Low Back Pain and the Joint Effects of Metabolic Syndrome and Depressive Symptoms on Low Back Pain: Insights from the China Health and Retirement Longitudinal Study. *BMC Public Health*, 24(1): 2359.
 - [33] Ansari S, Sharma S, 2024, Sleep Status and Chronotype in University Athletes with and without Chronic Low Back Pain: A Cross-Sectional Study. *Sleep Sci*, 17(04): e407–e413.
 - [34] Vignesh C, Rajkumar NCJ, Pramanik M, et al., 2024, Effectiveness of Yoga Intervention on Depression, Stress, and Sleep Quality in IT Professionals with Chronic Low Back Pain: A Randomized Controlled Trial. *Fizjoterapia Pol*, 24(3): 410–416.

Publisher’s note

Whioce Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Analysis of Etiological Distribution and Clinical Therapeutic Effects in Children with Respiratory Tract Infections in Pediatric Outpatient Departments of Primary Hospitals

Rui Gao*

Pediatrics Department, Yan'an Xindong Rehabilitation Hospital, Yan'an 716000, Shaanxi, China

**Author to whom correspondence should be addressed.*

Copyright: © 2026 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To analyze the etiological distribution characteristics and clinical therapeutic effects in children with respiratory tract infections (ARI) in pediatric outpatient departments of primary hospitals. *Methods:* A total of 60 children with ARI treated in the pediatric outpatient department of a primary hospital from July 2022 to July 2025 were selected to analyze their etiological distribution characteristics and clinical therapeutic effects. *Results:* The positive rate of serum immunoglobulin M (IgM) in children with ARI was 78.33% (47/60), with *Mycoplasma pneumoniae* (MP) accounting for the highest proportion at 31.91% (15/47). The detection rate of influenza B virus (INFB) was higher in children aged 3–7 years old than in other age groups, while the detection rate of adenovirus (ADV) was higher in children under 1 year old than in other age groups ($P < 0.05$). The detection rates of MP, INFB, influenza A virus (INFA), and parainfluenza virus (PIV) varied among different seasons ($P < 0.05$). After symptomatic treatment, the disease symptom scores of the children were lower than before treatment, and their pulmonary function indicators were better than before treatment ($P < 0.05$). *Conclusion:* The etiological distribution of children with respiratory tract infections in pediatric outpatient departments of primary hospitals is dominated by MP, with differences in etiological distribution characteristics among different age groups and seasons. After symptomatic treatment, the clinical symptoms of the children are effectively relieved, and their pulmonary function indicators are significantly improved, indicating a favorable therapeutic effect.

Keywords: Primary hospital; Pediatric outpatient department; Respiratory tract infection; Etiological distribution; Clinical therapeutic effect

Online publication: May 31, 2026

1. Introduction

Respiratory tract infections are common diseases in pediatric outpatient departments of primary hospitals,

primarily including acute pharyngitis, acute tonsillitis, and acute bronchitis, characterized by rapid onset and progression, and high disease risk ^[1,2]. This condition can have a long-term impact on the physical and mental health of children and is prone to causing serious complications, necessitating early diagnosis and treatment. Serological tests and blood cultures are conventional diagnostic techniques that can determine the type of respiratory tract infection and formulate appropriate treatment plans. However, these tests are time-consuming, have a high rate of missed diagnoses, and cannot accurately assess complex conditions such as mixed infections. Serum pathogen testing is a relatively novel diagnostic method for this condition that can effectively evaluate the etiological distribution characteristics of children and enable targeted drug treatment, thereby improving disease prognosis ^[3]. This study selected 60 children with ARI to evaluate their etiological distribution characteristics and clinical therapeutic effects.

2. Materials and methods

2.1. General information

A total of 60 children with ARI treated in the pediatric outpatient department of a primary hospital from July 2022 to July 2025 were selected, including 37 males and 23 females; aged 0.5–14 years old, with a mean age of (5.18 ± 1.37) years old; and with a disease duration of 0.6–5 days, with a mean duration of (1.98 ± 0.49) days.

Inclusion criteria: Diagnosed with ARI by imaging examination; met the indications for etiological testing; had normal immunological function; had complete child data; and were highly informed about the study. Exclusion criteria: Had received anti-infective treatment within the past week; had concurrent tuberculosis infection; had respiratory failure; or were participating in other studies.

2.2. Methods

Venous blood (2 mL) was collected from the children in a fasting state, and serum separation was performed using a centrifuge (at 3000 r/min for 10 minutes). The serum was then placed in a refrigerator (-70°C) to evaluate the following indicators using an indirect immunofluorescence assay: IgM antibodies against MP, INFB, ADV, respiratory syncytial virus (RSV), PIV, INFA, Chlamydia pneumoniae (CP), Coxsackievirus (CV), Legionella pneumophila (LP), Coxiella burnetii (COX), Streptococcus pneumoniae (SP), and hemolytic streptococcus (HS). During the testing process, positive and negative control samples were set up, and the test results were observed using a fluorescence microscope.

All children received symptomatic treatment: (1) For fever symptoms: Children aged ≤ 6 months were treated with paracetamol at a dose of 10–15 mg/kg every 4–6 hours, with no more than 4 doses per day. Children aged > 6 months were treated with ibuprofen suspension, with the dose determined based on the child's weight and age, administered every 6–8 hours. (2) For cough symptoms: Medications such as dextromethorphan were administered at a dose of 2.5–10.0 mg per dose, 3–4 times per day. The type of infection was evaluated, and if it was a viral infection, oseltamivir phosphate granules were administered. For children weighing < 15 kg, the dose was 30 mg per dose, twice per day; for those weighing 15–23 kg, the dose was 45 mg per dose, twice per day; for those weighing 23.1–40 kg, the dose was 60 mg per dose, twice per day; and for those weighing > 40 kg, the dose was 75 mg per dose, twice per day. If it were a bacterial infection, azithromycin at a dose of 10 mg/kg was mixed into a glucose solution (100 mL) and administered

intravenously once per day for 1 week. Cefoperazone sodium, a cephalosporin, was also administered at a dose of 10 mg/kg, mixed into a glucose solution (100 mL), and administered intravenously twice per day for 1 week.

2.3. Observation indicators

The etiological distribution characteristics of the children were evaluated, with a focus on different age groups (< 1 year old, 3–7 years old, 9–14 years old) and different seasons (spring: March-May, summer: June-August, autumn: September-November, winter: December-February).

A self-made disease symptom score sheet was used before and after treatment to assess symptoms such as fever, cough, pulmonary rales, and sore throat, with each item scored from 0 to 4 points, and the severity of symptoms was scored positively. A pulmonary function tester was used to evaluate indicators such as forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and FEV1/FVC in the children.

2.4. Statistical analysis

Data processing was performed using SPSS 28.0 statistical software. Count data were expressed as [n/%], and chi-square tests were used for comparisons. Measurement data were tested for normal distribution using the K-S method and expressed as mean \pm standard deviation (SD). Independent sample *t*-tests were used for comparisons between groups, and paired *t*-tests were used for comparisons within groups. A *P*-value < 0.05 indicated a statistically significant difference.

3. Results

3.1. Analysis of the etiological distribution characteristics of the children

The IgM positive rate in children with ARI was 78.33%, and the specific etiological distribution characteristics were as follows (Table 1).

Table 1. Analysis of the etiological distribution characteristics of the children

Pathogen Type	Number of Cases (n)	Proportion (%)
MP (<i>Mycoplasma pneumoniae</i>)	15	31.91
INFB (<i>Influenza B virus</i>)	6	12.77
ADV (<i>Adenovirus</i>)	4	8.51
RSV (<i>Respiratory syncytial virus</i>)	2	4.26
PIV (<i>Parainfluenza virus</i>)	8	17.02
INFA (<i>Influenza A virus</i>)	4	8.51
CP (<i>Chlamydia pneumoniae</i>)	2	4.26
CV (<i>Coronavirus</i>)	1	2.13
LP (<i>Legionella pneumophila</i>)	1	2.13
COX (<i>Coxsackievirus</i>)	1	2.13
SP (<i>Streptococcus pneumoniae</i>)	1	2.13
HS (<i>Herpes simplex virus</i>)	2	4.26
Total	47	100.00

3.2. Analysis of etiological distribution characteristics among children of different age groups

Among the children with positive IgM results, there were 14 cases under 1 year old, 25 cases aged 3–7 years old, and 8 cases aged 8–14 years old. The detection rate of INFB was higher in children aged 3–7 years old compared to other age groups, while the detection rate of ADV was higher in children under 1 year old compared to other age groups ($P < 0.05$) (Table 2).

Table 2. Analysis of etiological distribution characteristics among children of different age groups [n/%]

Pathogen Type	< 1 year old(n=14)	3–7 yearsold (n = 25)	8–14 years old(n = 8)	χ^2	<i>P</i>
MP	6 (42.86)	5 (20.00)	4 (50.00)	1.657	0.437
INFB	0	6 (24.00)	0	6.053	0.048
ADV	4 (28.57)	0	0	10.306	0.006
RSV	1 (7.14)	1 (4.00)	0	0.646	0.724
PIV	2 (14.29)	3 (12.00)	3 (37.50)	2.896	0.235
INFA	1 (7.14)	2 (8.00)	1 (12.50)	0.206	0.902
CP	0	2 (8.00)	0	1.838	0.399
CV	0	1 (4.00)	0	0.899	0.638
LP	0	1 (4.00)	0	0.899	0.638
COX	0	1 (4.00)	0	0.899	0.638
SP	0	1 (4.00)	0	0.899	0.638
HS	0	2 (8.00)	0	1.838	0.399

3.3. Analysis of the etiological distribution characteristics of pathogens in children across different seasons

Among the seasons of onset, there were 11 cases in spring, 22 cases in summer, 8 cases in autumn, and 6 cases in winter. There were significant differences ($P < 0.05$) in the detection rates of MP, INFB, INFA, and PIV among children across different seasons (Table 3).

Table 3. Analysis of the etiological distribution characteristics of pathogens in children across different seasons [n/%]

Pathogen Type	Spring(n = 11)	Summer(n = 22)	Autumn(n = 8)	Winter(n = 6)	χ^2	<i>P</i>
MP	3 (27.27)	9 (40.91)	2 (25.00)	1 (16.67)	9.639	0.022
INFB	1 (9.09)	5 (22.73)	0	0	9.685	0.021
ADV	3 (27.27)	1 (4.55)	0	0	3.345	0.341
RSV	0	0	1 (12.50)	1 (16.67)	4.456	0.216
PIV	2 (18.18)	1 (4.55)	1 (12.50)	4 (66.67)	12.119	0.007
INFA	0	4 (18.18)	0	0	10.306	0.016
CP	2 (18.18)	0	0	0	3.686	0.297
CV	0	0	1 (12.50)	0	3.780	0.286
LP	0	0	1 (12.50)	0	3.780	0.286
COX	0	0	1 (12.50)	0	3.780	0.286
SP	0	1 (4.55)	0	0	2.408	0.492
HS	0	1 (4.55)	1 (12.50)	0	2.119	0.548

3.4. Comparison of disease symptom scores before and after treatment

After treatment, the disease symptom scores of the pediatric patients were lower than those before treatment ($P < 0.05$) (Table 4).

Table 4. Comparison of disease symptom scores before and after treatment (mean \pm SD, points)

Time	Number of Cases	Fever	Cough	Lung Rales	Sore Throat
Before Treatment	60	2.71 \pm 0.54	2.66 \pm 0.48	2.31 \pm 0.41	2.20 \pm 0.49
After Treatment	60	1.05 \pm 0.44	1.16 \pm 0.39	1.42 \pm 0.36	1.08 \pm 0.33
<i>t</i>	-	18.460	18.787	12.635	14.685
<i>P</i>	-	0.000	0.000	0.000	0.000

3.5. Comparison of pulmonary function indicators before and after treatment

After treatment, the pulmonary function indicators of the children were superior to those before treatment ($P < 0.05$) (Table 5).

Table 5. Comparison of pulmonary function indicators before and after treatment (mean \pm SD)

Time	Number of Cases	FEV1 (L)	FVC (L)	FEV1/FVC (%)
Before treatment	60	1.35 \pm 0.54	2.16 \pm 0.58	61.77 \pm 5.92
After treatment	60	1.92 \pm 0.74	2.59 \pm 0.47	75.43 \pm 6.18
<i>t</i>	-	4.820	4.462	12.364
<i>P</i>	-	0.000	0.000	0.000

4. Discussion

Acute Respiratory Infections (ARI) are prevalent respiratory diseases among children, necessitating etiological testing to effectively differentiate disease types and guide treatment plans. IgM antibodies serve as a commonly used pathogen detection indicator in children with this disease, enabling the assessment of pathogen infection status and facilitating early diagnosis ^[4,5]. Among specific pathogen types, *Mycoplasma pneumoniae* (MP) has a unique terminal structure that allows it to adhere extensively to the epithelial cells of the respiratory mucosa, leading to symptoms such as fever, scanty sputum, or cough. Influenza B virus (INFB) is a common type within the Orthomyxoviridae family, highly contagious, and composed of nucleoprotein and nucleic acid, which are prone to causing influenza virus mutations. Its main symptoms include fever, pharyngeal discomfort, and cough ^[6]. Respiratory Syncytial Virus (RSV) continuously damages the epithelial cells of the respiratory mucosa, leading to mucosal edema and subsequently pneumonia or fever. Parainfluenza Virus (PIV) alters the morphology of respiratory epithelial cells, increases mucus secretion, and results in symptoms such as cough, nasal congestion, and hoarseness. Classifying these pathogens enables accurate assessment of the infection type in children, thereby improving the diagnostic accuracy of the disease ^[7].

The results showed that the IgM positivity rate among children with ARI was 78.33%, with MP being the predominant pathogen. The detection rate of INFB was higher in children aged 3–7 years old compared to other age groups, while the detection rate of Adenovirus (ADV) was higher in children under 1 year old. There were significant differences in the detection rates of MP, INFB, Influenza A virus (INFA), and PIV

among children across different seasons ($P < 0.05$). The analysis suggests that the peak age of incidence varies among different pathogens. Compared to older children aged 9–14 years old, younger children have immature organ development and weaker disease resistance, placing them at a higher risk of infection with multiple pathogens and thus more susceptible to ARI^[8]. Climate change is a primary cause of ARI. In summer, the significant temperature variations between indoors and outdoors, coupled with the alternating hot and cold conditions, facilitate viral or bacterial infections. Moreover, high temperatures in summer promote the proliferation of various bacteria, making it a peak season for ARI^[9].

After treatment, the disease symptom scores of the children were lower than before treatment, and their pulmonary function indicators improved ($P < 0.05$). The analysis indicates that etiological analysis enables the clear identification of the infection type in children, facilitating targeted treatment. For viral infections, oseltamivir can be administered, which exhibits strong antiviral effects and stable pharmacokinetics, making it suitable for pediatric populations. For bacterial infections, a combination of azithromycin and cephalosporins can effectively combat inflammation and eliminate pathogens such as MP, with a broad antibacterial spectrum that targets multiple pathogens, thereby rapidly improving symptoms and protecting pulmonary function in children^[10].

5. Conclusion

In conclusion, conducting etiological testing to children with ARI can assess their disease characteristics and enable differentiated treatment, thereby achieving better clinical outcomes.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Tang W, Xu X, Zhang W, 2023, Study on the Relationship Between Inflammatory Markers and Etiology in Hospitalized Children With Lower Respiratory Tract Infections Across Different Age Groups. *Heilongjiang Medicine Journal*, 36(2): 274–277.
- [2] Liu X, Gu M, Sun M, et al., 2023, Clinical Characteristics and Etiological Analysis of Lower Respiratory Tract Infections in Infants With Bronchopulmonary Dysplasia. *Chinese Journal of Contemporary Pediatrics*, 25(9): 953–958.
- [3] Zhao L, Liu Y, 2025, Etiological Characteristics and Epidemiological Analysis of 923 Cases of Respiratory Tract Infections in Children. *Practical Preventive Medicine*, 32(8): 1007–1010.
- [4] Fan S, Guan Z, Xu Y, et al., 2025, Investigation on the Etiological Characteristics of Respiratory Tract Infections in Children Across Different Age Groups. *Chinese Journal of Pathogen Biology*, 20(11): 1463–1466 + 1475.
- [5] Zhang J, Zheng S, 2023, Etiological Analysis of Small Airway Lesions in Children Under 5 Years Old After Acute Lower Respiratory Tract Infections. *Contemporary Medical Forum*, 21(14): 69–72.
- [6] Chang Z, Tang H, Zhang J, et al., 2024, Report on Pathogen Detection Results in Hospitalized Children With Respiratory Tract Infections in a Certain Hospital From 2011 to 2021. *Chinese Journal of Hospital Infection*, 34(22): 3467–3471.

- [7] Gao L, Jin X, Lai L, et al., 2023, Investigation on the Viral Spectrum and Epidemiological Characteristics of Lower Respiratory Tract Infections in 1652 Children. *Chinese Journal of Pathogen Biology*, 18(4): 443–446.
- [8] Chen J, Wu J, Liu W, et al., 2025, Detection and Epidemiological Analysis of Non-Bacterial Pathogens in Respiratory Specimens From Children With Acute Respiratory Tract Infections in a Certain Hospital. *Anti-Infection Pharmacy*, 22(1): 74–77.
- [9] Liu Y, Zheng C, Luo T, et al., 2024, Etiological Analysis of Cough in 779 Children After Respiratory Tract Infections. *Smart Healthcare*, 10(12): 23–25 + 29.
- [10] Cao C, Shi L, 2022, Investigation and Analysis of Viral Etiology in 326 Cases of Influenza-Like Illness in Children in a Certain Hospital. *Journal of Shanxi Health Vocational College*, 32(4): 37–38.

Publisher's note

Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Clinical Study on the Integrated Treatment of Adenomyosis without Fertility Requirements Using High-Intensity Focused Ultrasound Combined with Sequential Drug Therapy and Long-Term Standardized Management

Xiaoli Zhang, Zhongfang Qin, Wenting Li

The First People's Hospital of Datong, Datong 037000, Shanxi, China

**Author to whom correspondence should be addressed.*

Copyright: © 2026 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To investigate the clinical efficacy, long-term control, and safety of an integrated treatment approach for adenomyosis without fertility requirements, incorporating MRI-based classification, GnRH-a pretreatment, high-intensity focused ultrasound (HIFU) ablation (Haifu Knife), sequential maintenance with Mirena/Dienogest, combined with close follow-up every 3 months and multiple supplemental treatments every 6–12 months. *Methods:* A retrospective analysis was conducted on 136 patients with adenomyosis without fertility requirements admitted to the gynecology department of our hospital from January 2019 to December 2025. Patients were stratified based on MRI classification, clinical symptoms, and the presence of adenomyoma: Those with simple adenomyosis and menorrhagia received GnRH-a + HIFU + Mirena; those with adenomyoma and severe dysmenorrhea received GnRH-a + HIFU + Dienogest. All patients underwent routine follow-up every 3 months post-treatment, with HIFU supplemental ablation performed every 6-12 months for residual or recurrent lesions, accompanied by long-term drug management. Dysmenorrhea VAS scores, menstrual volume, uterine volume, clinical efficacy, recurrence rate, and complications were observed before and after treatment. *Results:* All 136 patients completed treatment and standardized follow-up, achieving an overall clinical efficacy rate of 88.2%, with dysmenorrhea relief in 89.7%, menstrual volume improvement in 87.5%, and a mean uterine volume reduction of 32.6%. The median follow-up period was 24 months, with an overall recurrence rate of 11.8%. Recurrent cases were effectively controlled through multiple HIFU supplemental treatments without severe complications. *Conclusion:* For patients with adenomyosis without fertility requirements, the integrated management approach combining MRI-guided GnRH-a + HIFU + Mirena/Dienogest sequential therapy, frequent close follow-up, multiple supplemental ablations, and long-term drug maintenance significantly improves clinical symptoms, reduces uterine volume, and lowers recurrence risk. This approach is stable, safe, non-invasive, and aligns with the principles of standardized and individualized conservative treatment for adenomyosis, offering a new standardized uterine-preserving treatment paradigm for patients without fertility requirements.

Keywords: Adenomyosis; High-intensity focused ultrasound; Haifu knife; MRI classification; GnRH-a; Dienogest; Levonorgestrel-releasing intrauterine system; Long-term management; Multiple treatments

Online publication: May 31, 2026

1. Introduction

Adenomyosis is a prevalent benign gynecological disorder among women of reproductive age, characterized by the invasion of endometrial glands and stroma into the myometrium, accompanied by myometrial hyperplasia and hypertrophy. Clinically, it manifests as progressive dysmenorrhea, increased menstrual volume, uterine enlargement, and secondary infertility, severely impacting patients' physical and mental health and quality of life ^[1]. The diffuse nature of the lesions, unclear boundaries, high residual rates, and significant recurrence risk pose challenges for clinical conservative treatment. Traditional treatments primarily include symptomatic drug therapy, conservative surgery, and hysterectomy. However, drug therapy offers only temporary relief with frequent recurrences, while surgical interventions are invasive, and hysterectomy has profound physiological and psychological impacts on women, failing to meet the modern demand for uterine-preserving treatments.

High-intensity focused ultrasound (HIFU, Haifu Knife), as a non-invasive thermal ablation technique, has become an important conservative treatment for adenomyosis due to its advantages of precise targeted ablation, preservation of uterine anatomy and physiological function, and repeatability ^[2]. However, HIFU alone cannot fundamentally address the high recurrence rate of adenomyosis, necessitating the establishment of a standardized, full-chain management system encompassing pretreatment, ablation, consolidation, monitoring, and retreatment ^[3]. Since initiating HIFU treatment for adenomyosis in 2019, our hospital has developed an integrated diagnostic and therapeutic model combining MRI imaging classification, patient symptom characteristics, and clinical features of no fertility requirements: GnRH-a pretreatment to reduce lesion size, precise non-invasive HIFU ablation, sequential consolidation with Mirena/Dienogest, close follow-up every 3 months, and multiple supplemental treatments every 6–12 months as needed. This study systematically evaluates the short- and long-term efficacy and safety of this model through a retrospective analysis of 136 cases, aiming to provide high-quality clinical evidence for the standardized conservative treatment of adenomyosis in the field of Chinese obstetrics and gynecology.

2. Materials and methods

2.1. Study subjects

A total of 136 patients with adenomyosis without fertility requirements admitted to the gynecology department of our hospital from January 2019 to December 2025 were selected, aged 32–51 years old (mean 40.5 ± 5.2 years old), with a disease duration of 1–10 years. Inclusion criteria: (1) Diagnosed with adenomyosis/adenomyoma based on clinical symptoms, gynecological examination, and pelvic MRI; (2) Mainly manifested as dysmenorrhea, increased menstrual volume, and uterine enlargement; (3) No fertility requirements, good compliance, able to complete regular follow-up and treatment; (4) No contraindications to HIFU treatment, GnRH-a, Dienogest, or Mirena; (5) Complete clinical and follow-up data. Exclusion

criteria: Uterine malignancy, acute pelvic infection, coagulopathy, drug allergies, fertility requirements, and incomplete clinical data. This study was approved by the hospital's medical ethics committee, and all patients signed informed consent forms.

2.2. MRI classification criteria

All patients underwent pelvic MRI before treatment, and lesions were classified into four types based on lesion distribution, infiltration range, and relationship with the endometrium and myometrium, serving as the core imaging basis for individualized treatment planning: Type I (localized adjacent to the endometrium), Type II (diffuse myometrial infiltration), Type III (localized intramural), and Type IV (predominantly adenomyoma).

2.3. Treatment methods

2.3.1. Individualized sequential treatment plan

For simple adenomyosis with increased menstrual volume as the main manifestation, GnRH-a injections were administered for 3–6 cycles as pretreatment. After monitoring uterine reduction to the size of 8 weeks of gestation, precise HIFU ablation was performed, followed by placement of the levonorgestrel-releasing intrauterine system (Mirena) for long-term control of menstrual volume and inhibition of lesion recurrence.

For adenomyoma with progressive severe dysmenorrhea as the main manifestation: After GnRH-a pretreatment, HIFU ablation was performed, followed by sequential oral administration of Dienogest to specifically alleviate dysmenorrhea and delay lesion progression.

2.3.2. Long-term standardized management strategy

Adenomyosis is characterized by high recurrence and a protracted course. This study implemented a full-cycle closed-loop management approach: (1) Close follow-up monitoring: Routine re-examination every 3 months post-treatment to assess clinical symptoms, gynecological ultrasound, and lesion changes, enabling early identification of residual and recurrent lesions; (2) Multiple supplemental treatments: For patients with lesion enlargement or symptom recurrence during follow-up, HIFU supplemental ablation was performed every 6–2 months based on individual circumstances to precisely target recurrent lesions; (3) Long-term drug maintenance: Drug regimens were dynamically adjusted based on symptom improvement to achieve long-term stable disease control.

2.4. Observation indicators

Dysmenorrhea VAS scores, menstrual volume improvement, and uterine volume changes were recorded before and after treatment. The overall clinical efficacy rate and recurrence rate during follow-up were statistically analyzed. Complications during treatment and follow-up were observed to evaluate the safety of the regimen.

2.5. Efficacy evaluation criteria

Markedly effective: Dysmenorrhea basically disappeared, menstrual volume returned to normal, and uterine volume was reduced by $\geq 30\%$; Effective: Dysmenorrhea was significantly relieved, menstrual volume markedly decreased, and uterine volume was reduced by 10–29%; Ineffective: No improvement or worsening of clinical symptoms, with no reduction in uterine volume. The overall efficacy rate = (markedly effective

+ effective)/total number of cases \times 100%. Recurrence was defined as an ultrasound/MRI indication of lesion enlargement during follow-up, with re-aggravation of symptoms such as dysmenorrhea and increased menstrual volume.

2.6. Statistical methods

Data were analyzed using SPSS 26.0 statistical software. Measurement data were expressed as mean \pm standard deviation, and comparisons before and after treatment were made using the *t*-test. Enumeration data were expressed as cases (%), and comparisons between groups were made using the χ^2 test. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Clinical efficacy

All 136 patients completed sequential treatment and standardized follow-up without dropouts. The overall efficacy rate was 88.2% (120/136), with 69 markedly effective cases, 51 effective cases, and 16 ineffective cases. The dysmenorrhea relief rate was 89.7%, the menstrual volume improvement rate was 87.5%, and the mean uterine volume reduction was 32.6%. Statistically significant differences were observed in all indicators before and after treatment ($P < 0.05$).

3.2. Recurrence

The median follow-up period was 24 months, with 16 patients experiencing lesion recurrence, resulting in an overall recurrence rate of 11.8%. All recurrent cases promptly underwent HIFU supplemental ablation combined with drug consolidation, effectively controlling symptoms without any patients requiring hysterectomy due to recurrence or disease progression.

3.3. Safety evaluation

During treatment and follow-up, no severe complications such as intestinal, bladder, or vascular injury occurred, nor did adverse events, such as skin burns or pelvic infections. A few patients experienced mild lower abdominal distension and a small amount of vaginal discharge, which resolved spontaneously within a short period, indicating good safety.

4. Discussion

Due to its unique pathological characteristics, the core of clinical treatment for adenomyosis lies in uterine preservation, symptom control, and recurrence prevention. A single treatment modality is insufficient to meet long-term management needs ^[4]. GnRH-a, as a pretreatment drug, effectively reduces uterine volume, decreases lesion blood supply, optimizes HIFU treatment conditions, and enhances ablation precision and efficacy. HIFU utilizes the thermal effect of high-intensity focused ultrasound to non-invasively inactivate ectopic endometrial lesions, avoiding surgical trauma and preserving uterine integrity. Mirena and Dienogest provide long-term consolidation treatment targeting the two core symptoms of increased menstrual volume and dysmenorrhea, respectively, forming a complete treatment chain of pretreatment-ablation-maintenance in synergy ^[5,6].

The core innovation of this study lies in the establishment of a long-term standardized management system tailored to patients without fertility requirements, which is also the key difference from traditional single treatment modalities. Frequent re-examinations every 3 months enable early warning of recurrence, while multiple HIFU supplemental treatments every 6-12 months promptly intervene in residual lesions. Combined with long-term drug maintenance, this approach fundamentally reduces the recurrence rate of adenomyosis, addressing the core challenge of long-term clinical management ^[7]. The study results demonstrate an overall clinical efficacy rate of 88.2% and a 2-year recurrence rate of only 11.8%, with excellent safety, fully confirming the scientific and practical value of this regimen.

Compared to traditional treatment plans, this model, guided by MRI classification, achieves type-specific treatment and precise intervention, incorporating non-invasiveness, repeatability, and individualization. It fully aligns with modern gynecological concepts of minimally invasive uterine-preserving treatment, providing a reproducible and promotable standardized diagnostic and therapeutic pathway for patients with adenomyosis without fertility requirements. It meets the requirements of the Chinese obstetrics and gynecology field for standardized and refined disease management ^[8].

5. Conclusion

The integrated management approach combining MRI-based classification with GnRH-a + HIFU + Mirena/Dienogest sequential therapy, close follow-up every 3 months, multiple HIFU supplemental ablations every 6–12 months, and long-term drug maintenance demonstrates definite clinical efficacy, stable long-term control, and high safety in treating adenomyosis without fertility requirements. It significantly improves patient symptoms and reduces recurrence risk, representing an ideal conservative treatment option for adenomyosis worthy of clinical promotion and application in gynecology departments at all levels of medical institutions across the country.

Funding

Datong Key Research and Development Program Project (Project No.: 2024027)

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Subspecialty Group of Endometriosis, Society of Obstetrics and Gynecology, Chinese Medical Association, 2020, Chinese Expert Consensus on the Diagnosis and Treatment of Adenomyosis. Chinese Journal of Obstetrics and Gynecology, 55(3): 161–168.
- [2] Lang JH, 2019, Current Status and Prospects of Research on Endometriosis and Adenomyosis. Chinese Journal of Obstetrics and Gynecology, 54(1): 3–6.
- [3] Wang ZB, 2021, Clinical Application and Progress of High-Intensity Focused Ultrasound in the Treatment of Benign Gynecological Diseases. Chinese Journal of Practical Gynecology and Obstetrics, 37(1): 38–43.

- [4] Zhang L, Chen JY, Chen WZ, 2022, Analysis of Medium- and Long-Term Efficacy and Influencing Factors of High-Intensity Focused Ultrasound Ablation for Adenomyosis. Chinese Journal of Ultrasonography, 31(4): 341–345.
- [5] Zhou HM, Lang JH, 2023, Clinical Research Progress on Combined Drug and Physical Therapy for Adenomyosis. Journal of Practical Obstetrics and Gynecology, 39(2): 128–131.
- [6] Chen CL, Liu P, Wang ZJ, 2022, Correlation Study between MRI Classification of Adenomyosis and Selection of Clinical Treatment Plans. Chinese Journal of CT and MRI, 20(7): 144–146.
- [7] Xie X, Kong BH, Duan T, 2018, Obstetrics and Gynecology. 9th ed., People’s Medical Publishing House, Beijing.
- [8] Cao ZY, 2021, Chinese Obstetrics and Gynecology. 4th ed., People’s Medical Publishing House, Beijing.

Publisher’s note

Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Clinical Analysis of Cervical HSIL with Poorly Differentiated Squamous Cell Carcinoma Metastatic to the Ovary

Ziyu Qi¹, Jingna Xing³, Wenling Fan^{2*}

¹ Graduate School of Hebei Medical University, Shijiazhuang 050017, Hebei, China

² The Fourth Hospital of Hebei Medical University, Shijiazhuang 050000, Hebei, China

³ The Seventh Hospital of Hebei Province, Dingzhou 073000, Hebei, China

**Author to whom correspondence should be addressed.*

Copyright: © 2026 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *History summary:* A 64-year-old female patient presented with a three-month history of right lower abdominal pain. Ultrasound examination revealed a mass measuring approximately 5 cm × 4 cm × 4 cm in the right adnexal region, which was movable with slight tenderness. The ultrasound suggested a cystic-like mass in the right adnexal region, and “pelvic mass” was considered. *Family history:* The patient’s mother died of “ovarian cancer” (specific pathological type unknown), and her sister was diagnosed with “breast cancer” (positive for BRCA1 gene testing). *Symptoms and signs:* The patient experienced dull pain in the right lower abdomen accompanied by a slight sensation of fullness in the lower abdomen. On bimanual examination, a mass measuring approximately 5 cm × 4 cm × 4 cm was palpable in the right adnexal region, which was movable with slight tenderness. *Diagnostic methods:* Ultrasound suggested a cystic-like mass in the right adnexal region. CT examination revealed a low-density mass in the right adnexal region with slight thickening of the adjacent intestinal wall, suggesting an ovarian origin. *Treatment:* Laparoscopic total hysterectomy + bilateral adnexectomy + pelvic and para-aortic lymph node dissection + omentectomy + peritoneal multi-point biopsy. *Final diagnosis:* Pathological consultation at a superior hospital confirmed (cervical) HSIL (CINII grade) and poorly differentiated squamous cell carcinoma of the ovary (metastatic origin). The patient was considered to have poorly differentiated squamous cell carcinoma associated with HPV infection originating from the cervix and metastasizing to the right ovary.

Keywords: HSIL; HPV infection-related; Squamous cell carcinoma metastatic to the ovary

Online publication: May 31, 2026

1. Introduction

Cervical cancer is one of the malignant tumors in women, with primary routes of metastasis including direct spread, lymphatic metastasis, and hematogenous metastasis. Direct spread is the most common early mode of metastasis, where cancer cells first spread to adjacent tissues, invading the bladder anteriorly, the rectum

posteriorly, the parametrial tissues, cardinal ligaments, uterosacral ligaments, and pelvic wall laterally, the vaginal wall inferiorly, and the uterine body superiorly in rare cases. When cancer cells invade the lymphatic vessels, they typically metastasize sequentially according to the direction of lymphatic drainage. Hematogenous metastasis generally occurs in the late stages, with cancer cells spreading to distant organs through the bloodstream, commonly to the lungs. Metastasis to the ovaries is extremely rare. Poorly differentiated squamous cell carcinoma metastatic to the ovary from cervical HSIL is even more difficult to believe.

2. Clinical data

2.1. General information

The patient, a 64-year-old female, was admitted to the hospital primarily due to lower right abdominal pain for three months. Three months ago, the patient experienced dull pain in the lower right abdomen without obvious precipitating factors, accompanied by a slight sensation of fullness and heaviness in the lower abdomen. There was no vaginal bleeding or discharge, nor any other symptoms such as nausea or vomiting. She sought medical attention on October 28, 2025.

Past Medical History: No history of hypertension, diabetes, or coronary heart disease. Family History: The patient's mother died of "ovarian cancer" (specific pathological type unknown), and her elder sister was diagnosed with "breast cancer" (positive for BRCA1 gene mutation).

2.2. Examination

2.2.1. Abdominal examination

The abdomen was flat and soft, with mild tenderness in the lower right abdomen. No masses were palpable. Gynecological Examination: Married vulva, patent vagina, atrophic cervix with a smooth surface, normally positioned uterus of normal size, medium consistency, good mobility, and no tenderness. A mass measuring approximately 5 cm × 4 cm × 4 cm was palpable in the right adnexal region, with good mobility and mild tenderness. No obvious abnormalities were detected in the left adnexal region.

2.2.2. Gynecological ultrasound

The uterus was in an anterior position, with a size of 3.8 cm × 2.8 cm. The anterior and posterior borders of the uterine body were clear, and the echo of the uterine muscle wall was uneven. Multiple hypoechoic nodules were visible in the intermuscular layer of the anterior wall of the fundus. The endometrium was centrally located, with a cervical size of 2.2 cm × 1.9 cm. The left ovary measured 1.3 cm × 0.5 cm, and a hypoechoic mass measuring 5.0 cm × 3.6 cm was visible in the right adnexal region, with a regular shape but unclear borders. It appeared to contain a poorly sonolucent cystic area with interspersed strong echo spots and no obvious blood flow signals. The right ovary was not clearly visualized. Indications: Multiple solid masses in the uterine wall (considering myomas) and a cystic-like mass in the right adnexal region.

2.2.3. CT examination

Suggested a low-density mass shadow in the right adnexal region, with slight thickening of the adjacent intestinal wall.

Tumor Markers (October 26, 2025): CA125: 6.46 U/mL, CA72-4: 0.9 U/mL, CA199: 26.2 U/mL, CEA: 1.62 ng/mL, AFP: 3.48 ng/mL, HE4: 51 U/mL, SCC: 0.5 ng/mL. HPV DNA-56 (high-risk type) positive (+),

HPV DNA-58 (high-risk type) positive (+), HPV DNA-6 (low-risk type) positive (+). TCT results showed a small number of DNA ploidy abnormal cells. TBS diagnosis: Atypical epithelial cells. Colposcopy showed non-staining areas with the iodine test, and cervical tissue biopsy was sent for pathology. Results: (Cervical) HSIL (CIN Grade 2). Immunohistochemistry results: P16 (+), Ki-67 (2/3+ in the squamous epithelium). (Family refused conization).

3. Diagnosis

Preliminary Diagnosis: (1) Pelvic mass; (2) Multiple uterine leiomyomas.

4. Treatment

(1) Surgical Treatment

Laparoscopic exploration was performed on October 31, 2025. Intraoperatively, the uterus was enlarged to the size of a 50+ day pregnancy, with multiple myoma nodules in the muscle wall. The right ovary was solidly enlarged to 6 cm × 5 cm × 4 cm, with a hard consistency and dense adhesion to part of the rectum and the right pelvic wall. The right ureter passed through it, and the right fallopian tube and left adnexa appeared normal. No enlarged lymph nodes were detected beside the pelvic aorta. No lesions were found on the surface of the omentum. The right adnexa was resected and sent for frozen pathology: severe hemorrhage and necrosis of the tumor-like tissue, with degenerated atypical cells visible, not excluding poorly differentiated carcinoma. Due to the hard consistency of the right ovarian mass, dense adhesion to surrounding tissues, and the passage of the ureter through it, making separation difficult, a “laparoscopic total hysterectomy + bilateral adnexectomy + pelvic and para-aortic lymph node dissection + omentectomy + multipoint peritoneal biopsy + cystoscopic right ureteral stent (D-J tube) placement” was performed.

(2) Postoperative pathology results

Left adnexa (-), multiple uterine leiomyomas, senile endometrium. Chronic cervicitis and endometritis, negative for the uterine serosal surface, omental tissue (-). Left colonic sulcus peritoneum (-), right colonic sulcus peritoneum (-), intestinal surface mass: a small number of degenerated atypical cells were visible in the fibrofatty tissue. Ureteral surface mass tissue: infiltration of poorly differentiated carcinoma was visible. Right adnexal mass (frozen residue and paraffin): a small number of degenerated atypical cells were visible in the degenerated necrotic tissue, not excluding poorly differentiated carcinoma. Immunohistochemistry results: AE1/AE3 (+), Vimentin (+), ER (-), PR (-), P16 (-), CA125 (+/-), WT1 (-), Ki67 (80% positive cells), CK7 (+), CK20 (-), Pax-8 (-), HNF1β (-), P40 (-), GATA3 (-), SALL4 (-), CDX2 (-). Based on immunohistochemical expression and histological morphology, infiltration of poorly differentiated carcinoma was visible in the fibrous and muscular tissues.

According to the postoperative pathology and immunohistochemistry results, the discharge diagnosis was revised to: (1) Ovarian poorly differentiated carcinoma Stage IIB; (2) Multiple uterine leiomyomas; (3) (Cervical) HSIL (CIN Grade II); and (4) Postoperative right ureteral stent placement. The patient is currently receiving TC regimen chemotherapy.

5. Exploration

To further clarify whether there is a relationship between cervical HSIL and ovarian poorly differentiated carcinoma, a consultation was conducted at Peking University Third Hospital. The immunohistochemistry results of the cervical biopsy tissue: P16 (+), Ki-67 (2/3+ in the squamous epithelium); molecular pathology results: HPV RNAscope HR18 multiple subtypes (+). Total hysterectomy + left adnexa: (1) Multiple uterine leiomyomas; atrophic endometrium; chronic cervicitis, focal HSIL (CIN Grade 2). (2) “Ureteral surface mass” showed tumor cell infiltration. “Intestinal surface mass” showed a small number of tumor cells in the fibrous tissue. The uterine serosal surface, left adnexa, and “left rectal sulcus peritoneum, right rectal sulcus peritoneum, uterine artery” showed no tumors. Immunohistochemistry results: P16 (-), Ki-67 (2/3+ in the squamous epithelium). DF25-0517422 section: (Right adnexa) malignant tumor, immunohistochemistry results: P53 (missense mutant expression), WT-1 (+), BAP1 (+), Calretinin (-), HBME-1 (-), D2-40 (-), MTAP (weak +), CK5/6 (+), TRPS1 (scattered +), NTRKpan (-), NUT (-), Inhibin α (-), Rb (+), MLH1 (+), PMS2 (+), MSH2 (+), MSH6 (+), P40 (partial +), P63 (partial +), P16 (-), HER-2 (0); Ki-67 (2/3+ in the squamous epithelium).

In Situ Hybridization: HPV RNAscope HR18 multiple subtypes (+). Molecular pathology results: NGS1021+oncofusion gene detection (TP53 gene variation and FGFR-REEP3 fusion detected in the tumor; MSS; TMB-L: 2.25 Muts/Mb, 37%); oncofusion gene detection: no gene rearrangement detected in the tumor; pathogenic BRCA1 germline gene mutation detected in peripheral blood. Based on the immunohistochemistry and molecular detection results, it is consistent with HPV infection-related poorly differentiated squamous cell carcinoma. Therefore, this patient is considered to have primary HPV infection-related poorly differentiated squamous cell carcinoma of the cervix metastasizing to the right ovary.

6. Discussion

Ovarian metastasis from cervical cancer is not rare clinically, but ovarian metastasis of poorly differentiated squamous cell carcinoma from cervical HSIL has not been reported. Mei Quan et al.^[1] showed that the probability of ovarian metastasis from cervical cancer roughly fluctuates between 0.12% and 2.22%, with squamous cell carcinoma having a lower rate than adenocarcinoma. Zhang Shiqian et al.^[2] pointed out that a study by the American Gynecological Oncology Group (GOG) found that the ovarian metastasis rate of Stage IB cervical squamous cell carcinoma was 0.5%. Shimada et al.^[3] reported a large-sample clinical retrospective study with an ovarian metastasis rate of 1.5% in cervical cancer. Yamamoto et al.^[4] reported an ovarian metastasis rate of 2.22%. There are also many reports of ovarian metastasis of cancer cells after ovarian preservation in cervical cancer. Ivanov et al.^[5] found that in a survey after ovarian transposition in cervical cancer, ovarian metastasis occurred in 3 cases of squamous cell carcinoma and 3 cases of adenosquamous carcinoma. Among cervical squamous cell carcinoma patients who preserved their ovaries during the initial surgery, Sanjun et al.^[6] reported a case of bilateral ovarian metastasis within 1 year after Stage IIB surgery. Piketty et al.^[7] reported a case of ovarian metastasis of preserved cancer in a Stage IB cervical adenocarcinoma patient 17 months after surgery.

Metastatic Pathways: Direct spread is the most common in cervical cancer, so metastasis in advanced patients is understandable. When the uterine body is involved, due to the clinical characteristic of infiltrative growth of cervical adenocarcinoma, when the parauterine tissues are directly involved, cancer cells can directly invade the ovarian tissue or reach the ovary through the blood vessels and lymphatic vessels of the cardinal and broad ligaments. Nakanishi et al.^[8] believed that in cervical cancer patients, the larger the tumor diameter, especially when it exceeds 3cm, the higher the chance of ovarian tissue involvement. Wen Qiang et

al.^[9] found that the probability of ovarian metastasis in cervical minimal deviation adenocarcinoma reached 30%, significantly higher than other tissue cell types. Regarding the ovarian metastasis rates of cervical cancer patients in Stages IB, IA, and IIB, Landoni et al.^[10] reported rates of 0.83%, 1.14%, and 3.33%, respectively, fully indicating a positive correlation between tumor stage and ovarian metastasis rate. How do early patients metastasize? And the patient's cervix only showed HSIL (Grade II). Samaila et al.^[11] believed that there is a significant positive correlation between vascular invasion of cervical cancer cells and ovarian metastasis, speculating that cervical cancer cells can invade the ovary through blood transportation. The reason why only HSIL without invasive squamous cell carcinoma was detected in the cervical site in this case may be: (1) Limited by the amount of tissue sampled, invasive cancer was not observed; (2) The invasive cancer focus was very small and metastasized into the bloodstream at an early stage. The latest tumor metastasis theory suggests that, in individual cases, metastasis can occur when the maximum diameter of the primary lesion is less than 1mm. Moreover, HSIL lesions (positive for high-risk HPV E6/E7 mRNA) were detected in both the biopsy and total resection specimens at the cervical site. High-risk HPV E6/E7 mRNA was detected in the poorly differentiated squamous cell carcinoma of the ovary using RNAscope technology, along with the expression of squamous differentiation markers such as CK5/6, P40, and P63, supporting that the ovarian metastasis originated from primary cervical squamous cell carcinoma.

Treatment and Prognosis: Treatment should consider both the primary cervical cancer and the metastatic lesions. For cervical cancer patients who undergo initial surgical treatment and subsequently develop ovarian metastasis, radiotherapy and chemotherapy are mainly recommended, with surgery as an adjunct. This patient is receiving TC regimen chemotherapy combined with radiotherapy, following the treatment principles for advanced cervical cancer. Patients with ovarian metastasis from cervical cancer generally have a poor prognosis. A study in the United States showed that the 5-year survival rates of cervical cancer patients in China, Japan, and Europe were 79%, 72%, and 62%, respectively. During the same period, similar to the study by Mei Quan et al.^[1], Shimada et al.^[3] reported a 5-year survival rate of 39.44% for cervical cancer patients with ovarian metastasis, and Ma Shaokang et al.^[12] reported only 17.65%. It can be considered that ovarian metastasis is one of the factors for a poor prognosis in cervical cancer.

7. Conclusion

Squamous cell carcinoma, neuroendocrine carcinoma, and adenocarcinoma of the cervix have all been reported to metastasize to the ovary. Although many patients have a known history of cervical canal tumors before the appearance of ovarian tumors, it is rare for ovarian masses to occur before cervical cancer. The difficulty in recognizing the potentially invasive behavior of certain clinically occult or microinvasive tumors makes diagnosis more challenging. Zhu Sijing et al.^[13] found that in postmenopausal women, cervical atrophy and inward migration of the squamocolumnar junction make it difficult to expose the high-incidence area of cervical lesions, making cytological examination more difficult to obtain and limiting the amount of tissue sampled, thus restricting a clear diagnosis. For ovarian squamous cell carcinoma, it is crucial to determine whether it is primary or metastatic and to exclude primary cervical metastatic SCC, as this plays a key role in the subsequent treatment of patients. Recently, Tamura K et al.^[14] found that serum lymphocyte chemokine (XCL1) has a certain value in differentiating the tissue origin of ovarian squamous cell carcinoma. XCL1 is specifically overexpressed in primary ovarian squamous cell carcinoma and not expressed in metastatic ovarian squamous cell carcinoma. For postmenopausal patients with HR-HPV infection, active and effective intervention should be implemented to avoid disease progression and delayed treatment.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Mei Q, Li S, Ma D, 2010, Research Progress on Ovarian Metastasis of Cervical Cancer. *Chinese Journal of Practical Gynecology and Obstetrics*, 26(3): 238–240.
- [2] Zhang S, Ni X, Lin Z, 2023, Expert Consensus on Indications for Ovarian Preservation in Cervical Adenocarcinoma Surgery (2023 Edition). *Chinese Journal of Practical Gynecology and Obstetrics*, 39(2): 185–188.
- [3] Shimada M, Kigawa J, Nishimura R, et al., 2006, Ovarian Metastasis in Carcinoma of the Uterine Cervix. *Gynecologic Oncology*, 101(2): 234–237.
- [4] Yamamoto R, Okamoto K, Yukiharu T, et al., 2001, A Study of Risk Factors for Ovarian Metastases in Stage Ib–IIb Cervical Carcinoma and Analysis of Ovarian Function After Transposition. *Gynecologic Oncology*, 82(2): 312–316.
- [5] Ivanov S, Zervoudis S, 2003, Metastatic Cancer in Transposed Ovaries After Radical Wertheim-Meigs Hysterectomy for Stage IB and IIA Cervical Cancer. *Akush Ginekol (Sofia)*, 42(5): 22–24.
- [6] Sanjuan A, Martinez Roman S, Martinez-Zamora MA, et al., 2007, Bilateral Ovarian Metastasis on Transposed Ovaries from Cervical Carcinoma. *International Journal of Gynecology and Obstetrics*, 99(1): 64–65.
- [7] Piketty M, Barranger E, Najat M, et al., 2005, Ovarian Recurrence After Radical Trachelectomy for Adenocarcinoma of the Cervix. *American Journal of Obstetrics and Gynecology*, 193(4): 1382–1383.
- [8] Nakanishi T, Wakai K, Ishikawa H, et al., 2001, A Comparison of Ovarian Metastasis Between Squamous Cell Carcinoma and Adenocarcinoma of the Uterine Cervix. *Gynecologic Oncology*, 82(3): 504–509.
- [9] Wen Q, Shao Z, Fang S, 2015, Clinical Analysis of Ovarian Metastasis in 321 Cases of Cervical Adenocarcinoma. *Progress in Modern Obstetrics and Gynecology*, 24(7): 501–503.
- [10] Landoni F, Zanagnolo V, Lovato-Diaz L, et al., 2007, Ovarian Metastases in Early-Stage Cervical Cancer (IA2–IIA): A Multicenter Retrospective Study of 1965 Patients (A Cooperative Task Force Study). *International Journal of Gynecological Cancer*, 17(3): 623–628.
- [11] Samaila M, Adesiyun AG, Oluwole P, 2008, Metastatic Ovarian Squamous Cell Carcinoma. *Singapore Medical Journal*, 49(5): E139–E141.
- [12] Ma S, Sun J, 1996, Analysis of 17 Cases of Ovarian Metastasis in Cervical Cancer. *Chinese Journal of Obstetrics and Gynecology*, 31(5): 305.
- [13] Zhu S, Li C, 2022, Characteristics, Diagnosis, and Treatment of Cervical Squamous Intraepithelial Lesions in Postmenopausal Women: Research Progress. *Journal of Geriatric Medicine Research*, 3(2): 64–65.
- [14] Tamura K, Yamamoto M, Nakayama T, et al., 2020, XCL1 Expression Correlates with CD8-Positive T Cells Infiltration and PD-L1 Expression in Squamous Cell Carcinoma Arising from Mature Cystic Teratoma of the Ovary. *Oncogene*, 39: 3541–3554.

Publisher's note

Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Evaluation of the Initiation Effect of QLB Combined with General Anesthesia in the “Painless Mode” during Gynecological Laparoscopic Surgery

Yu Jiao*

Taizhou Hospital of Traditional Chinese Medicine, Taizhou 225300, Jiangsu, China

**Author to whom correspondence should be addressed.*

Copyright: © 2026 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To evaluate the painless mechanism of the quadratus lumborum block at the level of the arcuate ligament (denoted as QLB) combined with general anesthesia during gynecological laparoscopic surgery. *Methods:* Forty patients undergoing gynecological laparoscopic surgery were selected and evenly divided by ball-drawing. The combined group received QLB combined with general anesthesia, while the reference group received only general anesthesia. The initiation effects of the painless mode were compared between the two groups. *Results:* The analgesic indicators in the combined group were significantly superior. Except for before 10 minutes of anesthesia (i.e., T₀), the hemodynamics in the combined group were more favorable. At different postoperative time points, the pain scores of the combined group were lower in both resting and active states, with $P < 0.05$ between the groups. *Conclusion:* QLB combined with general anesthesia can significantly improve the analgesic effect, stabilize hemodynamics, alleviate postoperative pain, and enhance anesthesia safety in patients undergoing gynecological laparoscopic surgery.

Keywords: Gynecological laparoscopy; QLB; General anesthesia; Painless mode; Initiation effect

Online publication: May 31, 2026

1. Introduction

Gynecological diseases encompass a wide variety of conditions, many of which require surgical treatment. Laparoscopic surgery is a novel surgical approach for gynecological diseases, offering distinct advantages in terms of minimally invasive procedures, painless procedures throughout the surgery, and shortened postoperative recovery time^[1]. However, laparoscopic surgery can affect the patient's respiratory and circulatory systems, leading to hemodynamic fluctuations. Therefore, it is crucial to select an appropriate anesthesia method. QLB demonstrates high feasibility for anesthesia during laparoscopic surgery, with a wide

range of blockage, a high success rate of anesthesia, and the ability to alleviate visceral pain and discomfort. Moreover, the precision of this anesthesia method is high when performed under ultrasound guidance, minimizing the specific dosage of anesthetic drugs and thus offering favorable safety benefits. When combined with general anesthesia, it can enhance the analgesic effect through a synergistic mechanism, thereby fully leveraging the advantages of minimally invasive surgery ^[2]. Combined anesthesia can reduce the irritation of laparoscopic surgery on the patient's body under the premise of achieving a "painless mode," thereby improving surgical outcomes. It can also alleviate postoperative pain, enabling patients to navigate the perioperative period. Based on this, this study enrolled 40 patients undergoing gynecological laparoscopic surgery to analyze the implementation effects of QLB combined with general anesthesia.

2. Materials and methods

2.1. General information

Forty patients who underwent gynecological laparoscopic surgery between October 2024 and April 2025 were selected and evenly divided by ball-drawing. The specific information for each group is as follows (**Table 1**).

Table 1. Comparison of information content between groups [mean \pm SD, n/%]

Group	Number of Cases	Age (years old)	ASA Grade		Operation Time(min)
			Grade I	Grade II	
Combined Group	20	44.65 \pm 4.84	11	9	133.56 \pm 17.95
Reference Group	20	45.01 \pm 4.70	12	8	132.09 \pm 18.40
<i>t</i> / χ^2	-	0.239	0.102		0.256
P	-	0.813	0.749		0.800

2.2. Methods

Patients were required to fast for more than 6 hours and abstain from drinking for more than 4 hours before surgery, and their body temperature, blood pressure, and other vital signs were measured. In the combined group, QLB anesthesia was administered. The patients were placed in a prone position, and under precise ultrasound guidance, the quadratus lumborum muscle at the level of the arcuate ligament (bilateral) was marked. At the first lumbar vertebra on the dorsal spine, specifically between the diaphragm at the apex of the transverse process and the adjacent quadratus lumborum muscle, and at the lower edge of the twelfth rib (bilateral), ropivacaine was injected, with a dose of 20 mL (0.375%) on each side. The reference group did not receive QLB anesthesia. The anesthesia induction methods were consistent between the two groups, involving intravenous administration of 0.02 mg/kg midazolam, 1.5 to 2.0 mg/kg propofol, 0.5 μ g/kg sufentanil, and 0.2 mg/kg cisatracurium. Subsequently, tracheal intubation was performed, and anesthesia was maintained by pumping propofol (at a dose of 4 to 12 mg/kg per hour) + remifentanyl (at a dose of 0.05 to 0.20 μ g/kg per hour). Cisatracurium was administered intermittently to maintain muscle relaxation, with the bispectral index (BIS) maintained between 40 and 60, and fluctuations in blood pressure and heart rate were kept within 30% of the baseline values. The ventilator's tidal volume (VT) parameter was set at 500 ml, maintaining the end-tidal carbon dioxide partial pressure (PETCO₂) between 35 and 45 mmHg, with an inspiratory-to-expiratory ratio of 1:2 and a respiratory rate of 8 to 12 breaths per minute. After surgery, a subcutaneous analgesic pump was implanted in the patient's left upper limb, mixing sufentanil (100 μ g) and

lidocaine (10 mL, 2%) with physiological saline to prepare a 100 mL solution. Each injection was 2 ml at a rate of 2 ml/h, with a lockout time of 15 minutes for the analgesic pump.

2.3. Observation indicators

- (1) Analgesic indicators: The consumption of remifentanil and propofol was recorded.
- (2) Hemodynamics: The mean arterial pressure (MAP) and heart rate (HR) were measured at T0 (before anesthesia), T1 (1 minute after tracheal intubation), T2 (5 minutes after pneumoperitoneum establishment), and T3 (at the end of surgery).
- (3) Pain scores: From 2 to 48 hours postoperatively, a visual analog scale (VAS) ranging from 0 to 10 points was used to assess pain levels under resting and active conditions, with higher scores indicating greater pain intensity.

2.4. Statistical analysis

Data were processed using SPSS 28.0 software. Continuous variables were compared using t-tests, and categorical variables were compared using chi-square tests. Statistical significance was considered when the *P*-value was less than 0.05.

3. Results

3.1. Comparison of analgesic indicators between groups

The analgesic indicators in the combined group were significantly superior, with $P < 0.05$ between the groups (Table 2).

Table 2. Comparison of analgesic indicators between groups [mean \pm SD, χ^2]

Group	Number of Cases	Remifentanil dosage (mg)	Propofol dosage (mg)	Number of analgesic pump presses within 48h postoperatively	Rescue analgesia rate (%)
Combination Group	20	0.75 \pm 0.23	336.85 \pm 19.74	1.02 \pm 0.39	1 (5.0)
Reference Group	20	1.21 \pm 0.35	401.56 \pm 20.83	2.05 \pm 0.47	6 (30.0)
<i>t</i> / χ^2 value	-	4.912	10.084	7.542	4.329
<i>P</i> value	-	<0.001	<0.001	<0.001	0.038

3.2. Comparison of hemodynamics among groups

Except for T0, the hemodynamic parameters in the combined group were consistently lower at other time points, with a statistically significant difference between groups ($P < 0.05$) (Table 3).

Table 3. Comparison of hemodynamics among groups [mean \pm SD]

Group	Number of Cases	MAP (mmHg)				HR (beats/min)			
		T0	T1	T2	T3	T0	T1	T2	T3
Combination Group	20	75.68 \pm 5.62	77.86 \pm 6.81	79.86 \pm 5.28	78.44 \pm 4.67	84.19 \pm 6.25	84.12 \pm 5.61	83.59 \pm 4.15	77.98 \pm 4.13
Reference Group	20	75.71 \pm 5.53	82.52 \pm 6.45	84.06 \pm 5.34	82.02 \pm 4.53	81.24 \pm 6.22	88.04 \pm 5.63	87.18 \pm 4.50	81.02 \pm 4.10

Group	Number of Cases	MAP (mmHg)				HR (beats/min)			
		T0	T1	T2	T3	T0	T1	T2	T3
t	-	0.017	2.222	2.501	2.461	1.496	2.206	2.623	2.336
P	-	0.987	0.032	0.017	0.019	0.143	0.034	0.012	0.025

3.3. Comparison of pain scores among groups

At different postoperative time points, under both resting and active conditions, the combined group exhibited lower pain scores, with a statistically significant difference between groups ($P < 0.05$) (Table 4).

Table 4. Comparison of pain scores among groups [mean \pm SD, points]

Group	Number of Cases	Rest				Activity			
		Post-op 2h	Post-op 12h	Post-op 24h	Post-op 48h	Post-op 2h	Post-op 12h	Post-op 24h	Post-op 48h
Combination Group	20	2.35 \pm 0.42	2.04 \pm 0.34	1.55 \pm 0.41	0.44 \pm 0.15	2.89 \pm 0.56	2.35 \pm 0.45	2.05 \pm 0.47	1.15 \pm 0.36
Reference Group	20	4.07 \pm 0.44	3.49 \pm 0.38	3.36 \pm 0.47	1.13 \pm 0.21	5.91 \pm 0.63	5.18 \pm 0.49	4.41 \pm 0.52	1.82 \pm 0.42
t	-	12.646	12.717	12.978	11.957	16.023	19.024	15.058	5.417
P	-	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

4. Discussion

Gynecological laparoscopic surgery is a frequently performed surgical procedure that involves making a small incision of 0.5 to 1.5 cm in the abdomen to insert laparoscopic instruments for targeted surgical treatment^[3,4]. The success of this procedure is closely related to the anesthetic effect, necessitating a rational selection of anesthesia protocols to ensure painlessness while enhancing the safety of anesthetic drug dosages, thereby reducing postoperative adverse reactions.

General anesthesia is a commonly used anesthetic method for gynecological laparoscopic surgery, capable of inhibiting the hypothalamic projection system and the limbic system of the cerebral cortex, providing effective analgesia. However, general anesthesia cannot block the central nervous conduction caused by traumatic procedures, lacking a significant inhibitory mechanism on the neural conduction process. This continues to interfere with the patient's sympathetic-adrenal medullary system, increasing the overall release of catecholamines, affecting the patient's circulatory system, and thereby reducing the anesthetic effect^[5].

Quadratus lumborum block (QLB) is a novel anesthetic block technique that can be combined with general anesthesia, offering high feasibility for abdominal surgery anesthesia. QLB reduces the dosage of anesthetic drugs during general anesthesia and alleviates postoperative pain, leading to faster postoperative recovery. Performing QLB under ultrasound guidance allows the anesthetic to directly reach the anterior aspect of the quadratus lumborum muscle in the lateral region of the arcuate ligament. This enables efficient action on the lower thoracic paravertebral space, thereby achieving excellent intraoperative and postoperative analgesic effects. This anesthetic technique prevents the continuous transmission of stressful stimuli to the patient's central nervous system, enhancing anesthetic safety. Moreover, QLB combined with general

anesthesia provides a wide range of block planes, is easy to perform, and has a long duration of anesthetic action, ensuring the smooth progress of laparoscopic surgery.

The results showed that the analgesic indicators in the combined group were significantly superior, with a statistically significant difference between groups ($P < 0.05$). The reason for this is that QLB, combined with general anesthesia, can rapidly exert an anesthetic effect and provide extensive blockage, thereby enhancing the effectiveness of general anesthetic drugs and reducing their maintenance dosage. Simultaneously, it prevents the continuous resistance of the cerebral cortex to general anesthetic drugs, resulting in a lower rate of rescue analgesia in patients. QLB combined with general anesthesia allows local anesthetics to act on regions such as the paravertebral space, regulating the neural innervation function of the T7-L1 segments and alleviating incisional pain in the abdominal wall muscles. It also acts on the sympathetic nerves of the T5-6 segments, providing a strong blocking effect on the sympathetic chain, thereby reducing visceral traction pain during surgery. Combined anesthesia blocks the transmission of nociceptive stimuli to the cerebral cortex or spinal nerves, preventing central sensitization and reducing the required dosage of general anesthetic drugs such as propofol during surgery. QLB has a preemptive analgesic effect, preventing significant fluctuations in vital signs during surgery, thus maintaining BIS values without the need for additional propofol and reducing its dosage [6]. During QLB anesthesia, ropivacaine is selected as the anesthetic drug, with a blocking effect lasting approximately 24 hours, providing a long-lasting blocking effect and strong coverage during the acute postoperative pain phase, reducing the frequency of analgesic pump use. Combined anesthesia prevents the continuous transmission of peripheral pain signals, thereby downregulating the pain memory effect and stably exerting the analgesic pump's effect without the need for frequent pressing.

Except for T0, the hemodynamic parameters in the combined group were consistently lower at other time points, with a statistically significant difference between groups ($P < 0.05$). At the T1 time point, tracheal intubation produces significant traumatic stimulation to the body, continuously activating the sympathetic nerves in the tracheal region and increasing vagal nerve excitability, leading to an elevation in MAP levels and an accelerated heart rate. The blocking effect of QLB on the thoracolumbar segments reduces the body's tissue pain sensitivity, thereby decreasing the stress response to tracheal intubation. Administering sufentanil before tracheal intubation exerts a synergistic effect, alleviating the intubation response and, in combination with QLB anesthesia, stabilizing the patient's intraoperative hemodynamics. Moreover, maintaining anesthesia with propofol reduces the cardiovascular response caused by tracheal intubation, dilating blood vessels and stabilizing blood pressure values. At the T2 time point, creating a pneumoperitoneum produces strong stimulation to tissues such as the uterus or peritoneum, exciting the sympathetic nerves and causing visceral pain. QLB, combined with general anesthesia, acts on the sympathetic chain, relieving visceral traction pain and reducing the adverse effects of pneumoperitoneum on peritoneal tissues. Pneumoperitoneum increases the patient's intra-abdominal pressure, activating mechanical receptors in the abdominal wall region. QLB combined with general anesthesia inhibits abdominal wall nerve sensitivity, thereby reducing abdominal wall pressure and preventing excessive hemodynamic fluctuations. Furthermore, pneumoperitoneum elevates hormone levels such as norepinephrine in the body. Combined anesthesia inhibits catecholamine release, preventing the continuous transmission of nociceptive signals, thereby stabilizing hormone levels in the body and avoiding significant hemodynamic fluctuations. At the T3 time point, ropivacaine continues to exert its analgesic mechanism, allowing the patient to awaken smoothly.

Additionally, the controllable dosage of anesthetic drugs in combined anesthesia reduces drug accumulation, preventing rebound tachycardia and other conditions.

The pain scores at different postoperative time points in the combined group were consistently lower, with a statistically significant difference between groups ($P < 0.05$). The reason for this is that ultrasound-guided anesthesia allows the anesthetic to precisely reach specific regions, fully exerting a paravertebral-like blocking effect and achieving excellent analgesic results. Moreover, the anesthetic can slowly and continuously exert its analgesic effect, reducing postoperative pain. Combined anesthesia employs QLB, general anesthesia, and an analgesic pump, providing high synergistic effects, prolonging postoperative analgesia time, and doubly blocking the peripheral and central nervous systems, thereby exhibiting strong analgesic effectiveness.

5. Conclusion

In conclusion, adopting QLB combined with general anesthesia during gynecological laparoscopic surgery yields excellent results, reducing the dosage of anesthetic drugs, decreasing the frequency of analgesic pump presses, stabilizing perioperative hemodynamics, and alleviating postoperative pain, offering high anesthetic safety benefits. However, before anesthesia, it is essential to assess the patient's individual circumstances, such as medication history and surgical history, to exclude contraindications to combined anesthesia. Simultaneously, educate patients on anesthesia cooperation methods to ensure they have a high level of understanding of anesthetic knowledge and can efficiently cooperate with the anesthesia process as instructed by the doctor. To enhance anesthetic effectiveness, closely monitor the patient's vital signs during surgery, promptly identify adverse anesthetic events, and provide targeted treatment to prevent severe adverse reactions.

Disclosure statement

The author declares no conflict of interest.

References

- [1] Guo X, Wang D, Hong H, et al., 2025, The Effect of Ultrasound-Guided Anterior Quadratus Lumborum Block at the Arcuate Ligament Level on Postoperative Recovery Quality in Patients Undergoing Laparoscopic Surgery. *Chinese Journal of Anesthesiology*, 45(3): 325–328.
- [2] Wang L, Qiu S, Gao J, et al., 2022, Optimization Strategy for Anesthesia in Laparoscopic Gynecological Surgery: Anterior Quadratus Lumborum Block at the Arcuate Ligament Level Combined with General Anesthesia. *Chinese Journal of Anesthesiology*, 42(5): 581–585.
- [3] Zhou G, Yang X, Ren Y, et al., 2024, The Effect of Quadratus Lumborum Block at the Arcuate Ligament Level on Postoperative Analgesia After Total Laparoscopic Hysterectomy in Gynecology. *Journal of Clinical Anesthesiology*, 40(4): 389–392.
- [4] Zhang X, Ma Y, Yu X, et al., 2025, The Anesthetic Effect of Quadratus Lumborum Block at the Arcuate Ligament Level Combined with General Anesthesia in Patients Undergoing Total Laparoscopic Hysterectomy. *Zhejiang Journal of Traumatic Surgery*, 30(4): 765–768.

- [5] Huang Y, Chen G, Zhou W, 2025, Analgesic Effect of Quadratus Lumborum Block at the Arcuate Ligament Level During Total Laparoscopic Hysterectomy. *Journal of Rare and Uncommon Diseases*, 32(2): 154–156.
- [6] Yang J, Ji K, He K, et al., 2025, Application of Quadratus Lumborum Block at the Arcuate Ligament Level in Laparoscopic Hepatectomy. *China Modern Medicine*, 32(9): 90–95.

Publisher's note

Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Research on Establishing a Prediction Model for Pregnancy Outcomes Based on Retrospective Analysis of 1,131 Cases of Frozen-Thawed Single Embryo Transfer

Lijun Lou, Zhengfang Zhang

Affiliated Dongyang Hospital of Wenzhou Medical University, Dongyang 322100, Zhejiang, China

**Author to whom correspondence should be addressed.*

Copyright: © 2026 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* This study is based on preliminary clinical data from a public welfare project funded by the Jinhua Science and Technology Bureau. A total of 1,131 cases of frozen-thawed single embryo transfer were retrospectively enrolled to investigate clinical indicators such as patient age, embryo developmental stage, and endometrial type. Key factors influencing pregnancy outcomes were identified, and a predictive model was constructed. This provides a prerequisite for analyzing the correlation between the immune functional status of Treg lymphocytes and pregnancy outcomes following embryo transfer, and also serves as a reference for clinical immune assessment and individualized embryo transfer strategies in assisted reproduction. This research intends to set up a pregnancy outcome prediction model relying on 1131 frozen-thawed single embryo transfer instances. It takes into account elements like patients age, d3 embryo transfer, d4 fused embryo, d5 or d6 blastocyst, endometrial thickness and type, etc. *Methods:* Via systematic data gathering, which encompasses fundamental patient details, data associated with embryo development, and endometrial data, and by utilizing statistical instruments like SPSS and R software for univariate analysis and multivariate logistic regression analysis, independent factors influencing pregnancy results were screened. Based on this situation, a prediction model for pregnancy outcomes was built by using a nomogram. *Results:* Validated through ROC curves and AUC values, the model showed good discriminatory ability and calibration, efficiently forecasting the pregnancy result of single embryo transfer and offering a significant reference for clinical decision-making. *Conclusion:* It is feasible to set up a pregnancy outcome prediction model for single embryo transfer, and it has high precision.

Keywords: Single embryo transfer; Pregnancy outcome; Prediction model; Endometrial thickness; Embryo development

Online publication: May 31, 2026

1. Introduction

1.1. Research

Background With the continuous advancement of assisted reproductive technology, Single Embryo Transfer (SET) has emerged as one of the primary strategies for optimizing pregnancy outcomes. Its significance in enhancing pregnancy rates while substantially reducing the risk of multiple pregnancies has become increasingly evident ^[1]. Recent outcomes from selective SET practices during Frozen Embryo Transfer (FET) cycles indicate that this strategy can achieve high clinical pregnancy and implantation rates in specific populations, particularly for women under 33 years of age, where Day 5 Blastocyst Transfer (SBT-D5) demonstrates superior advantages compared to other protocols ^[2]. Furthermore, research on nomogram-based predictive models for clinical pregnancy in single-blastocyst transfer during thaw cycles underscores the importance of precise prediction. This study selects independent influencing factors through multivariate regression analysis, providing a scientific basis for formulating individualized treatment plans ^[3]. However, the dynamic compatibility between endometrial receptivity and embryo quality remains a primary factor influencing pregnancy outcomes. The complexity of this compatibility significantly increases prediction challenges, especially across different age groups and embryo types ^[4,5]. Therefore, constructing a pregnancy outcome prediction model that integrates multiple key factors not only facilitates the optimization of embryo transfer protocols but also provides clinicians with more accurate decision-making references. Although SET has demonstrated notable success in assisted reproductive technology, current research on pregnancy outcome prediction still faces significant limitations. Most studies focus on single-factor or limited-variable analyses, with insufficient in-depth exploration of the synergistic effects of multiple factors ^[6,7]. For example, although existing studies have shown that endometrial thickness and embryo type play major roles in pregnancy outcomes, such research often fails to fully account for the interplay of multiple factors, including patient age, embryo development rate, and endometrial type ^[8]. Furthermore, the discrimination and calibration of existing predictive models still require improvement; in particular, the applicability of traditional statistical methods is significantly limited when dealing with non-normally distributed data ^[7]. Thus, constructing a predictive model that comprehensively incorporates factors such as patient age, Day 3 embryo transfer status, Day 5/6 blastocyst development, endometrial thickness, and type plays a crucial role in enhancing the accuracy of pregnancy outcome predictions and their clinical relevance.

1.2. Research objectives

This study aims to construct a pregnancy outcome prediction model based on 1,131 SET cases, incorporating factors such as patient age, Day 3 embryo transfer status, Day 5/6 blastocyst development, endometrial thickness, and type. Through systematic analysis of these key factors, the study seeks to determine their independent and interactive effects on pregnancy outcomes while developing visual prediction tools like nomogram models to assist clinicians in formulating personalized embryo transfer protocols ^[9]. This model is expected to provide scientific support for optimizing embryo transfer timing and selecting optimal embryo types, thereby improving clinical pregnancy and live birth rates in SET cycles. Furthermore, the model's development will offer new insights and methodologies for future clinical research in assisted reproductive technology, promoting further refinement and advancement of pregnancy outcome prediction models.

2. Materials and methods

2.1. Study population

2.1.1. Case source

The data for this study were obtained from the reproductive medicine center at Dongyang People's Hospital, covering thaw cycle SET cases and patient databases for assisted reproductive technology treatments from January 2021 to December 2025. Embryo transfer cycles involving SET during the thaw phase, derived from embryos fertilized via in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI), were included in this study. Case selection adhered to criteria of data completeness and representativeness to ensure the included cases reflect the current real-world practice of SET ^[2]. After screening through the database, information from 1,131 eligible patients was extracted to form the core dataset for this study.

2.1.2. Inclusion and exclusion criteria

To ensure the reliability of the study population and comparability of results, strict inclusion and exclusion criteria were established. The inclusion criteria were as follows: women aged 21 to 45 years old; undergoing thaw cycle SET; embryo developmental stages including Day 3 embryo transfer, Day 4 fused embryo, and Day 5/6 blastocyst transfer; and possession of complete clinical data, such as embryo quality assessment, endometrial thickness, and type. The exclusion criteria were as follows: history of uterine malformations, endometriosis, or adenomyosis affecting pregnancy outcomes; chromosomal abnormalities in either partner; and patients who had undergone more than three assisted reproductive treatments (i.e., beyond the third transfer cycle). After rigorous screening based on these criteria, 1,131 eligible cases were ultimately selected for analysis ^[2].

2.2. Data collection

2.2.1. Patient baseline information

Patient baseline information constitutes a primary component of this study, encompassing female age, duration of infertility, baseline hormonal status (e.g., FSH, LH, and AMH), endometrial preparation method for the transfer cycle (including natural cycle, hormone replacement cycle, and low-dose stimulation cycle), and past pregnancy history. This information was obtained by reviewing electronic medical records and cross-verified by two independent researchers to ensure data accuracy. Age was recorded as a continuous variable and analyzed in groups based on interquartile ranges. The definition of duration of infertility is the time interval from the first attempt to conceive to the initiation of assisted reproductive technology treatment, and it should be recorded as a continuous variable. Additionally, past pregnancy history, including the number of natural pregnancies, miscarriages, and history of ectopic pregnancy, was obtained through detailed patient interviews and corroborated with medical records.

2.2.2. Embryo-related data

Embryo-related data were collected in strict accordance with international standardized protocols. Day 3 embryo quality was assessed using a morphological scoring system, focusing on key indicators such as the number of blastomeres, uniformity, and fragmentation percentage. For Day 4 fused embryos, further documentation of fusion status was required, including partial fusion, complete fusion, and early blastocyst formation. These data were recorded by experienced embryologists based on microscopic observation and then verified against the data stored in the laboratory information system. For Day 5/6 blastocysts, the

Gardner scoring system was employed to grade expansion status, inner cell mass quality, and trophectoderm quality. All embryo-related data were collected before transfer to ensure timeliness and accuracy.

Additionally, parameters of the embryo culture environment were included in data collection, such as incubator temperature ($37.0 \pm 0.1^{\circ}\text{C}$), CO_2 concentration ($5.0 \pm 0.1\%$), and humidity (saturated humidity). All culture conditions strictly adhered to the ISO 15189 laboratory quality management system standards to ensure standardization of the embryo culture process. For frozen-thawed embryos, vitrification and rapid thawing methods were used, with documentation of post-thaw survival status (fully viable, partially viable, or non-viable) and morphological changes. The number of embryos transferred was determined based on clinical guidelines and patient preferences, recorded as a single transfer, with annotation of the specific developmental stage of the transferred embryo (Day 3 cleavage-stage embryo, Day 4 fused embryo, or Day 5/6 blastocyst). All embryo-related data were entered into the laboratory information management system (LIMS) in a structured format, with data entry permissions and automatic validation rules established to prevent manual entry errors. Monthly internal cross-comparisons of embryo morphological scores were conducted to ensure consistency among embryologists, and annual participation in at least one national-level embryo morphological quality assessment program validated the accuracy and reliability of the scoring standards.

2.2.3. Endometrial data

Measurements of endometrial thickness and type were performed via transvaginal ultrasound on the day of embryo transfer, the day of progesterone conversion, and the day before conversion. Endometrial thickness was defined as the maximum vertical distance between the anterior and posterior uterine wall muscular layers and the endometrial interface, with results recorded in millimeters. Endometrial types based on ultrasonographic echogenicity characteristics can be classified into three types: type A (triple-line sign), type B (homogeneous moderate echogenicity), and type C (hyperechogenicity) ^[4]. All measurements were independently performed by two experienced ultrasonographers, with the final result taken as the average of their measurements. Additionally, endometrial thickness measurements were timed on the day of luteal conversion or the day before transfer to minimize measurement errors ^[4].

2.3. Research methods

2.3.1. Statistical analysis methods

This study used SPSS 20.0 and R software (version 3.5.0) to perform statistical analyses. First, potential factors associated with pregnancy outcomes were selected based on univariate analysis, including patient age, duration of infertility, embryo development stage, endometrial thickness and type. Count data were presented as frequencies (percentages) and compared using the chi-square test or Fisher's exact test. For measurement data that were not normally distributed, results were expressed as median (interquartile range), and analyzed using the Mann-Whitney U test or the Kruskal-Wallis H test ^[9]. Variables that were statistically significant in the univariate analysis were then incorporated into a multivariate logistic regression model, and a stepwise backward LR method was applied to select the variables ultimately retained in the model. The discriminatory ability of the model was assessed using the receiver operating characteristic curve (ROC) and the area under the curve (AUC), while calibration was evaluated using the Hosmer-Lemeshow test.

2.3.2. Model construction methods

Based on the results of multivariate regression analysis, this study constructed a nomogram-based pregnancy outcome prediction tool. The nomogram model converts regression coefficients of independent factors into intuitive scoring scales, enabling clinicians to estimate pregnancy probabilities based on patient-specific conditions. The specific steps were as follows: first, determine the contribution weight of each factor to pregnancy outcomes and map it to the corresponding scoring axis; next, sum the scores of all factors to obtain a total score, then refer to the predicted pregnancy probability scale. This model was established using the rms package in R software and evaluated for stability and reliability through internal validation methods such as Bootstrap resampling^[10]. The final nomogram model demonstrates high predictive accuracy and excellent clinical practical value, providing an important reference for personalized treatment decisions in SET patients.

3. Results

3.1. Patient baseline characteristics

This study included a total of 1,131 cases of single-embryo transfers. The age range of patients was from 23 to 45 years, with a median age of 32 years old (interquartile range: 28–37 years old). The primary causes of infertility were tubal factors (45.3%), male factors (27.8%), endometriosis (15.4%), and various other causes (11.5%). Based on the duration of infertility, most patients had infertility lasting between 2 and 8 years, with a median duration of 4 years (interquartile range: 2–6 years). Additionally, the distribution of pregnancy history among patients exhibited a skewed pattern, with 63.7% of patients having no prior pregnancies and 36.3% having had one or more pregnancies. Analysis of patient baseline characteristics revealed significant differences in age groups and causes of infertility across the overall sample, laying the groundwork for further investigation into the impact of these factors on pregnancy outcomes^[3].

3.2. Embryo development and endometrial conditions

In terms of embryo development, the formation rate of fused embryos on Day 4 (D4) after Day 3 (D3) embryo transfer was 78.3%, while the formation rate of blastocysts on Day 5 (D5) or Day 6 (D6) was 65.7%. The distribution of embryo developmental stages indicated that D5 blastocysts accounted for the highest proportion (37.2%), followed by D6 blastocysts (28.5%) and D4 fused embryos (21.4%). Regarding endometrial data, on the day of embryo transfer, the mean endometrial thickness was 9.8 mm (interquartile range: 8.5–11.2 mm), with 84.6% of patients having an endometrial thickness greater than 8 mm. The endometrial types were primarily Type A (56.3%), Type B (32.1%), and Type C (11.6%), with Type A endometrium being significantly more prevalent than the other types. The findings suggest that embryo developmental stages and endometrial characteristics in this study exhibited diverse distribution patterns, and these variables may play a crucial role in pregnancy outcomes^[4,5].

3.3. Univariate analysis results

Univariate analysis revealed significant correlations between patient age, embryo developmental stage, endometrial thickness and type, and pregnancy outcomes. Specifically, clinical pregnancy rates declined with increasing age, with patients aged 35 and above having significantly lower pregnancy rates than those under 35 ($p < 0.001$). In terms of embryo developmental stages, D5 blastocyst transfers yielded the highest

clinical pregnancy rate (64.63%), followed by D6 blastocysts (45.7%) and D4 fused embryos (38.6%), with statistically significant differences between groups ($p < 0.001$). Additionally, patients with endometrial thickness greater than 9 mm had significantly higher pregnancy rates than those with thickness less than 9 mm ($p = 0.002$); Type A endometrium also had significantly higher pregnancy rates than Types B and C ($p < 0.001$). These initial findings provide a basis for subsequent multivariate regression analysis.

In single-embryo transfer cycles, after controlling for age as a confounding factor, the impact of D3 cleavage-stage embryo scoring and blastocyst evaluation on pregnancy outcomes was as follows:

- (1) Impact of D3 Cleavage-Stage Embryo Scoring
 - (a) Embryos were evaluated based on cell number, fragmentation rate, and symmetry according to ISCE criteria:
 - (b) Implantation: Embryos with 8 cells and a fragmentation rate $<10\%$ had a significantly higher implantation rate (48.2%) than those with 6 cells or a fragmentation rate $>20\%$ (29.5%, OR = 2.31, 95%CI 1.52-3.50).
 - (c) Miscarriage: High-quality D3 cleavage-stage embryos (8-10 cells, fragmentation rate $<10\%$) had a 42% lower miscarriage rate (15.3%) compared to low-scoring embryos (26.4%, $P < 0.05$).
 - (d) Key Conclusion: D3 cleavage-stage embryos with 8-10 cells, a fragmentation rate $<10\%$, and good symmetry had significantly better pregnancy outcomes than low-scoring embryos.
- (2) Impact of Blastocyst Evaluation. Blastocysts were evaluated based on expansion status, inner cell mass quality, and trophectoderm morphology using the Gardner scoring system:
 - (a) Clinical Pregnancy: High-quality blastocysts (AA/AB grade) had a clinical pregnancy rate of 52.3%, significantly higher than non-high-quality blastocysts (BC/CB grade, 31.7%, $P < 0.001$).
 - (b) Biochemical Pregnancy: High-quality blastocysts had a 43% lower biochemical pregnancy rate (64.3%) compared to non-high-quality blastocysts (21.3%, $P < 0.01$).
 - (c) Live Birth Probability: AA-grade blastocysts had a live birth probability of 58.3% under favorable endometrial receptivity conditions, significantly higher than BC-grade blastocysts (OR=2.15, 95%CI 1.33-3.48).
- (3) Comparative Analysis of Embryo Types (after controlling for age):
 - (a) Single blastocyst transfers had a clinical pregnancy rate and implantation rate of 64.53%, significantly higher than those of D3 cleavage-stage embryos (48.26%), with an absolute difference of approximately 16.5%.
 - (b) High-quality blastocysts (AA/AB grade) had better pregnancy outcomes than high-quality D3 cleavage-stage embryos; however, D3 cleavage-stage embryos meeting the criteria of 8 cells and a fragmentation rate $< 10\%$ still achieved a relatively good implantation rate of 48.2%.

3.4. Multivariate regression analysis results

Multivariate logistic regression analysis further identified independent factors affecting clinical pregnancy rates, including patient age, embryo developmental stage, endometrial thickness, and type. For each additional year of patient age, the odds ratio (OR) for clinical pregnancy decreased to 0.92 (95% confidence interval: 0.88–0.96, $p < 0.001$). In terms of embryo developmental stages, compared to D4 fused embryos, D5 blastocysts had an OR of 1.56 for clinical pregnancy (95%CI: 1.23-1.98, $p < 0.001$), while D6 blastocysts had an OR of 1.32 (95%CI: 1.05–1.66, $p = 0.017$). For each additional millimeter of endometrial thickness,

the OR for clinical pregnancy increased by 1.15 (95%CI: 1.08–1.23, $p < 0.001$). Additionally, compared to Type C endometrium, Type A endometrium had an OR of 1.84 for clinical pregnancy (95%CI: 1.36–2.48, $p < 0.001$). These regression coefficients provide quantitative support for constructing a clinical pregnancy prediction model and reveal the relative importance of each factor on pregnancy outcomes.

3.5. Prediction model construction and validation

3.5.1. Model construction

Based on the results of multivariate regression analysis, this study utilized a nomogram model to establish a pregnancy outcome prediction model. This model considered patient age, developmental stages of D3 embryos and D5 or D6 blastocysts, endometrial thickness, and type as primary predictive variables. Each variable was assigned a corresponding score based on its regression coefficient, and individualized pregnancy probabilities were calculated based on the total score. For example, a 30-year-old patient transferring a D5 blastocyst with an endometrial thickness of 10 mm and Type A endometrium would have a predicted pregnancy probability of approximately 60%. The advantage of the nomogram model is its intuitive display of the overall impact of each factor on pregnancy outcomes and its facilitation of rapid evaluation by clinicians in practical work ^[3]. A model related to clinical pregnancy and birth rate was also established.

3.5.2. Model validation

To evaluate the predictive performance of the model, this study validated its discriminatory ability using the receiver operating characteristic (ROC) curve and the area under the curve (AUC), as well as assessed its calibration using the Hosmer-Lemeshow test. The results showed that the AUC of the model's ROC curve was 0.832 (95% confidence interval: 0.798–0.866, $p < 0.001$), indicating high discriminatory ability. Additionally, the Hosmer-Lemeshow test results demonstrated good calibration of the model ($\chi^2 = 7.23$, $df = 8$, $p = 0.518$), meaning a high degree of consistency between predicted probabilities and actual observed probabilities. These validation metrics sufficiently demonstrate the reliability and effectiveness of the prediction model in clinical applications.

4. Clinical significance

When performing single-embryo transfer, prioritizing the selection of high-quality blastocysts (AA/AB grade) can significantly enhance the likelihood of a successful pregnancy while reducing the risk of early pregnancy loss.

If D3 cleavage-stage embryos are chosen, preference should be given to transferring embryos with 8 cells and a fragmentation rate of less than 10% to optimize pregnancy outcomes.

Embryo quality and endometrial receptivity have a synergistic effect: high-quality embryos placed in a receptive endometrium (with a thickness of 8–12 mm and Type A) can further increase the live birth rate to 58.3%.

The aforementioned conclusions are based on stratified analyses that exclude age as a confounding factor, providing more precise reference evidence for embryo selection in single-embryo transfer.

5. Discussion

5.1. Analysis of research findings

This study included 1,131 cases of single embryo transfer (including data from both elective and non-elective single embryo transfers) and developed a predictive model for pregnancy outcomes that incorporates multiple factors, including patient age, day 3 embryo transfer status, day 5/day 6 blastocyst development, endometrial thickness, and type. Due to the small number of day 4 transfer cycles, they were not included in the subgroup statistical analysis. The findings indicate that patient age is one of the primary factors influencing pregnancy outcomes, which is consistent with previously published literature^[8,11]. Age-stratified analysis revealed that the clinical pregnancy rate in patients under 35 years of age was significantly higher than that in patients aged 35 years or older, with a similar trend observed for live birth rate, aligning with the findings of Huang Ya et al.^[11]. Furthermore, blastocyst quality and developmental speed also significantly affect pregnancy outcomes; notably, in younger patient populations, the live birth rate following day 5 blastocyst transfer was significantly higher than that following day 6 blastocyst transfer, further confirming the importance of blastocyst developmental speed on pregnancy outcomes^[12].

Analysis of endometrial characteristics revealed a significant correlation between endometrial thickness and pregnancy outcomes. Clinical pregnancy rates were significantly higher when endometrial thickness ranged from 8 to 12 mm, a finding consistent with existing literature^[4]. However, the influence of endometrial type on pregnancy outcomes was not clearly established, which may be attributable to the relatively broad classification criteria for endometrial type used in this study. Of note, this study also found that the multiple pregnancy rate in the single cleavage embryo or blastocyst transfer group was significantly lower than that in the double embryo transfer group, a finding consistent with reference^[1], further highlighting the advantage of elective single embryo transfer in reducing the risk of multiple pregnancy.

Compared with existing research, the predictive model developed in this study demonstrates certain innovations in terms of the comprehensiveness of included factors and the depth of data analysis. For example, in addition to considering patient age and blastocyst quality, the model also incorporates endometrial thickness and type, providing a more comprehensive reflection of the key factors influencing pregnancy outcomes. Moreover, the identification of independent influencing factors through multivariate regression analysis further enhances the predictive accuracy of the model^[13].

5.2. Advantages and limitations of the model

This predictive model for pregnancy outcomes developed in this study has several notable advantages. First, the model integrates multiple factors, including patient age, embryonic development stage, and endometrial characteristics, enabling a more comprehensive assessment of the patient's reproductive capacity. Second, the use of a nomogram model provides a visual tool that allows clinicians to perform individualized predictions based on each patient's specific condition, thereby offering scientific support for embryo transfer decisions^[14]. Furthermore, validation of the model's discrimination and calibration indicates high predictive accuracy, providing reliable references for clinical practice^[9].

However, this study also has some limitations. First, the sample size is relatively small, including only 1,131 cases of single embryo transfer, which may limit the model's generalizability. Second, data were collected from a single reproductive medicine center, potentially introducing regional or institution-specific biases that may affect the model's general applicability to some extent^[9]. Additionally, the classification

criteria for some variables are relatively broad; for example, the categorization of endometrial types lacks detail, which may reduce the model's ability to capture specific factors ^[4]. Finally, due to the retrospective study design, information bias may exist during data collection, which could also affect the accuracy of the model ^[9].

5.3. Guidance for clinical practice

The predictive model for pregnancy outcomes established in this study holds significant guiding value in clinical practice. First, this model can assist clinicians in more accurately assessing patients' reproductive potential, thereby facilitating the development of personalized treatment plans. For example, for patients of advanced age or with insufficient endometrial thickness, adjusting the timing of embryo transfer or optimizing endometrial preparation protocols can increase the likelihood of successful pregnancy ^[15]. Second, the model emphasizes blastocyst quality and developmental speed, providing scientific support for embryo selection. Particularly in single embryo transfer strategies, prioritizing high-quality, rapidly developing blastocysts not only improves the chances of pregnancy but also effectively reduces the risk of multiple gestations.

Moreover, this model serves as an effective tool for communication between clinicians and patients. Based on the nomogram model, patients can intuitively understand their probability of pregnancy, thereby gaining an understanding of the risks and benefits associated with the treatment process. Such transparent information delivery enhances patient trust and compliance, ultimately improving overall treatment outcomes. Finally, the establishment of this model guides future advancements in assisted reproductive technology. For instance, incorporating more influencing factors or expanding the sample size could further enhance the model's predictive performance, thereby better serving clinical applications.

6. Conclusion

This study successfully developed a predictive model for pregnancy outcomes based on 1,131 cases of single embryo transfer, comprehensively considering multiple factors, including patient age, the developmental status of D3 embryos and D5/D6 blastocysts, as well as endometrial thickness and type. Univariate analysis and multivariate regression analysis were used to determine the independent effects of each factor on pregnancy outcomes, and a nomogram model was constructed to enable intuitive prediction of pregnancy probability. Model validation results demonstrated that the model has good discriminatory ability and calibration, providing a reliable basis for clinical decision-making.

The main value of this predictive model lies in its ability not only to improve the accuracy of pregnancy outcome predictions for single embryo transfer but also to offer clinicians a quantitative reference. For instance, when formulating individualized transfer strategies, clinicians can use the model to assess pregnancy probabilities under different embryo developmental stages and endometrial conditions, thereby selecting the optimal timing for transfer and the most suitable embryo type. Furthermore, the comprehensiveness and practicality of this model give it broad application prospects in the field of assisted reproductive technology, helping to optimize resource allocation, reduce the risk of multiple pregnancies, and improve overall treatment efficacy.

However, this study has certain limitations. First, the sample data were derived from a single reproductive medicine center, which may introduce biases related to regional characteristics and

specific population features. Future multicenter, large-sample studies are needed to further validate the generalizability of the model. Second, although the model incorporated several important factors, to minimize the impact of ovulation induction medications and high estrogen levels on pregnancy outcomes, only data from frozen-thawed single embryo transfer cycles were analyzed. Other variables that may influence pregnancy outcomes, such as the patient's metabolic status, immunological factors, ovulation induction protocols, and embryo fertilization methods, were not fully considered. Third, embryo quality assessment did not include time-lapse culture data; the model was established based solely on D3 embryo evaluations across all single embryo transfer cycles. Modeling criteria based on blastocyst assessment might offer better predictive capability. Therefore, future research should focus on exploring additional relevant factors to further refine this predictive model.

In addition, with the rapid development of artificial intelligence and machine learning technologies, the potential applications of these emerging tools in medical predictive models are becoming increasingly evident. Future studies could attempt to introduce machine learning algorithms into the field of pregnancy outcome prediction, using more complex model frameworks to uncover nonlinear relationships within the data and thereby further improve predictive performance. Interdisciplinary collaboration may also bring new opportunities for development in this area, such as analyzing embryo gene expression data through bioinformatics approaches to gain a more comprehensive understanding of embryo developmental potential.

In summary, the pregnancy outcome prediction model established in this study provides a key scientific tool for clinical practice in frozen-thawed single embryo transfer, though continuous improvement and refinement through subsequent research are necessary. It is hoped that future studies will achieve breakthroughs in expanding sample sizes, incorporating additional influencing factors, and adopting advanced technologies, thereby contributing more significantly to the advancement of precision medicine in assisted reproductive technology.

Funding

Sub-topic of the Public Welfare Project of Jinhua Science and Technology Bureau (Project No.: 2022-4-279)

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Chen M, Peng S, Lin H, et al., 2022, Analysis of the Application Effect of Elective Single Embryo Transfer Strategy in Frozen-Thawed Embryo Transfer Cycles. *Journal of Reproductive Medicine*, 31(7): 918–925.
- [2] Jiao Y, Wang Y, Song N, et al., 2023, Analysis of Pregnancy Outcomes After Fresh Transfer of Different Grades of D3 Embryos and D5 Blastocysts in Patients With Ectopic Pregnancy. *Journal of Medical Research*, 52(3): 27–31.
- [3] Shen Y, Deng X, Yu H, et al., 2020, Development and Validation of a Nomogram Model for Predicting Clinical Pregnancy After Single Blastocyst Transfer in Frozen-Thawed Cycles. *Progress in Modern Obstetrics and Gynecology*, 29(3): 194–198.
- [4] Zhao F, Shi Z, Zhang Y, et al., 2023, Effects of Endometrial Thickness and Transferred Embryo Type on Clinical

- Outcomes of Frozen-Thawed Embryo Transfer Cycles. *Journal of Reproductive Medicine*, 32(1): 125–129.
- [5] Tao L, Zheng B, Dai F, et al., 2023, Effect of D4 Embryo Development Rate on Pregnancy Outcomes in IVF-ET. *Journal of Reproductive Medicine*, 32(9): 1355–1362.
 - [6] Shen C, Zhang J, Du S, et al., 2021, Relationship Between Cell Number on Day 2 and Day 3 of Single Cleavage-Stage Embryo Transfer and Pregnancy Rate. *Journal of Zhengzhou University (Medical Sciences)*, 56(1): 119–122.
 - [7] Deng X, Han Y, Peng W, et al., 2023, Effect of Zygote Pronuclear Area Difference and Mean Cytoplasmic Diameter on Live Birth After Single Blastocyst Transfer. *China Practical Medicine*, 18(2): 15–19.
 - [8] Guo N, Yuan X, Deng T, et al., 2020, Analysis of Factors Affecting Live Birth Outcomes in Single Blastocyst Frozen-Thawed Transfer Cycles. *Journal of Reproductive Medicine*, 29(6): 716–721.
 - [9] Liu Z, Xiong F, Zhang H, et al., 2021, Research Progress on Prediction Models for IVF-ET Pregnancy Outcomes. *Journal of Reproductive Medicine*, 30(5): 695–700.
 - [10] Dong Y, Jian N, La X, 2022, Effect of Hormone Levels on the Day of Endometrial Transformation on FET Pregnancy Outcomes in Advanced-Age Women. *Chinese Journal of Reproductive Health*, 33(3): 277–280.
 - [11] Fang L, Huang Y, Xu J, et al., 2021, Effect of D3 Embryo Morphological Score on Clinical Outcomes of Single Blastocyst Frozen-Thawed Transfer Cycles. *Journal of Reproductive Medicine*, 30(10): 1300–1306.
 - [12] Zhu X, Zhao Z, Du Y, et al., 2020, Effect of Blastocyst Evaluation Parameters on Clinical Outcomes and Transfer Selection in Frozen-Thawed Cycles. *Journal of Reproductive Medicine*, 29(11): 1439–1445.
 - [13] Xu H, Cai G, Xu W, et al., 2021, Analysis of Factors Influencing the Outcomes of Artificial Cycle Frozen-Thawed Embryo Transfer. *Journal of Reproductive Medicine*, 30(7): 901–906.
 - [14] Wen W, Zhou H, Meng B, et al., 2020, Analysis of Factors Affecting Pregnancy Outcomes in Frozen Embryo Transfer Cycles. *Journal of Clinical Practical Medicine*, 24(9): 80–83.
 - [15] Ji Y, Zheng A, Ding J, et al., 2022, Analysis of Pregnancy Outcomes in Optimized Elective Single Cleavage-Stage Embryo Transfer Strategy. *Journal of Reproductive Medicine*, 31(8): 1022–1029.

Publisher's note

Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Case Analysis of Cervical Cancer Complicated with Von Hippel-Lindau Syndrome

Xiaojing Sun, Li Li*, Hongyun Shi

Department of Radiotherapy, Affiliated Hospital of Hebei University, Baoding 071000, Hebei, China

**Author to whom correspondence should be addressed.*

Copyright: © 2026 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To explore the clinical characteristics, diagnostic approach, and multidisciplinary management strategies of cervical cancer complicated with Von Hippel-Lindau syndrome (VHL), and to enhance clinical awareness of rare and complex cases. *Methods:* A retrospective analysis was conducted on the clinical data of a patient with cervical cancer complicated by VHL syndrome. The patient's medical history, family genetic background, laboratory tests, imaging findings, pathological results, diagnostic process, and multidisciplinary treatment were organized and analyzed in conjunction with relevant literature. *Results:* The patient was a 77-year-old female presenting with vaginal bleeding and lower abdominal distension. Cervical biopsy pathology indicated cervical squamous cell carcinoma, staged as IIIC1r. Further examination revealed abnormal changes in multiple systems, including the liver, pancreas, kidneys, and adrenal glands, along with a clear family genetic background of VHL. After comprehensive evaluation through imaging, pathology, and multidisciplinary consultation, the patient was ultimately diagnosed with cervical cancer complicated by VHL syndrome. This case was characterized by advanced age at onset, pronounced family clustering, multi-organ involvement, and complex diagnosis and treatment. *Conclusion:* Cervical cancer complicated by VHL syndrome is relatively rare in clinical practice. For patients with a special family history and multi-system involvement, it is essential to enhance awareness of hereditary tumor syndromes, strengthen multidisciplinary collaboration, and conduct individualized assessments to improve the diagnostic proficiency and clinical management capabilities for complex cases.

Keywords: Cervical cancer; Von Hippel-Lindau syndrome; VHL syndrome; Multidisciplinary treatment; Case analysis

Online publication: May 31, 2026

1. Introduction

Von Hippel-Lindau (VHL) syndrome is a rare autosomal dominant disorder characterized by multiple tumors and cysts in various organ systems. Cervical cancer is not a classic component of VHL syndrome, and its coexistence is extremely rare. Here, we present a case of a 77-year-old female with locally advanced cervical squamous cell carcinoma concurrently diagnosed with VHL syndrome, highlighting the diagnostic and

management challenges of such rare complex cases.

2. Medical condition presentation

The patient, a 77-year-old female from Hebei Province, was admitted to the hospital due to “intermittent vaginal bleeding for over three months accompanied by lower abdominal distension and pain.” Since January 2026, the patient has experienced intermittent, slight vaginal bleeding without apparent cause, which is bright red, intermittent, and without significant blood clots, accompanied by a sensation of lower abdominal distension and mild pain in the lower back, without notable symptoms such as frequent urination, urgency, or constipation. She sought medical attention at the Affiliated Hospital of Hebei University, where a gynecological examination revealed a cervical mass, prompting further investigations. A gynecological ultrasound indicated reduced local echo in the cervix, measuring approximately 3.1 cm × 1.2 cm, with unclear borders. TCT showed atypical squamous cells, and HPV16 was positive. A cervical biopsy pathology report indicated a malignant tumor, consistent with squamous cell carcinoma, based on immunohistochemical results. Immunohistochemistry results showed: P40 (+), P63 (+), P16 (+), Ki-67 (70%+), CK7 (+), EGFR (+). Relevant case data were sourced from uploaded medical records. The patient has a history of hypertension for over 30 years, treated with long-term oral amlodipine besylate and valsartan; diabetes for over 20 years, controlled with long-term Novolin 30R. She has smoked for over 50 years, approximately 7-8 cigarettes per day, with no history of alcohol consumption, trauma, blood transfusion, or major surgery. The family history is notably distinctive. The patient’s son carries the VHL gene; her brother underwent surgical treatment for central nervous system and renal tumors; both sisters died from multiple tumors; her nephew was diagnosed with VHL syndrome, indicating a familial clustering of the disease.

Upon admission, physical examination revealed an obese body type with a BMI of 26.8, clear consciousness, and no palpable enlargement of superficial lymph nodes. Gynecological examination showed the disappearance of the original cervical shape, with an irregular, hard mass on the surface measuring approximately 5 cm × 4 cm, significantly invading the left parametrium, disappearance of the vaginal fornix, and thickening of the left parametrium reaching the pelvic wall, which was fixed. A tripartite examination indicated that the sacral ligaments were not thickened, the rectal mucosa was smooth, the left parametrium was significantly thickened, reaching the pelvic wall and fixed, and the right side was slightly thickened.

Pelvic MRI revealed a localized mass-like abnormal signal in the cervix, measuring approximately 2.8 cm × 2.7 cm × 3.0 cm, with the lesion invading the upper one-third of the vagina and the left parametrium, extending to the pelvic wall, and enlarged lymph nodes beside the left iliac vessels. Thoracoabdominal pelvic enhanced CT showed scattered nodules in both lungs, multiple liver cysts, multiple pancreatic cysts, multiple left renal cysts, multiple right renal space-occupying lesions, and bilateral adrenal nodules, suggesting the possibility of VHL syndrome.

Laboratory tests showed: white blood cells at $11.71 \times 10^9/L$; significantly elevated urinary white and red blood cells; D-dimer at 0.70 µg/mL; glycated hemoglobin at 10.4%; significantly elevated squamous cell carcinoma antigen at 8.850 ng/mL.

3. Diagnostic basis

The patient, an elderly female, presented primarily with vaginal bleeding and lower abdominal distension.

Gynecological examination revealed a space-occupying lesion in the cervix, and cervical biopsy pathology confirmed squamous cell carcinoma. Pelvic MRI showed parametrial and pelvic wall invasion, along with pelvic lymph node metastasis, meeting the diagnostic criteria for stage IIIC1r cervical cancer. The patient has a typical VHL family genetic background, with multiple first- and second-degree relatives having a history of VHL-related tumors. Imaging studies revealed multiple renal space-occupying lesions and cysts, multiple pancreatic cysts, liver cysts, and bilateral adrenal lesions, consistent with the multi-system involvement characteristic of VHL syndrome. Although cranial MRI did not reveal hemangioblastomas, the diagnosis of VHL syndrome does not rely on a single organ manifestation but requires a comprehensive analysis based on genetic background and multi-organ imaging features ^[1]. MDT discussion concluded that the diagnosis of VHL syndrome was established.

4. Diagnostic results

- (1) Cervical squamous cell carcinoma, stage IIIC1r;
- (2) Von Hippel-Lindau syndrome (VHL syndrome);
- (3) Right renal space-occupying lesion (suspected clear cell renal carcinoma);
- (4) Multiple pancreatic cysts;
- (5) Multiple liver cysts;
- (6) Bilateral renal cysts;
- (7) Type 2 diabetes mellitus;
- (8) Hypertension.

5. Analysis report

Von Hippel-Lindau syndrome (VHL) is a rare autosomal dominant hereditary tumor syndrome caused by mutations in the VHL tumor suppressor gene located on the short arm of chromosome 3 (3p25-26). The VHL gene encodes a protein involved in the degradation regulation of hypoxia-inducible factor (HIF). When the VHL gene undergoes loss-of-function mutations, HIF cannot be normally degraded, continuously activating downstream pro-angiogenic factors such as vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and transforming growth factor (TGF), further promoting abnormal angiogenesis, cell proliferation, and tumorigenesis. Given its involvement in metabolic regulation in multiple tissues and organs, VHL syndrome is characterized by multi-organ, multifocal, and lifelong progression ^[2].

The clinical manifestations of VHL syndrome are complex and can involve multiple organ systems, including the central nervous system, kidneys, adrenal glands, pancreas, reproductive system, retina, and inner ear. Classic manifestations include central nervous system hemangioblastomas, clear cell renal carcinoma, renal cysts, pancreatic cysts, pheochromocytomas, endolymphatic sac tumors, and epididymal cystadenomas. Literature reports an incidence of approximately 1/36,000, with over 95% of patients developing initial symptoms before age 34 and nearly 100% penetrance after age 70. The average lifespan is approximately 59.4 years for males and 48.4 years for females, with central nervous system hemangioblastomas and renal cell carcinoma being the primary causes of death. Relevant case data also suggest that VHL syndrome is a hereditary disease characterized by multi-system, multi-organ tumorigenesis.

This patient, at 77 years old, was first systematically identified and diagnosed with VHL syndrome,

significantly later than the commonly reported age of onset in the literature, which is a rare occurrence. Further analysis reveals a prominent family genetic background. Both of the patient's sons carry the VHL gene; her brother underwent surgical treatment for central nervous system and renal tumors; both sisters died from multiple tumors throughout the body; her nephew was diagnosed with VHL syndrome after surgical treatment for a central nervous system tumor at a superior hospital, indicating a clear familial clustering of the disease. These characteristics are consistent with an autosomal dominant inheritance pattern. The risk of VHL syndrome in first-degree relatives can reach 50%, making family history crucial for disease diagnosis.

Imaging studies showed scattered tiny nodules in both lungs, multiple liver cysts, multiple pancreatic cysts, multiple left renal cysts, a space-occupying lesion in the right kidney, and bilateral adrenal nodular thickening on thoracoabdominal pelvic enhanced CT. The right renal lesion is suspected to be clear cell renal carcinoma, while the pancreas and liver primarily exhibit cystic lesions, consistent with the common distribution of affected organs in VHL syndrome. Although cranial MRI enhancement did not reveal central nervous system hemangioblastomas, and fundus examination did not find retinal hemangiomas, VHL syndrome exhibits significant clinical heterogeneity, and not all patients present with a complete disease spectrum. Some patients may initially present with abnormalities in only one system, necessitating a comprehensive judgment based on family history, imaging, and organ involvement.

On the other hand, this patient also has cervical squamous cell carcinoma. Cervical cancer is a common malignant tumor in the female reproductive system, closely related to persistent high-risk HPV infection, with HPV16 being the primary high-risk subtype. This patient tested positive for HPV16, and TCT indicated atypical squamous cells. Biopsy pathology, combined with immunohistochemical results, confirmed the diagnosis of squamous cell carcinoma. Immunohistochemistry showed positive P16 expression and a Ki-67 proliferation index of 70%, indicating active tumor cell proliferation, consistent with the molecular biological characteristics of HPV-related cervical cancer.

Pelvic MRI further indicated a cervical lesion measuring approximately 2.8 cm × 2.7 cm × 3.0 cm, with the lesion invading the upper one-third of the vagina, left parametrial tissue, and pelvic wall, accompanied by enlarged lymph nodes beside the left iliac vessels. Gynecological examination revealed the disappearance of the original cervical shape, with an irregular, hard mass significantly invading the left side, disappearance of the vaginal fornix, and thickened parametrial tissue reaching and fixing to the pelvic wall. Combined with imaging and clinical manifestations, this is consistent with the presentation of locally advanced cervical cancer, stage IIIC1r.

The uniqueness of this case is mainly reflected in the following aspects. First, the co-occurrence of VHL syndrome and cervical cancer is extremely rare, with few related reports domestically and internationally, and cervical cancer is not part of the classic tumor spectrum of VHL, so there is a lack of clear research evidence on whether there is a common molecular mechanism between the two. Second, the patient simultaneously has renal space-occupying lesions, pancreatic cysts, liver cysts, and adrenal lesions, requiring differentiation between metastatic lesions, secondary tumors, and VHL-related lesions. Third, the patient is elderly and has comorbidities such as diabetes, hypertension, and a long smoking history, increasing treatment risks and diagnostic and therapeutic challenges. Fourth, this case involves issues in gynecological oncology, genetics, imaging, pathology, and multidisciplinary comprehensive management, making it a typical complex case.

Therefore, this case is not a simple case of cervical malignancy but a complex and special case influenced by genetic background, multi-system involvement, and advanced age with comorbidities. For such

patients, clinical management should not only focus on controlling the primary lesion but also emphasize screening for systemic lesions, genetic counseling, and family management. Multidisciplinary collaboration is essential to achieve precise and individualized diagnosis and treatment, providing a reliable basis for long-term disease management.

6. Treatment plan

Given the patient's complex condition, the focus of treatment is on controlling local cervical lesions while simultaneously assessing the risk of VHL-related lesions. For general treatment, nutritional support and management of underlying diseases are provided, with enhanced monitoring of blood glucose and blood pressure to control risk factors. For VHL syndrome, a comprehensive systemic screening is conducted, including brain MRI, fundus examination, urinary system imaging, and multi-organ evaluation to determine the extent of involvement. Ophthalmology consultation and OCT reveal diabetic retinopathy and cataracts in both eyes; brain MRI does not reveal any mass in the central nervous system. After the patient's admission, an MDT multidisciplinary consultation is held, involving pathology, urology, radiology, and hepatobiliary surgery departments. Pathology suggests a full genetic blood test due to the patient's family history of VHL; urology considers the possibility of clear cell renal carcinoma in the right kidney; radiology recommends further PET-CT to assess the nature of the lesions; hepatobiliary surgery suggests no immediate intervention for pancreatic and liver cysts, recommending dynamic observation. After comprehensive analysis, it is determined that the current cervical cancer lesion is large, accompanied by significant vaginal bleeding and pelvic wall invasion, representing the primary issue at hand. Therefore, priority is given to addressing the cervical lesion.

7. Clinical measures

After integrating MDT opinions and fully communicating with the patient's family, and considering the patient's clear family history of VHL, the family requests prioritizing local treatment for cervical cancer and temporarily refuses PET-CT and hematological genetic testing. Subsequently, a precise pelvic radiotherapy plan is formulated, with the radiation target area covering the primary cervical lesion, bilateral obturator lymph nodes, and high-risk parametrial regions. GTVnd is defined as visible enlarged obturator lymph nodes. CTV includes the cervix, uterus, parametrium, and pelvic lymphatic drainage areas, with stratified dose designs based on different risk areas. The specific dose regimen is as follows: PTV is administered at 4500 cGy in 25 fractions, PTV1 at 5400 cGy in 25 fractions, PTV2 at 5200 cGy in 25 fractions, and PGTVnd at 6000 cGy in 25 fractions. Starting from the fourth weekend, CT-guided intravaginal three-dimensional brachytherapy is added, with a single dose of 600 cGy, planned for five sessions, ultimately achieving an EQD2 of ≥ 8500 cGy in the tumor area. During treatment, vital signs monitoring, blood glucose control, and nutritional support are conducted simultaneously, with continuous assessment of renal masses and changes in VHL-related lesions. Given the patient's advanced age and multi-organ disease background, close attention is paid to the risks of bone marrow suppression, urinary system injury, and complications during treatment. After local radiotherapy, once the overall condition improves, further consultation with urology for renal mass resection is planned, with close follow-up on masses and cysts in other organs throughout the body.

8. Summary and discussion

VHL syndrome is a rare hereditary tumor syndrome with complex clinical manifestations involving multi-system lesions^[3]. This case involves an elderly patient with locally advanced cervical cancer, renal masses, and cystic lesions in the pancreas and liver, presenting a complex diagnostic process and challenging treatment decisions. Due to the rarity of concurrent cervical cancer and VHL syndrome, clinical experience is limited, necessitating enhanced recognition of family history and multi-system imaging abnormalities. For complex tumor patients, the MDT model should be emphasized, with joint decision-making across gynecology, pathology, genetics, imaging, and surgery to achieve individualized management. Particularly for patients with a genetic background, family screening and genetic counseling should be prioritized to improve early detection rates and provide a basis for subsequent precise treatment. This case can offer some reference for the diagnosis and treatment of clinically rare cases.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Ye J, Fu Z, Li R, Zhou C, Liang Z, Zhai W, 2014, A Case of von Hippel-Lindau Syndrome. *Chinese Journal of Hepatobiliary Surgery*, 20(12): 2.
- [2] Li X, Yu Z, Zhang G, 2024, Comprehensive Treatment of von Hippel-Lindau Syndrome: A Case Report. *Chinese Medical Journal Case Report Database*, 6(1): E2813–E2813.
- [3] Shi Y, Xu Z, Mo Y, et al., 2022, Imaging Findings of Typical von Hippel-Lindau Syndrome: A Case Report. *Chinese Journal of Magnetic Resonance Imaging*, 13(2): 2.

Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

A Phenomenological Study on Ovarian Reserve Health Risk Experiences, Fertility Difficulties, and Support Needs among Obstetric, Gynecologic, and Pediatric Nurses

Ruizhi Huang, Shuang Zhang, Jialin Ye*

The First Affiliated Hospital of Sun Yat-sen University, Guangzhou 510062, Guangdong, China

**Author to whom correspondence should be addressed.*

Copyright: © 2026 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To explore the lived experiences of ovarian reserve health risks, fertility difficulties, and support needs among obstetric, gynecologic, and pediatric nurses. *Methods:* A descriptive phenomenological approach was adopted. Semi-structured, in-depth interviews were conducted with nine nurses from obstetrics, gynecology, pediatrics, reproductive medicine, and delivery room departments at a tertiary hospital in China. Data were analyzed using Colaizzi's seven-step method, with sample size determined by data saturation. *Results:* Four core themes emerged: (1) Health risk awareness originated from high occupational exposure, while delayed childbearing was impeded by multiple barriers including economic constraints, career demands, relationship challenges, and work intensity; (2) Health risks and uncertainty triggered stratified negative emotions and differential fertility confidence; (3) Structural conflicts existed between occupational demands and reproductive health maintenance, with individual coping being passive and limited; (4) Organizational support gaps were pronounced, with strong demands for fertility-friendly institutional support. *Conclusions:* Ovarian reserve health anxiety among obstetric, gynecologic, and pediatric nurses primarily stemmed from high clinical exposure and occupational stress, with emotions and fertility experiences exhibiting stratified characteristics. Night shifts, occupational exposures, promotion-related involution, and fertility needs were difficult to reconcile. Hospitals should urgently implement supportive measures, including reduced night shifts, free ovarian function screening, optimized occupational protection protocols, and promotion policy adjustments favoring reproductive health.

Keywords: Obstetric, gynecologic, and pediatric nurses; Ovarian reserve; Health risks; Fertility difficulties; Qualitative research

Online publication: May 31, 2026

1. Introduction

Diminished ovarian reserve (DOR) refers to a reduction in the quantity and/or quality of oocytes within the ovary, leading to decreased fertility, accompanied by reduced anti-Müllerian hormone (AMH), decreased antral follicle count (AFC), and elevated follicle-stimulating hormone (FSH) ^[1]. In recent years, DOR has shown an increasing trend among women of reproductive age, with occupational exposure, psychological stress, and circadian rhythm disruption identified as significant contributing factors ^[2]. As of the end of 2023, China had 5.63 million registered nurses, the vast majority of whom are women ^[3].

Nurses working in obstetrics, gynecology, pediatrics, reproductive medicine centers, and delivery rooms hold a dual identity as both “reproductive health caregivers” and “populations at high risk for reproductive health problems.” They are chronically exposed to cases of infertility, ovarian decline, and assisted reproduction, while simultaneously facing multiple occupational hazards, including rotating night shifts, exposure to chemotherapeutic agents and disinfectants, high-pressure on-call duties, and intense promotion competition. These factors create multidimensional conflicts between their professional responsibilities and reproductive planning ^[9].

At the occupational exposure level, Jiang et al.’s ^[4] nationwide survey of female nurses in China demonstrated that exposure to antineoplastic drugs increased the risk of preterm birth by approximately 2.2-fold (OR = 2.169), while exposure to disinfectants significantly increased the risk of threatened miscarriage (OR = 2.293). Nouri et al.’s ^[5] meta-analysis confirmed that occupational exposure to antineoplastic drugs nearly doubled the risk of spontaneous abortion. Regarding night shift work, Jaafarzadeh et al.’s ^[6] meta-analysis established a significant association between rotating shift work and menstrual disorders, and demonstrated that frequent night shifts (> 25 times) during the first trimester could increase the risk of preterm birth by 2–3 fold, with the underlying mechanism involving melatonin suppression-induced dysfunction of the hypothalamic–pituitary–ovarian (HPO) axis. Furthermore, Zhu et al.’s ^[2] comprehensive review indicated that various environmental toxins and persistent psychological stress could accelerate follicular depletion, suggesting that obstetric, gynecologic, and pediatric nurses face superimposed ovarian damage risks from chemical, physical, and psychological stressors.

At the psychological experience level, Hammond and Marczak’s ^[7] thematic synthesis of ten qualitative studies on premature ovarian insufficiency (POI) revealed that diagnosed women commonly experienced identity disruption, with barriers to accessing support exacerbating emotional distress. Eftekhari et al.’s ^[8] quantitative survey found that only 35% of nurses planned to have children within three years, with occupational stress being the primary negative predictor. However, existing research has several limitations: it predominantly focuses on diagnosed patients, neglecting the unique experiences of nurses who harbor concerns but remain undiagnosed; it relies mainly on quantitative methods, lacking in-depth qualitative exploration of ovarian health risk experiences; and research on nurses’ fertility-friendly organizational support needs is extremely limited.

This study employed a phenomenological qualitative approach to conduct in-depth interviews with nine obstetric, gynecologic, and pediatric nurses spanning different risk statuses, including confirmed DOR, health concerns, menstrual irregularities, and high occupational exposure, aiming to reveal their authentic experiences and provide evidence for constructing an occupational reproductive health protection system for nursing personnel.

2. Methods

2.1. Study design

A descriptive phenomenological qualitative research design was adopted, following the Colaizzi analytic tradition and focusing on obstetric, gynecologic, and pediatric nurses' subjective experiences and meaning-making regarding ovarian reserve health risks.

2.2. Participants

A combined strategy of purposive sampling and maximum variation sampling was employed. Inclusion criteria: (1) currently employed nurses in obstetrics, gynecology, pediatrics, neonatology, reproductive medicine, or delivery room departments; (2) aged 28–30 years; (3) meeting at least one of the following statuses: confirmed DOR, existing ovarian health concerns, menstrual irregularities accompanied by reproductive anxiety, or prolonged high exposure to reproductive clinical cases without explicit concerns; (4) informed consent provided. Exclusion criteria: non-target department assignment, inability to complete the interview due to communication barriers, refusal of audio recording, or withdrawal during the study. The final sample size was determined by data saturation; by the ninth interview, no new themes emerged, indicating information saturation. All nine participants were female, aged 28–30 years; eight were unmarried, one was married; all were nulliparous. Their departmental distribution was: four from pediatrics, one from neonatology, one from gynecology, one from the delivery room, one from obstetrics, and one from reproductive medicine.

2.3. Data collection

One-on-one, face-to-face, semi-structured in-depth interviews were conducted. The interviews explored the following core areas: sources and perception processes of ovarian health risk awareness; the impact of health concerns on emotions and fertility planning; experiences of conflict between the occupational environment and reproductive health maintenance; and coping strategies and organizational support needs. Interviews were conducted in a quiet, private room, lasting 25–45 minutes each, and were audio-recorded in full. Verbatim transcriptions were completed within 24 hours and returned to participants for member checking.

2.4. Data analysis

Data were analyzed using Colaizzi's seven-step method. Two researchers independently coded the data and held regular discussions to reach consensus.

3. Results

3.1. Participant characteristics

Table 1 presents the demographic and risk status information of the nine participants.

Table 1. General participant information (n = 9)

No.	Age	Marital Status	Department	Ovarian Reserve Health Risk Status
N1	28	Unmarried	Pediatrics	Normal test results; concerned
N2	30	Unmarried	Pediatrics	AMH not tested; highly concerned
N3	29	Unmarried	Pediatrics	Confirmed DOR

No.	Age	Marital Status	Department	Ovarian Reserve Health Risk Status
N4	28	Unmarried	Neonatology	Confirmed DOR
N5	28	Married	Pediatrics	No concerns; high exposure only
N6	28	Unmarried	Reproductive Medicine	Normal test results; concerned
N7	30	Unmarried	Gynecology	Irregular menstruation; concerned
N8	29	Unmarried	Delivery Room	Mild concern; long-distance relationship
N9	28	Married	Obstetrics	Irregular menstruation; concerned

3.2. Core themes

Through Colaizzi's seven-step analysis, four core themes were identified.

3.2.1. Theme 1: Health risk awareness originating from high occupational exposure, fertility planning delayed by multiple practical barriers

All participants' knowledge of ovarian reserve originated from their clinical rotation experiences and informal exchanges about colleagues' cases, rather than from systematic health education. Participant N6 stated: "In the reproductive medicine center, I see many young colleagues with very low AMH. If you don't get tested, you're fine. Once tested, anxiety sets in." N1 shared: "During my rotation in the reproductive department, I encountered patients around age 30 with AMH as low as 0.1–0.2, close to my own age. It worried me enormously." Delayed fertility planning was hindered by multiple factors: economic pressure (high child-rearing costs, insufficient material security); occupational pressure (promotion requirements, publications, competitions, night shifts consuming substantial energy); relationship barriers (limited social circles, long-distance relationships); and work intensity (frequent night shifts leading to physical and mental exhaustion), collectively creating a predicament of "wanting to have children but being unable to."

3.2.2. Theme 2: Health risks and uncertainty triggering stratified emotions and differential fertility confidence

Participants' emotional responses and fertility confidence exhibited clear stratification according to health risk status. The confirmed diagnosis group (N3, N4) initially experienced fear and shock as predominant emotions, gradually transitioning to acceptance, with fertility confidence markedly diminished, where N4 described: "It was terrifying and shocking, to experience ovarian decline at such a young age is hard to believe." The concerned/irregular menstruation group (N1, N2, N6, N7, N9) manifested persistent anxiety, closely monitoring their menstrual cycles and test indicators, with some proactively advancing their fertility plans, where N9 stated: "With so many night shifts and frequently delayed menstruation, I am very worried about my ovaries." The low-anxiety group (N5, N8) exhibited emotional stability, more influenced by practical constraints, regarding assisted reproduction as a psychological fallback, where N8 expressed: "With IVF as a backup, I'm not anxious; it's mainly the long-distance situation holding things up." A common feature across all groups was that clinical scenarios continuously intensified their anxiety levels, forming a cycle of "witnessing cases → self-projection → heightened emotion."

3.2.3. Theme 3: Structural conflicts between occupational demands and reproductive health maintenance, with passive and limited individual coping

Four levels of core conflict were repeatedly mentioned: (1) night shift-induced circadian disruption leading

to irregular menstruation and endocrine abnormalities (N9, N6); (2) direct reproductive harm from exposure to chemotherapeutic agents, formaldehyde, and infectious environments (N1, N6); (3) persistent tension from 24-hour work phone on-call duties and resuscitation emergencies; and (4) promotion criteria tied to night shift quotas, forcing a binary choice between career advancement and fertility (N7). In terms of coping, participants generally adopted passive strategies such as menstrual monitoring, regular check-ups, dietary supplementation, health products, and traditional Chinese medicine regulation, none of which could adequately offset occupational harm. N1 frankly acknowledged: “Night shifts are unavoidable—I can only monitor my sleep, supplement my energy, and self-regulate to minimize physical depletion.”

3.2.4. Theme 4: Pronounced organizational support gaps and strong demands for fertility-friendly support

Participants’ demands for organizational support spanned five dimensions, expressed with high consistency and urgency: scheduling support, reduced night shifts and flexible scheduling for those preparing for pregnancy, of reproductive age, or with menstrual disorders (N8, N9); health support, adding AMH, sex hormones, and ovarian ultrasound to health examinations and providing free screening (N3, N9); environmental support, reassignment of pregnancy-planning personnel away from chemotherapy, high-risk infection, and formaldehyde exposure posts (N1); career support, reducing promotion-related involution and eliminating unreasonable night shift quota requirements (N2, N6); and security and psychological support, increasing salaries, including assisted reproduction in health insurance coverage (N9), and organizing health lectures and psychological counseling (N6). The high consistency of these multidimensional needs indicates a significant gap in reproductive health dimensions within existing occupational health systems.

4. Discussion

This study revealed that the core source of ovarian health anxiety among obstetric, gynecologic, and pediatric nurses was not merely somatic symptoms but a dual driver of “high clinical exposure + occupational stress.” Zhu et al.’s ^[2] review had already confirmed occupational factors and environmental toxins as significant external triggers for DOR, while Jiang et al. ^[4] and Nouri et al. ^[5] corroborated the reproductive hazards of occupational chemical exposure at the quantitative level. This study offers experiential-level evidence revealing that even with normal test results, this population remains in a state of heightened vigilance—a phenomenon of “premature vigilance” that constitutes a unique finding of the present study, suggesting that occupational exposure has been “internalized” into psychological risk perception, extending beyond the objective risk scope described in the literature ^[4,5].

Regarding the emotional and fertility confidence dimension, Hammond and Marczak’s ^[7] thematic synthesis of qualitative studies on diagnosed POI women showed that diagnosed individuals experienced identity disruption and barriers to support access. The present study confirmed and extended this finding: not only did the confirmed diagnosis group experience identity disruption, but the concerned/irregular menstruation group and the low-anxiety group exhibited distinct experiential patterns, indicating a broad “gray zone” between “diagnosis” and “complete absence of concerns,” where a domain that previous research exclusively focused on diagnosed patients ^[7] could not capture. Eftekhari et al. ^[8] found that only 35% of nurses planned to have children within three years; from a qualitative perspective, the present study reveals

that declining fertility confidence does not exist in isolation but is produced through the intertwining of health uncertainty, occupational stress, economic burden, and relationship difficulties, with dominant barriers differing across risk statuses, suggesting that support strategies should be stratified.

The structural contradiction between occupation and reproductive health represents another core finding. Jaafarzadeh et al. ^[6] confirmed the biological mechanisms linking rotating shift work and menstrual disorders; the present study supplements this from a sociological dimension: even when participants fully recognized the harm of night shifts, at the institutional level they were still “unavoidable” (N1), and the institutional design tying promotion criteria to night shift quotas actively positioned career development against reproductive health (N7). The highly passive nature of individual coping strategies further confirms the institutional origin of the problem. This stands in contrast to the requirements of the “Healthy China” strategy for whole-life-cycle health protection of occupational populations.

Regarding support needs, the multidimensional and highly consistent demands of participants indicate that this population exists in a state of quadruple superimposition: “high exposure, high risk, high stress, low support,” filling an empirical gap in the field of occupational reproductive health protection for nurses. The innovation of this study lies in being the first to systematically include populations across four risk statuses, revealing the “stratified” nature of experiences, and deeply exploring the pathway of “high occupational exposure → risk internalization → psychological anxiety.” Limitations include the single-center design, small sample size ($n = 9$), and concentration of participants within the 28–30 age range with nulliparous status, limiting external validity; additionally, the exclusive use of qualitative methods precludes quantification of exposure–effect dose–response relationships. Future research could adopt multi-center, mixed-methods designs, include nurses across different ages and parity statuses, and incorporate biomarkers such as AMH testing to establish a more comprehensive evidence base.

5. Conclusion

Ovarian reserve health risk perception among obstetric, gynecologic, and pediatric nurses is significantly amplified by high occupational exposure, with the phenomenon of “premature vigilance” being prevalent. Emotional responses and fertility confidence exhibit stratified differences. Structural conflicts exist between night shifts, occupational exposure, high-pressure on-call duties, promotion-related involvement, and reproductive health maintenance, with individual coping being passive and limited. Organizational support gaps are pronounced across scheduling, health screening, occupational protection, and promotion burden reduction dimensions. It is recommended that hospitals optimize scheduling systems, integrate ovarian function indicators into free health examinations, establish standardized protocols for reassigning pregnancy-planning personnel, and reduce the degree of promotion-related involution, thereby constructing a fertility-friendly occupational environment.

6. Future Directions

Future multi-center, large-sample studies incorporating quantitative analyses of occupational factors are warranted. Intervention studies should be designed to verify the effectiveness of fertility-friendly policies. Research perspectives could be broadened by including nurses of different ages and parity statuses.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Expert Consensus Group on Clinical Diagnosis and Treatment of Diminished Ovarian Reserve, 2022, Expert Consensus on Clinical Diagnosis and Treatment of Diminished Ovarian Reserve. *Journal of Reproductive Medicine*, 31(4): 425–434.
- [2] Zhu Q, Li Y, Ma J, et al., 2023, Potential Factors Result in Diminished Ovarian Reserve: A Comprehensive Review. *Journal of Ovarian Research*, 16(1): 208.
- [3] National Health Commission of the People's Republic of China, 2024, 2023 Statistical Bulletin on the Development of Health Services in China, Beijing.
- [4] Jiang M, Liu F, Luo Y, et al., 2023, Effect of Occupational Hazardous Factor Exposure on Adverse Pregnancy Outcomes Among Female Nurses in China. *Reproductive Health*, 20(1): 138.
- [5] Nouri M, Soltani A, Bastani P, et al., 2023, Occupational Exposure to Antineoplastic Drugs and Adverse Reproductive Outcomes in Nurses: A Meta-analysis. *Nursing Open*, 10(10): 6727–6737.
- [6] Jaafarzadeh F, Rajabalizadeh N, Razavi M, et al., 2023, The Relationship Between Shift Work and Menstrual Disturbances: A Systematic Review and Meta-analysis. *SSM – Population Health*, 24: 101522.
- [7] Hammond ER, Marczak M, 2023, Women's Experiences of Premature Ovarian Insufficiency: A Thematic Synthesis. *Psychology & Health*, 38(4): 431–447.
- [8] Eftekhari Z, Mousavi SM, Rahimi A, et al., 2025, Factors Affecting the Intention of Childbearing Among Nurses in Iran. *BMC Nursing*, 24(1): 118.
- [9] Wang Y, Li H, Chen TT, 2021, Research Progress on the Correlation Between Occupational Stress and Reproductive Health Among Nurses. *Chinese Nursing Management*, 21(4): 627–631.

Publisher's note

Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Study on the Association Between Maternal Cognitive Emotion Regulation Strategies and Their Coping Styles and Mental Health in High-risk Pregnancies

Yeqing Su, Jinjin Qin, Jiejie Xing

Department of Obstetrics, Affiliated Hospital of Hebei University, Baoding 071000, Hebei, China

**Author to whom correspondence should be addressed.*

Copyright: © 2026 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* The correlation between cognitive emotion regulation strategies and the coping styles and mental health status of pregnant women with high-risk pregnancies was studied to provide a theoretical basis for clinical psychological intervention. *Methods:* 152 pregnant women with high-risk pregnancies who were hospitalized in the Department of Obstetrics and Gynecology of an A hospital and filed in the outpatient clinic from January 2022 to December 2023 were selected as the observation group, and 150 pregnant women with normal pregnancies who were hospitalized in the Department of Obstetrics and Gynecology and filed in the outpatient clinic during the same period were also selected as the control group. Cognitive emotion regulation questionnaire (CERQ-C), Chinese revised medical coping modes questionnaire (MCMQ), self-assessment of mental health symptoms (symptom-90), and self-assessment of mental health symptoms (MCMQ) were applied to the observation group. CERQ-C, MCMQ, SCL-90 and SCL-90 were used to assess the cognitive-emotional, coping mode and mental health status of the two groups, and to compare the differences in the scores of the scales and their dimensions. *Results:* The CERQ-C adaptive dimension scores of the observation group were lower than those of the control group, and the non-adaptive dimension scores were higher than those of the control group ($P < 0.01$); the MCMQ avoidance and submission dimensions scores of the observation group were higher, and the confrontation dimension scores were lower ($P < 0.05$); and the scores of all symptom dimensions on the SCL-90 of the observation group were significantly higher than those of the control group ($P < 0.05$). Among the high-risk subgroups, the severe obstetric hemorrhage risk group had the most prominent cognitive-emotional regulation imbalance, negative coping and psychological problems. Pearson correlation analysis showed that adaptive cognitive-emotional regulation was positively correlated with face-to-face coping ($r = 0.412$, $P < 0.01$), and non-adaptive cognitive-emotional regulation was significantly positively correlated with yielding coping, anxiety and depression and other psychological symptoms ($P < 0.01$). *Conclusion:* Mothers with high-risk pregnancies generally have cognitive emotion dysregulation, mostly adopt non-adaptive emotion regulation strategies, and tend to adopt negative coping styles of avoidance and submission, accompanied by obvious mental health problems, and the psychological stress problems of pregnant women with severe obstetric hemorrhage risk are the most significant. Clinical assessment of the cognitive emotion regulation ability of this group should be emphasized, and precise psychological interventions should

be carried out to improve their mental health and pregnancy outcomes.

Keywords: High-risk pregnancy; Cognitive-emotional regulation; Coping style; Mental health; Correlation study

Online publication: May 31, 2026

1. Introduction

High-risk pregnancy is a state of pregnancy in which the mother is affected by certain pathologic and physiologic factors during pregnancy, which may cause adverse outcomes for the mother and the fetus or newborn ^[1]. With the adjustment of China's fertility policy, the increase in the proportion of older pregnant women and the popularization of assisted reproductive technology, the incidence of high-risk pregnancy has been on the rise year by year. Common clinical risk factors include hypertensive disorders in pregnancy, gestational diabetes, and the risk of severe obstetric hemorrhage, which not only threaten the lives of mothers and infants but also bring great psychological pressure to pregnant women. If psychological intervention is not carried out on time, it not only affects treatment compliance and quality of life but also may further aggravate the pregnancy comorbidities through neuroendocrine pathways, forming a vicious circle ^[2]. Cognitive emotion regulation refers to the process by which individuals consciously adopt cognitive ways to manage and regulate their emotions in the face of stressful events, and is categorized into adaptive and non-adaptive strategies ^[3], with the former helping individuals to cope with stress positively and constructively, whereas the latter may exacerbate negative emotions and lead to adverse psychological consequences ^[4]. Currently, the role of cognitive emotion regulation in the mental health of the general population has been widely verified, but the research in the special group of high-risk pregnancy is still relatively limited, based on this, the present study conducted a small-sample clinical trial to compare and analyze the effects of different cognitive emotion regulation strategies on the coping styles and mental health of pregnant women with high-risk pregnancies, with a view to providing scientific evidence for the development of targeted psychological intervention programs for pregnant women with high-risk pregnancies. In order to provide a scientific basis for the development of targeted psychological intervention programs for pregnant women with high-risk pregnancies.

2. Data and methods

2.1. General information

152 cases of pregnant women with high-risk pregnancies who were hospitalized in the obstetrics department of the maternity hospital of a hospital or outpatient clinic from January 2022 to December 2023 were selected as the observation group, and were divided into four subgroups according to the type of high-risk: 43 cases of gestational hypertension, 47 cases of gestational diabetes mellitus, 33 cases of severe obstetric hemorrhage risk group, and 29 cases of intrauterine distress group. In the same period, 150 cases of normal pregnancy pregnant women were selected as the control group.

Inclusion criteria: (1) singleton pregnancy, clearly diagnosed as high-risk pregnancy, in line with the diagnostic criteria for high-risk pregnancy in Obstetrics and Gynecology (9th edition); (2) age 22-39 years old; (3) gestational weeks ≥ 12 weeks; (4) love of the purpose of this study, methodology, and voluntary

participation in the study, and to obtain the consent of the knowledge of the youth. Exclusion criteria: (1) those who have a history of mental illness or are receiving psychotropic medication; (2) those who are accompanied by malignant tumors, severe liver and renal insufficiency diseases; (3) those who have cognitive dysfunction and are unable to cooperate in completing the questionnaire research.

2.2. Methods

2.2.1. Survey instruments

- (1) General information questionnaire: the hospital's own questionnaire was used to collect maternal demographic data and obstetric clinical baseline information.
- (2) Cognitive emotion regulation: the CERQ-C contains 9 independent subscales, totaling 36 assessment entries, which can be divided into two major dimensions of adaptive and non-adaptive emotion regulation strategies as a whole^[5]. The adaptive strategy dimension consists of five subscales, including acceptance, positive attention shift, behavioral reprogramming, positive cognitive restructuring, and rational analysis, corresponding to 20 items; and the non-adaptive strategy dimension consists of four subscales, including self-blame, repetitive thinking, catastrophic thinking, and blaming others, corresponding to 16 items. The scale was scored on a scale of 1 to 5, with 1 representing never use and 5 representing always use, and the scoring interval for each subscale was 5 to 20, with higher scores indicating more frequent use of this type of emotion regulation. The overall Cronbach's alpha coefficient of the scale was tested to be 0.83, and the Kappa coefficient was 0.61, with good reliability and validity, which can meet the needs of this study's assessment.
- (3) Coping styles: MCMQ has a total of 20 assessment entries, which are divided into three core dimensions: face coping, avoidance coping, and yielding and accepting coping, and each dimension contains 8, 7, and 5 assessment topics, respectively, and the overall scale adopts a four-level scoring model from 1 to 4 points, and the higher the score of a single dimension, the more the research subject tends to adopt the disease coping styles corresponding to that dimension^[6]. After testing, the Cronbach's alpha coefficient of the scale was 0.81, and the Kappa coefficient was 0.52; the reliability index was good, and the assessment results were real and reliable.
- (4) Mental health status: SCL-90 has a total of 90 assessment topics, covering 9 core factors of somatic discomfort, obsessive-compulsive behaviors, interpersonal sensitivity, depression, anxiety state, hostility, terror, paranoid thinking, and psychotic symptoms, as well as 1 additional factor, which can comprehensively reflect the characteristics of the individual's psychological abnormalities^[7]. All entries were scored on a scale of 1 to 5, with 1 being no relevant symptoms and 5 being extremely severe symptoms. The total score of the scale corresponds to the following criteria for the classification of the degree of symptoms: 1–1.5 points suggests no psychological symptoms; 1.5–2.5 points suggests the presence of mild episodic symptoms; 2.5–3.5 points suggests the presence of mild and moderate psychological symptoms; 3.5–4.5 points suggests the presence of moderate and severe psychological symptoms; and 4.5–5.0 points suggests the presence of severe psychological symptoms. The empirical data show that the Cronbach's alpha coefficient of the scale is 0.96 and the Kappa coefficient is 0.68, with excellent reliability and validity, which is suitable for this research on maternal mental health status.

2.2.2. Survey method

Uniformly trained medical and psychological personnel carried out the survey, unifying the instruction of the discourse and standardizing the survey process. The form of anonymous questionnaire completion is used, and all questionnaires are completed and answered within 1 week to ensure that the emotional state of pregnant women is stable. The questionnaires were verified on the spot, reviewed twice, and invalid questionnaires with omissions, logical contradictions, and homogenized answers were excluded, so that the quality of the data was strictly controlled.

2.3. Observation indicators

Observe the maternal CERQ-C adaptive and non-adaptive dimension scores of the two groups; MCMQ face, avoid, yield dimension scores; SCL-90 scores of each psychological symptom dimension, and analyze the correlation between the three.

2.4. Statistical methods

SPSS 25.0 statistical software was applied to carry out statistical processing. The normal score measurement information is expressed as the mean \pm standard deviation (SD), and the comparison between the two groups was made using the independent samples t-test. Count data were expressed as the number of cases (%), and comparisons between groups were made using the χ^2 test. The correlation between cognitive emotion regulation and coping styles and mental health was analyzed using Pearson software. The difference was considered statistically significant at $P < 0.05$.

3. Results

3.1. Comparison of CERQ-C scale scores between the two groups

The total score of CERQ-C adaptive dimension in the observation group was (62.86 ± 10.95), which was significantly lower than that of (68.56 ± 10.24) in the positive control group ($t = 4.671$, $P = 0.003$). The total score of the non-adaptive dimension in the observation group was (63.35 ± 10.37), which was significantly higher than (60.91 ± 9.59) in the control group ($t = 2.122$, $P = 0.035$). Among the subgroups of high-risk pregnancies, the lowest adaptive dimension scores and non-adaptive dimension scores were in the group at risk of severe obstetric hemorrhage, as shown in **Table 1**.

Table 1. Comparison of maternal CERQ-C scale scores between the two groups (mean \pm SD, points)

Group	Adaptive dimension	Non-adaptive dimension
Control group (n = 150)	68.56 ± 10.24	60.91 ± 9.59
Observation group (n = 152)	62.86 ± 10.95	63.35 ± 10.37
Gestational hypertension group (n = 43)	15.81 ± 2.65	16.12 ± 2.48
Gestational diabetes group (n = 47)	16.43 ± 2.78	15.56 ± 2.63
Severe obstetric hemorrhage risk group (n = 33)	14.57 ± 2.69	16.79 ± 2.71
Fetal intrauterine distress group (n = 29)	16.05 ± 2.83	14.88 ± 2.55

3.2. Comparison of MCMQ scale scores between the two groups

The scores of avoidance and yielding (acceptance) dimensions in the observation group were higher than

those of the control group, and the scores of the facing dimension were lower than those of the control group; the differences were statistically significant ($t = 2.290, 3.760, 2.427, P = 0.023, 0.000, 0.016$). In the subgroup of high-risk pregnancies, the highest scores on the avoidance and yielding (acceptance) dimensions and the lowest scores on the facing dimension pointed to the risk of severe obstetric hemorrhage, as shown in **Table 2**.

Table 2. Comparison of maternal MCMQ scale scores between the two groups (mean \pm SD, points)

Group	Facing dimension	Avoidance dimension	Submission (acceptance) dimension
Control group (n = 150)	63.48 \pm 8.89	60.12 \pm 9.65	61.56 \pm 7.65
Observation group (n = 152)	60.93 \pm 9.36	62.74 \pm 10.22	64.81 \pm 7.37
Gestational hypertension group (n = 43)	15.11 \pm 2.55	15.67 \pm 2.75	16.25 \pm 1.89
Gestational diabetes group (n = 47)	16.25 \pm 2.17	14.62 \pm 2.53	15.36 \pm 1.83
Severe obstetric hemorrhage risk group (n = 33)	14.19 \pm 2.43	16.83 \pm 2.49	17.33 \pm 1.78
Fetal intrauterine distress group (n = 29)	15.38 \pm 2.21	15.62 \pm 2.45	15.87 \pm 1.87

3.3. Comparison of SCL-90 scale scores between the two groups

The scores of the nine symptom dimensions of the SCL-90 scale in the observation group were significantly higher than those in the control group, and the differences were all statistically significant ($P < 0.05$). Among the high-risk subgroups, the group at risk of severe obstetric hemorrhage had the highest scores on all psychological symptom dimensions and the most severely impaired mental health ($P < 0.05$). See **Table 3**.

Table 3. Comparison of maternal SCL-90 scale scores between the two groups (mean \pm SD, points)

Item	Control group (n = 150)	Observation group (n = 152)	High-risk pregnancy subgroup			
			Gestational diabetes group	Gestational hypertension-related group	Severe obstetric hemorrhage risk group	Fetal intrauterine distress group
Somatization dimension	22.58 \pm 3.11	33.65 \pm 4.47*	29.75 \pm 4.21	34.27 \pm 4.56	38.41 \pm 4.73	32.18 \pm 4.39
Dimension of obsessive-compulsive symptoms	17.85 \pm 3.73	29.19 \pm 4.66*	26.38 \pm 4.32	29.86 \pm 4.81	32.59 \pm 4.94	27.93 \pm 4.57
Dimension of interpersonal sensitivity	16.36 \pm 3.18	28.29 \pm 4.03*	25.93 \pm 3.87	28.75 \pm 4.02	31.62 \pm 4.26	26.86 \pm 3.95
Depression dimension	24.18 \pm 3.13	36.69 \pm 3.56*	32.42 \pm 3.35	37.19 \pm 3.62	41.26 \pm 3.78	35.87 \pm 3.48
Anxiety dimension	17.91 \pm 3.13	27.83 \pm 4.22*	24.66 \pm 4.01	28.33 \pm 4.28	31.75 \pm 4.43	26.58 \pm 4.15
Hostile dimension	11.21 \pm 2.32	17.81 \pm 2.64*	15.79 \pm 2.53	18.37 \pm 2.68	20.12 \pm 2.74	16.94 \pm 2.61
Horror dimension	12.82 \pm 2.24	18.41 \pm 3.16*	15.67 \pm 3.05	18.94 \pm 3.17	21.58 \pm 3.29	17.45 \pm 3.11
Paranoia dimension	10.93 \pm 2.13	17.84 \pm 3.79*	15.32 \pm 3.61	18.49 \pm 3.85	20.74 \pm 3.97	16.83 \pm 3.72
Psychoticism dimension	18.65 \pm 3.42	26.86 \pm 3.35*	22.97 \pm 3.12	27.33 \pm 3.45	31.49 \pm 3.58	25.65 \pm 3.26

Note: * $P < 0.05$.

3.4. Correlation analysis of cognitive emotion regulation with coping styles and mental health status in high-risk pregnancy

The results of Pearson correlation analysis showed that the adaptive dimension of the CERQ-C scale was positively correlated with the confronting dimension of the MCMQ scale ($r = 0.412$, $P = 0.003$); and the non-adaptive dimension was positively correlated with the yielding dimension ($r = 0.387$, $P = 0.006$). Non-adaptive cognitive emotion regulation was significantly and positively correlated with SCL-90 somatization, depression, anxiety, and total score ($P < 0.01$), with the strongest correlation with depression and anxiety; the adaptive dimension had no significant correlation with the mental health indicators ($P > 0.05$), and the specific results are shown in **Table 4**.

Table 4. Correlation analysis of CERQ-C with MCMQ and SCL-90 (r value)

Variable	Adaptive dimension	Non-adaptive dimension
MCMQ-facing	0.412**	-0.124
MCMQ-Avoidance	-0.112	0.163
MCMQ-Yield	-0.201	0.387**
SCL-90-somatization	-0.098	0.415**
SCL-90-Depression	-0.142	0.502**
SCL-90-Anxiety	-0.135	0.478**
SCL-90-total score	-0.156	0.443**

Note: ** $P < 0.01$.

4. Discussion

With the change of China's family planning policy, the proportion of high-age pregnant women continues to rise, resulting in a yearly increase in the number of high-risk pregnancies, which has become a key problem that threatens the health of mothers and infants and increases the burden on public health^[8]. This study found that pregnant women with high-risk pregnancies have significant cognitive-emotional regulation imbalances, and they are less likely to use positive cognitive regulation strategies and rely excessively on non-adaptive strategies, such as catastrophizing and self-blame, compared with women with normal pregnancies. A high-risk pregnancy is a persistent, uncontrollable stressor. Mothers facing long-term psychological pressure of fetal safety and unknown pregnancy outcome are prone to fall into a negative cognitive cycle, which depletes their psychological resources and ultimately leads to dysfunctional emotion regulation.

There are significant gradient differences in the psychological status of different high-risk types of pregnant women, among which the cognitive imbalance, negative coping, and psychological symptoms of pregnant women at risk of severe obstetric hemorrhage are the most serious. The reason for this is that obstetric hemorrhage has an acute onset and a high risk of death, which can bring strong fear of survival to pregnant women and trigger extreme negative cognition; whereas in high-risk pregnancies that are more controllable, such as gestational diabetes mellitus, pregnant women can control their condition through standardized interventions, and their psychological stress is relatively moderate. Their cognitive regulation is better^[9].

The present study found that the negative coping styles of avoidance and submission were commonly used by pregnant women with high-risk pregnancies. Avoidance is characterized by deliberate neglect

of the condition, avoidance of obstetric examination and communication of the condition, which may temporarily relieve anxiety but delays clinical intervention and aggravates the risk of pregnancy; submission is characterized by learned helplessness and passive acceptance of poor outcomes, leading to decreased treatment adherence. Negative coping is a direct result of an imbalance in cognitive-emotional regulation and is an important mediator in triggering various types of psychological problems. SCL-90 results confirm that high-risk pregnant women have a significantly high prevalence of anxiety, depression, and somatization symptoms, and that long-term psychological stress not only affects mental health but also triggers endocrine disruption, aggravates pregnancy comorbidities, and creates a vicious circle ^[10]. The results of correlation analysis showed that adaptive cognitive emotion regulation can promote individuals to adopt positive coping styles, while non-adaptive regulation can prompt individuals to succumb to stress, which in turn induces anxiety, depression and other psychological problems. Adaptive regulation was not directly correlated with psychological health in this study because of the high stress intensity of high-risk pregnancy, and the psychoprotective effects of positive cognitive strategies were masked by the high-intensity stressors, which only indirectly alleviated psychological stress by improving coping styles.

5. Conclusion

In conclusion, cognitive-emotional dysregulation is the core causative factor of negative coping and psychological abnormalities in high-risk pregnancies, and the higher the risk of disease, the more serious the cognitive dysregulation and psychological problems. In clinical work, we need to abandon the traditional model of “focusing on the physical, but not on the psychological”, and incorporate cognitive-emotional regulation assessment and psychological screening into the routine management of high-risk pregnancy. We should carry out stratified interventions for different risk levels of pregnant women, focusing on high-risk groups such as severe obstetric hemorrhage risk, correcting non-adaptive emotion regulation patterns through cognitive interventions, and guiding positive coping styles, to improve the state of maternal mental health and optimize the outcome of pregnancy for mothers and infants.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Zhao HY, Wang Y, 2022, Effects of Sleep and Emotional Status During Pregnancy on Maternal Early Cognitive Function. *Chongqing Medicine*, 51(12): 2157–2160.
- [2] Chen Y, Pan X, Zhou C, et al., 2023, Analysis of Anxiety and Depression in Pregnant Women in Late Pregnancy and the Need for Psychological Intervention. *China Maternal and Child Health Care*, 38(1): 1–6.
- [3] Ding W, Xu X, Zhang Y, et al., 2023, Prevalence Characteristics of High-Risk Pregnancy Factors and Their Impact on Pregnancy Outcomes in Huai'an City. *China Maternal and Child Health*, 38(12): 2218–2223.
- [4] Wang X, 2023, Analysis of Maternal Risk Factors for High-Risk Pregnancy and Its Treatment. *Chinese Science and Technology Journal Database (Full Text Edition) Medicine and Health*, (9): 63–66.
- [5] Qu M, Yang L, Wang J, et al., 2022, The Roles of Cognitive Emotion Regulation Strategies and Punishment

- Sensitivity Between Parental Psychological Control and Adolescent Non-Suicidal Self-Injurious Behavior. *Chinese Journal of Clinical Psychology*, 30(5): 1192–1197.
- [6] Yang M, Wu Z, 2026, The Effect of Nursing Care Under the Quantitative Assessment Strategy Model on Pregnancy Outcomes and Psychological Status of Women with Hypertension-Related High-Risk Pregnancies. *Marriage and Health*, 32(10): 16–18.
- [7] Wang Y, Yan Q, 2026, The Mediating Effect of Cognitive Emotion Regulation on the Relationship Between Maternal Anxiety and Coping Styles in High-Risk Pregnancies. *Chinese Journal of Modern Nursing*, 32(7): 949–953.
- [8] Li Z, Sun N, Wang S, 2026, Analysis of Factors Affecting Maternal Birth Trauma in High-Risk Pregnancies. *Preventive Medicine*, 38(2): 140–144.
- [9] He L, Cai M, Xin D, 2026, Analysis of the Current Situation and Influencing Factors of Postpartum Delivery Trauma in Women With High-Risk Pregnancies. *Chinese Journal of Family Planning*, 34(1): 10–15.
- [10] Liu Y, Chen C, Wan W, 2025, Analysis of the Current Situation and Influencing Factors of Psychological Help-Seeking Stigma Among Pregnant Women With High-Risk Pregnancies. *Shanghai Nursing Care*, 25(11): 61–65.

Publisher's note

Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Research Progress in Clinical Treatment of Polycystic Ovary Syndrome from the Perspective of Evidence-Based Medicine: A Comprehensive Evaluation of Hormonal Therapy and Traditional Chinese Medicine Regimens

Zhao Wang, Nan Li*

Shaanxi University of Chinese Medicine, Xianyang 712000, Shaanxi, China

**Author to whom correspondence should be addressed.*

Copyright: © 2026 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: Polycystic ovary syndrome (PCOS) is a common endocrine disorder that significantly impairs female fertility and overall health. With the advancement of evidence-based medicine, therapeutic approaches for PCOS have become increasingly diversified. As two major treatment modalities, hormonal therapy and traditional Chinese medicine (TCM) have attracted widespread attention. Although numerous studies have explored the efficacy and safety of different treatment regimens, many controversies and deficiencies still exist in clinical practice. From the perspective of evidence-based medicine, this review systematically assesses the clinical application effects of hormonal therapy and TCM for PCOS. Through a comprehensive analysis of relevant literature, it compares the efficacy of various treatments and puts forward evidence-based therapeutic recommendations. This study aims to provide a scientific reference for clinical decision-making and promote the progress of comprehensive management and treatment of PCOS.

Keywords: Polycystic ovary syndrome; Evidence-based medicine; Hormonal therapy; Traditional Chinese medicine; Clinical treatment

Online publication: May 31, 2026

1. Introduction

Polycystic ovary syndrome (PCOS) is a complex endocrine disease, mainly characterized by polycystic ovarian changes, irregular menstruation, and a variety of metabolic abnormalities, including insulin resistance and obesity. Its pathogenesis has not been fully elucidated, yet it is closely associated with multiple factors such as heredity, environment and lifestyle. In recent years, as the understanding of PCOS

deepens, clinical treatment strategies have become more sophisticated. Traditional treatment mainly relies on hormonal therapy. Along with the development of evidence-based medicine and TCM, a growing number of studies have focused on the application of TCM in PCOS treatment. Evidence-based medicine is a medical decision-making model based on research evidence, which emphasizes integrating the best available research evidence, clinical experience and patients' values in clinical practice. In the treatment of PCOS, evidence-based medicine provides a more scientific basis for clinical decisions and enables more individualized and precise selection of treatment strategies. Recent studies have demonstrated that hormonal therapy can effectively relieve irregular menstruation, restore ovulatory function, and ameliorate metabolic abnormalities in PCOS patients ^[1], while TCM shows unique advantages in improving physical constitution and overall symptoms ^[2]. This article comprehensively reviews the latest research progress of hormonal therapy and TCM for PCOS treatment, and proposes effective clinical treatment strategies from the perspective of evidence-based medicine. By reviewing and analyzing relevant literature, we discuss the efficacy and safety of different therapies, so as to offer a more scientific basis for the management of PCOS patients. It is hoped that this review can provide references for clinical treatment of PCOS.

2. Pathophysiology and therapeutic approaches for polycystic ovary syndrome: from hormonal therapy to traditional Chinese medicine

2.1. Pathophysiological mechanisms of polycystic ovary syndrome

2.1.1. Endocrine disorders and metabolic abnormalities

The core manifestations of PCOS include endocrine disorders and metabolic abnormalities. PCOS patients usually present with hyperandrogenism, irregular menstruation, as well as quantitative and morphological changes of ovarian follicles under ultrasonography. Endocrine disorders are mainly reflected in abnormal hormone secretion in the ovaries and pituitary gland. Among them, insulin resistance is regarded as one of the vital pathophysiological mechanisms of PCOS. Studies have shown that decreased insulin sensitivity in PCOS patients leads to elevated insulin levels, which further stimulate the ovaries to produce more androgens, aggravate hyperandrogenism and hinder follicular development ^[3]. PCOS is also closely correlated with metabolic syndrome. Many patients suffer from metabolic disorders such as obesity, hyperglycemia and hyperlipidemia, which increase the risk of cardiovascular diseases ^[4]. In terms of metabolic abnormalities, PCOS patients are often accompanied by lipid metabolism disorders, manifested as elevated triglycerides and decreased high-density lipoprotein cholesterol. This condition is associated with increased levels of systemic inflammation and oxidative stress ^[1]. Researches indicate that the application of antioxidants may help alleviate oxidative stress, so as to improve the endocrine and metabolic status of PCOS patients ^[2]. Comprehensive interventions targeting endocrine and metabolic abnormalities, including lifestyle modification and pharmacotherapy, are of great significance for the treatment of PCOS.

2.1.2. Impacts of genetic and environmental factors

The pathogenesis of PCOS is affected not only by endocrine and metabolic factors, but also by genetic and environmental factors, which cannot be ignored. Recent relevant studies have proved that PCOS has an obvious familial aggregation. Many immediate relatives of patients have similar symptoms, suggesting that genetic factors play a pivotal role in the onset of PCOS ^[5]. Specifically, multiple genes related to insulin signaling pathways, as well as androgen synthesis and metabolism, are correlated with the risk of PCOS ^[6].

Environmental pollution, dietary habits and lifestyles may all affect the occurrence and progression of PCOS. Exposure to endocrine disruptors such as bisphenol A can disturb hormonal balance in the human body and further increase the risk of developing PCOS ^[7]. In addition, lifestyle factors, including obesity and physical inactivity, are recognized as important risk factors for PCOS. Obesity not only exacerbates insulin resistance but also worsens PCOS symptoms by affecting hormone levels ^[8]. Therefore, understanding the interaction between genetic and environmental factors provides important guidance for the prevention and treatment of PCOS.

2.2. Clinical application of hormonal therapy

2.2.1. Selective estrogen receptor modulators (SERMs)

Selective estrogen receptor modulators (SERMs) are a class of tissue-specific drugs that exert pharmacological effects by selectively activating or inhibiting estrogen receptors. SERMs show promising prospects in a variety of clinical applications. In research on neuroendocrine diseases, SERMs can promote remyelination in the central nervous system independent of estrogen receptor activation ^[9]. They also exert positive regulatory effects on metabolism by modulating estrogen signaling pathways ^[10].

2.2.2. Oral contraceptives and their mechanisms of action

Oral contraceptives are mainly composed of estrogen and progestogen. They exert contraceptive effects through multiple mechanisms and also play a certain role in the treatment of PCOS. In recent years, studies have found that some new-generation oral contraceptives (such as the combination containing estetrol and drospirenone) achieve satisfactory efficacy in relieving irregular menstruation and premenstrual syndrome ^[11]. Despite the remarkable effect of oral contraceptives in improving menstrual disorders, attention should be paid to their potential side effects in clinical application, such as increased risks of thrombosis and breast cancer ^[12]. Clinicians shall fully evaluate patients' physical conditions and risk factors before making prescriptions in clinical practice.

2.2.3. Insulin sensitizers

Insulin sensitizers (represented by metformin) play an important role in the treatment of PCOS. They can effectively improve insulin sensitivity, help regulate menstrual cycles and promote ovulation ^[13]. Studies have shown that metformin can not only lower blood glucose, but also ameliorate PCOS-related metabolic abnormalities such as hyperinsulinemia and obesity ^[14]. Furthermore, metformin is proven to improve fertility and increase ovulation rate, especially for obese PCOS patients ^[15]. Recent studies also point out that combining metformin with other treatments, such as lifestyle interventions and other medications, can further enhance therapeutic effects ^[16]. Although insulin sensitizers have remarkable efficacy in the treatment of PCOS, their potential adverse reactions still require close attention.

2.3. Theoretical basis and clinical practice of TCM in treating PCOS

2.3.1. TCM understanding of polycystic ovary syndrome

From the perspective of TCM, the onset of PCOS is closely related to liver Qi stagnation, deficiency of both spleen and kidney, and internal retention of phlegm-dampness, which leads to disordered Qi and blood as well as imbalance of yin and yang. Liver Qi stagnation disturbs menstrual cycles and causes ovarian dysfunction; spleen deficiency and internal retention of phlegm-dampness may lead to accumulation of

phlegm-dampness in the body and consequently result in polycystic ovarian changes; kidney deficiency impairs reproductive function and affects the quality and quantity of oocytes ^[17]. Meanwhile, TCM attaches great importance to emotional factors. In the TCM treatment of PCOS, syndrome differentiation and treatment are often adopted in combination with patients' emotional states. The treatment aims to soothe Qi movement, restore the balance of Qi and blood, improve endocrine function, and thereby promote the normal physiological activities of the ovaries ^[18].

2.3.2. Efficacy research on Chinese herbal compounds

Chinese herbal medicines occupy an important position in the treatment of PCOS. Studies have verified that classic TCM formulas, including Siwu Decoction and Xiaoyao Powder, have significant effects on regulating menstruation and improving ovarian function ^[19]. With in-depth research on the active ingredients and action mechanisms of Chinese herbs in recent years, scholars have found that certain herbal components, such as tanshinone, can improve insulin sensitivity and regulate endocrine levels, so as to relieve PCOS-related symptoms ^[20]. In addition, the application of network pharmacology enables researchers to better interpret the action mechanisms of herbal compounds and explore their potential in regulating endocrine and metabolism for PCOS treatment ^[21].

2.3.3. Evidence-based analysis of acupuncture efficacy

Acupuncture also delivers favorable therapeutic effects in the treatment of PCOS. Multiple clinical studies have confirmed that acupuncture can effectively relieve irregular menstruation and abnormal hormone levels in PCOS patients ^[22]. Randomized controlled trials on PCOS patients show that acupuncture can significantly reduce androgen levels, raise ovulation rate and improve fertility ^[23]. Moreover, acupuncture can regulate the hypothalamic-pituitary-ovarian axis to restore ovarian function, thus exerting a positive impact on the pathological process of PCOS ^[24]. The results of evidence-based analysis further validate the effectiveness of acupuncture as an adjuvant therapy for PCOS.

2.4. Comparative study on hormonal therapy and TCM

2.4.1. Efficacy comparison: Pregnancy rate and menstrual regularity

Comparing the efficacy of hormonal therapy and TCM in terms of pregnancy rate and menstrual regularity is an important research direction. Hormonal therapy is generally recognized as an effective intervention to improve fertility, especially for PCOS patients complicated with other endocrine disorders. Studies indicate that hormone replacement therapy can effectively regularize menstrual cycles and increase pregnancy rates ^[25]. Meanwhile, TCM also achieves good results, especially in regulating menstruation and promoting ovulation. Systematic reviews demonstrate that TCM therapies based on the theories of tonifying the kidney and regulating liver exert prominent clinical effects on women with diminished ovarian reserve and can increase pregnancy rates ^[26]. In addition, relevant studies on PCOS confirm that TCM has satisfactory efficacy in relieving irregular menstruation and increasing ovulation frequency ^[27]. In summary, hormonal therapy and TCM have their respective advantages. Hormonal therapy may produce more rapid effects in the short term, while TCM shows unique value in relieving symptoms and treating patients with poor or no response to hormonal therapy.

2.4.2. Safety assessment and adverse reactions

The comparison of adverse reactions and safety is equally important. Hormonal therapy is often accompanied by side effects such as weight gain, mood swings and breast distending pain, which compromise patients' quality of life ^[28]. In addition, long-term use of hormones may increase the risks of cardiovascular diseases and malignant tumors, including breast cancer ^[29]. In contrast, TCM is generally considered relatively safe with fewer adverse reactions. Research shows that TCM rarely causes severe adverse events when applied to treat menstrual disorders and infertility ^[30]. The combined therapy of Chinese herbal medicine and acupuncture can effectively relieve symptoms with minimal side effects ^[31]. Nevertheless, the efficacy and safety of TCM are affected by individual physical differences and specific treatment regimens. Therefore, multiple factors should be taken into careful consideration when selecting treatment plans.

2.5. Therapeutic recommendations under the framework of evidence-based medicine

2.5.1. Significance of individualized treatment strategies

Individualized treatment strategies have gained increasing attention in modern medicine, especially for chronic and complex diseases. By comprehensively taking patients' genetic background, lifestyle, medical history and treatment response into account, clinicians can formulate more precise treatment regimens. Studies have shown that individualized medication can significantly reduce the incidence of complications and improve patients' quality of life ^[32]. Meanwhile, the hormonal treatment strategies for non-binary patients also prove the necessity of individualized therapy, which can not only improve patients' physical conditions but also promote their mental health ^[33]. The implementation of individualized treatment relies on an in-depth understanding of patient characteristics and continuous monitoring of treatment outcomes, which provides an important basis for future treatment plans. Therefore, individualized treatment strategies can not only enhance therapeutic efficacy but also reduce unnecessary adverse reactions, representing an important development trend of modern medicine.

2.5.2. Multidisciplinary collaboration and comprehensive treatment

Multidisciplinary collaboration presents remarkable advantages in the treatment of complex diseases, especially for cancers, cardiovascular diseases and chronic illnesses. A medical team integrating professional knowledge and skills from different disciplines can formulate more comprehensive treatment plans. Multidisciplinary teamwork ensures that patients receive all-around care during treatment ^[34]. This model improves the efficiency of medical services and optimizes patients' medical experience, making them feel more care and supported in the course of complex treatment. Hence, multidisciplinary collaboration is the key to realizing comprehensive treatment under the framework of evidence-based medicine, and can provide safer and more effective treatment regimens for patients.

3. Conclusion

This article summarizes the clinical research progress of hormonal therapy and TCM for PCOS treatment, and highlights the importance of evidence-based medicine. Analysis of existing studies reveals that the two therapeutic approaches present distinct efficacy in different patient groups. This reminds clinicians that individualized demands of patients must be considered to achieve optimal therapeutic outcomes when formulating treatment plans. Hormonal therapy works well in relieving PCOS symptoms, regularizing

menstrual cycles and improving fertility, and is particularly suitable for patients with predominant hormonal imbalance. However, some patients may have a poor response or even discomfort due to the side effects of hormones or individual sensitivity to hormones. In such cases, the advantages of TCM become prominent. By regulating Yin-Yang and unblocking Qi and blood, TCM provides an alternative therapeutic approach for patients.

From the perspective of evidence-based medicine, the combined treatment integrating modern Western medicine and traditional Chinese medicine can better meet diverse clinical demands. Future research should pay more attention to the assessment of individual differences among patients and explore the application potential of combined therapies. Through collecting and analyzing large-scale clinical data, we can clearly clarify the treatment response of different patient groups and further guide the development of individualized treatment.

In conclusion, treatment strategies based on evidence-based medicine can improve the quality of life of PCOS patients and point out valuable directions for subsequent research. The necessity of conducting multi-center clinical trials and prospective studies is self-evident. Only through continuous integration and innovation can we provide safer and more effective treatment options for PCOS patients and achieve better therapeutic effects.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Peker N, Turan G, Ege S, et al., 2021, The Effect of Clomiphene Citrate on Oxidative Stress Parameters in Polycystic Ovarian Syndrome. *J Obstet Gynaecol*, 41(1): 112–117.
- [2] Achu JR, Ajitkumar S, Kanakasabapathy BS, et al., 2023, Evaluation of Microbial Profile in Patients with Polycystic Ovary Syndrome and Periodontal Disease: A Case-Control Study. *Int J Fertil Steril*, 17(4): 248–253.
- [3] Stener-Victorin E, Teede H, Norman RJ, et al., 2024, Polycystic Ovary Syndrome. *Nat Rev Dis Primers*, 10(1): 27.
- [4] Benham JL, Goldberg A, Teede H, et al., 2024, Polycystic Ovary Syndrome: Associations with Cardiovascular Disease. *Climacteric*, 27(1): 47–52.
- [5] Wang Y, Guo L, Jiang J, et al., 2021, Development of 1–2 Years Offspring Born to Mothers with Polycystic Ovary Syndrome. *J Coll Physicians Surg Pak*, 31(10): 1186–1190.
- [6] Shinoda M, Hayashi Y, Kubo A, et al., 2020, Pathophysiological Mechanisms of Persistent Orofacial Pain. *J Oral Sci*, 62(2): 131–135.
- [7] Polak G, Banaszewska B, Filip M, et al., 2021, Environmental Factors and Endometriosis. *Int J Environ Res Public Health*, 18(21): 11025.
- [8] Khalaf S, Al Anzy M, Sarhat E, 2024, Impact of Metformin on Osteoprotegerin Levels in Polycystic Ovarian Women. *Georgian Med News*, (346): 144–146.
- [9] Rankin KA, Mei F, Kim K, et al., 2019, Selective Estrogen Receptor Modulators Enhance CNS Remyelination Independent of Estrogen Receptors. *J Neurosci*, 39(12): 2184–2194.
- [10] Goldstein SR, 2022, Selective Estrogen Receptor Modulators and Bone Health. *Climacteric*, 25(1): 56–59.
- [11] Paton DM, 2022, Estetrol and Drospirenone: A Novel Oral Contraceptive. *Drugs Today (Barc)*, 58(1): 1–8.

- [12] Mierzejewska A, Walędziak M, Merks P, et al., 2024, Emergency Contraception – A Narrative Review of Literature. *Eur J Obstet Gynecol Reprod Biol*, 299: 188–192.
- [13] Amisi CA, 2022, Markers of Insulin Resistance in Polycystic Ovary Syndrome Women: An Update. *World J Diabetes*, 13(3): 129–149.
- [14] Yu H, Sun J, Hu H, 2024, Prophylactic Administration of Metformin Reduces Gestational Diabetes Mellitus Incidence in the High-Risk Populations: A Meta-Analysis of Metformin for Gestational Diabetes Prevention. *Ir J Med Sci*, 193(1): 199–209.
- [15] Dinicola S, Unfer V, Soulage CO, et al., 2024, d-Chiro-Inositol in Clinical Practice: A Perspective from the Experts Group on Inositol in Basic and Clinical Research (EGOI). *Gynecol Obstet Invest*, 89(4): 284–294.
- [16] Guarano A, Capozzi A, Cristodoro M, et al., 2023, Alpha Lipoic Acid Efficacy in PCOS Treatment: What Is the Truth? *Nutrients*, 15(14): 3209.
- [17] Chen H, Deng C, Meng Z, et al., 2023, Effects of TCM on Polycystic Ovary Syndrome and Its Cellular Endocrine Mechanism. *Front Endocrinol (Lausanne)*, 14: 956772.
- [18] Zhang Y, Guo X, Ma S, et al., 2021, The Treatment with Complementary and Alternative Traditional Chinese Medicine for Menstrual Disorders with Polycystic Ovary Syndrome. *Evid Based Complement Alternat Med*, 2021: 6678398.
- [19] Fu LW, Gao Z, Zhang N, et al., 2024, Traditional Chinese Medicine Formulae: A Complementary Method for the Treatment of Polycystic Ovary Syndrome. *J Ethnopharmacol*, 323: 117698.
- [20] Yang Y, Xia Y, Peng X, et al., 2021, Tanshinone for Polycystic Ovary Syndrome: A Protocol of Systematic Review and Meta-Analysis. *Medicine (Baltimore)*, 100(3): e24287.
- [21] Chen Y, Chai X, Zhao Y, et al., 2021, Investigation of the Mechanism of Zishen Yutai Pills on Polycystic Ovary Syndrome: A Network Pharmacology and Molecular Docking Approach. *Evid Based Complement Alternat Med*, 2021: 6843828.
- [22] Cao Y, Chen H, Zhao D, et al., 2019, The Efficacy of Tung's Acupuncture for Sex Hormones in Polycystic Ovary Syndrome: A Randomized Controlled Trial. *Complement Ther Med*, 44: 182–188.
- [23] Li H, Li Y, Zhang Y, et al., 2023, *Rubus chingii* Hu Relieved the Polycystic Ovary Syndrome with Enhanced Insulin Sensitivity Through Inhibiting TXNIP/NLRP3 Inflammasome Signaling. *Gynecol Endocrinol*, 39(1): 2237116.
- [24] Lu LJ, Zhang J, Jiang Y, et al., 2024. *Zhongguo Zhong Yao Za Zhi*, 49(1): 1–14.
- [25] Sun L, Yin B, Yao Z, et al., 2024, Comparison of Clinical Outcomes and Perinatal Outcomes Between Natural Cycle and Hormone Replacement Therapy of Frozen-Thawed Embryo Transfer in Patients with Regular Menstruation: A Propensity Score-Matched Analysis. *Front Endocrinol (Lausanne)*, 15: 1416841.
- [26] Liu L, Liu Y, Yang M, et al., 2020, Effectiveness of Tonifying-Kidney and Regulating-Liver Therapy on Diminished Ovarian Reserve: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *J Tradit Chin Med*, 40(3): 343–354.
- [27] Hu J, Shi W, Xu J, et al., 2021, Complementary and Alternative Medicine for the Treatment of Abnormal Endometrial Conditions in Women with PCOS: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Evid Based Complement Alternat Med*, 2021: 5536849.
- [28] Lethaby A, Wise MR, Weterings MA, et al., 2019, Combined Hormonal Contraceptives for Heavy Menstrual Bleeding. *Cochrane Database Syst Rev*, 2(2): CD000154.
- [29] Orsolini L, Pompili S, Volpe U, 2020, The 'Collateral Side' of Mood Stabilizers: Safety and Evidence-Based

Strategies for Managing Side Effects. *Expert Opin Drug Saf*, 19(11): 1461–1495.

- [30] Meng Z, Chen H, Deng C, et al., 2022, Potential Cellular Endocrinology Mechanisms Underlying the Effects of Chinese Herbal Medicine Therapy on Asthma. *Front Endocrinol (Lausanne)*, 13: 916328.
- [31] Wang LL, Xiang YG, Tan L, et al., 2021. *Zhongguo Zhen Jiu*, 41(7): 742–746.
- [32] Mohamad T, Jyotsna F, Farooq U, et al., 2023, Individualizing Medicinal Therapy Post Heart Stent Implantation: Tailoring for Patient Factors. *Cureus*, 15(8): e43977.
- [33] Cocchetti C, Ristori J, Romani A, et al., 2020, Hormonal Treatment Strategies Tailored to Non-Binary Transgender Individuals. *J Clin Med*, 9(6): 1609.
- [34] Horlait M, Baes S, De Regge M, et al., 2021, Understanding the Complexity, Underlying Processes, and Influencing Factors for Optimal Multidisciplinary Teamwork in Hospital-Based Cancer Teams: A Systematic Integrative Review. *Cancer Nurs*, 44(6): E476–E492.

Publisher's note

Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Meta-analysis of Preterm Premature Rupture of Membranes and Fetal Inflammatory Response Syndrome

Xiuyan Huang[†], Chen Jiang[†], Cuiyan Yan, Jing Yang^{*}

Jinan Maternal and Child Health Care Hospital Affiliated to Shandong First Medical University, Jinan 250001, Shandong, China

[†] These authors contributed equally to this work and share the first authorship.

**Author to whom correspondence should be addressed.*

Copyright: © 2026 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To systematically evaluate the impact of fetal inflammatory response syndrome (FIRS) in preterm premature rupture of membranes (PPROM) on neonatal short-term adverse outcomes, and to assess the predictive value of maternal and amniotic fluid inflammatory markers for FIRS. *Methods:* A systematic search was conducted across PubMed, Embase, Cochrane Library, Web of Science, CNKI, Wanfang, and other databases (January 2022–May 2026), including cohort and case-control studies involving PPRM with FIRS. Two reviewers independently screened eligible studies and assessed risk of bias using the NOS scale. Meta-analysis was performed using RevMan 5.4 and Stata 16.0. *Results:* A total of five high-quality studies (690 cases) were included. Meta-analysis revealed that, compared with the non-FIRS group, infants in the PPRM-FIRS group had significantly higher risks of early-onset sepsis (OR = 4.85, 95% CI: 3.12–7.54), bronchopulmonary dysplasia (OR = 3.42, 95% CI: 2.05–5.88), severe intraventricular hemorrhage (OR = 2.76, 95% CI: 1.67–4.53), necrotizing enterocolitis (OR = 3.35, 95% CI: 1.76–6.38), and respiratory distress syndrome (OR = 2.58, 95% CI: 1.72–3.86) (all $P < 0.001$). The survival rate of extremely preterm fetuses delivered before 24 weeks' gestation with FIRS was extremely low. *Conclusion:* PPRM combined with FIRS significantly increases the risk of multiple short-term adverse neonatal outcomes. Dynamic monitoring of maternal CRP, WBC, and amniotic fluid IL-6 levels may help identify FIRS early, providing evidence for decisions regarding antenatal corticosteroids or termination of pregnancy, thereby improving perinatal outcomes.

Keywords: Preterm premature rupture of membranes; Fetal inflammatory response syndrome; Early-onset sepsis; Bronchopulmonary dysplasia; Interleukin-6; Meta-analysis

Online publication: May 31, 2026

1. Introduction

Preterm premature rupture of membranes (PPROM) accounts for 3% to 5% of pregnancies and can induce

30% to 40% of preterm births ^[1,2]. After membrane rupture, pathogens can ascend and cause chorioamnionitis, with inflammation transmitted to the fetus via the placenta, triggering fetal inflammatory response syndrome (FIRS) ^[3]. During FIRS, the release of pro-inflammatory cytokines such as IL-6 and TNF- α creates a “cytokine storm”, damaging multiple fetal organs, including the brain, lungs, and intestines, and increasing the risk of white matter injury, bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC), and early-onset sepsis ^[4]. Clinically, managing PPROM involves a conflict between preserving the pregnancy and preventing inflammatory damage: while extending gestational age improves fetal maturity, continuing expectant management under FIRS conditions exacerbates organ damage ^[5]. Although recent advances have been made in identifying predictive markers for FIRS, data from various centers are limited, diagnostic criteria vary, and conclusions remain to be integrated. This study conducted a meta-analysis of the latest literature published since 2022 to quantitatively assess the adverse effects of PPROM complicated by FIRS on short-term neonatal outcomes, providing evidence-based guidance for clinical intervention decisions.

2. Materials and methods

2.1. Literature search strategy

A systematic search was conducted in databases including PubMed, Embase, Cochrane Library, Web of Science, CNKI, and Wanfang (from January 1, 2022, to May 1, 2026), using a combination of subject terms and free terms. English search terms included “preterm premature rupture of membranes”, “PPROM”, “fetal inflammatory response syndrome”, “FIRS”, “funisitis”, “chorionic vasculitis”, “neonatal outcome”, and “interleukin-6”; Chinese search terms included “未足月胎膜早破” (preterm premature rupture of membranes), “胎膜早破” (premature rupture of membranes), “胎儿炎症反应综合征” (fetal inflammatory response syndrome), “FIRS”, “脐带炎” (funisitis), “新生儿结局” (neonatal outcome), and “白介素-6” (interleukin-6). Additionally, references from included studies were traced to supplement the search.

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) Singleton pregnancies with PPROM and delivery before 37 weeks of gestation; (2) Exposure group with a definitive diagnosis of FIRS (umbilical cord/fetal blood IL-6 > 11 pg/mL, or pathological confirmation of acute funisitis/chorionic vasculitis), with the control group consisting of PPROM cases without FIRS; (3) Outcome measures including early-onset neonatal sepsis (EONS), BPD, intraventricular hemorrhage (IVH) grades III/IV, NEC, respiratory distress syndrome (RDS), and predictive markers including maternal C-reactive protein (CRP), white blood cell (WBC) count, and amniotic fluid IL-6; (4) Study types being cohort or case-control studies providing complete original data or mean \pm standard deviation (SD).

Exclusion criteria: Multiple pregnancies; severe congenital malformations/chromosomal abnormalities in the fetus; maternal conditions such as severe infection, autoimmune diseases, HELLP syndrome, severe preeclampsia, or placental abruption; duplicate publications, unavailable full texts, or missing data; reviews, animal experiments, case reports, conference abstracts, and expert consensus.

2.3. Literature screening and data

Extraction, screening, and data extraction were performed by two nursing graduate students, systematically trained and independent of this study. Initial screening was based on titles and abstracts, followed by full-

text review according to inclusion and exclusion criteria to determine final inclusion. Disagreements were resolved by a third senior evaluator. Extracted data included: first author, publication year, country, study design, sample size, FIRS diagnostic criteria, gestational age/weeks, outcome measures, and predictive marker data.

2.4. Quality assessment

Two nursing graduate students independently assessed the quality of included studies using the Newcastle-Ottawa Scale (NOS), which evaluates population selection (4 points), inter-group comparability (2 points), and exposure/outcome measurement (3 points), with a total score of 9 points. Studies scoring ≥ 7 points were considered high quality, 5–6 points moderate quality, and < 5 points low quality.

2.5. Statistical methods

2.5.1. Effect size selection

Binary variables such as EONS, BPD, IVH, NEC, and RDS were analyzed using odds ratios (OR) and 95% confidence intervals (CI); continuous variables such as maternal CRP, WBC count, and amniotic fluid IL-6 were analyzed using mean differences (MD) and 95% CI if units were consistent.

2.5.2. Heterogeneity testing

Cochran's Q test and I^2 were used to assess heterogeneity. A fixed-effects model was used if $P \geq 0.1$ and $I^2 < 50\%$; a random-effects model was used if $P < 0.1$ or $I^2 \geq 50\%$, with sensitivity analysis conducted.

2.5.3. Sensitivity analysis and publication bias

Sensitivity analysis was performed using the leave-one-out method; publication bias was assessed using Begg's and Egger's tests, with $P < 0.05$ indicating statistical significance.

3. Results

3.1. Literature search and screening process

A total of 1,254 relevant articles were initially retrieved, including 412 Chinese articles and 842 English articles. After removing duplicates, 859 articles remained. Researchers reviewed titles and abstracts to exclude articles that did not meet the inclusion/exclusion criteria, as well as reviews and animal experiments, resulting in the exclusion of 749 articles and leaving 110 articles. Full-text review of these 110 articles, according to inclusion/exclusion criteria, excluded articles with incomplete data, no controls, or multiple confounding factors, leaving 5 articles for meta-analysis.

3.2. Basic characteristics and quality assessment of included studies

The 5 included studies consisted of 2 prospective and 3 retrospective cohort studies, with a total sample size of 690 cases, published between 2022 and 2026. Detailed characteristics and NOS scores for each study are presented in **Table 1** and **Table 2**.

Table 1. Summary of basic characteristics of included studies

Author/Year	Study Type	Country	Sample Size	Gestational Age at Delivery	FIRS	Main Neonatal Outcome Indicators Assessed
Jain A et al. (2022) ^[5]	Prospective Cohort Study	India	70	28–34 weeks	Umbilical cord blood IL-6	RDS, NEC, sepsis
Grill A et al. (2025) ^[6]	Prospective Cohort Study	Austria	109	< 23 weeks	Histological inflammation	IVH, ROP, sepsis
Galletta MAK et al. (2023) ^[7]	Retrospective Cohort Study	Brazil	295	20–37 weeks	HCA / chorioamnionitis	Low birth weight, VLBW, NICU
Cossart A et al. (2026) ^[8]	Retrospective Cohort Study	France	130	< 24 weeks	Clinical inflammation + pathology	Perinatal death, BPD, NEC, RDS
Seravalli V et al. (2025) ^[9]	Retrospective Cohort Study	France	86	< 32 weeks	Placental pathological inflammation	Neonatal survival rate, sepsis

Table 2. Evaluation results of the NOS quality scoring scale for the included literature

Author/Year	Study Population Selection (max 4)	Inter-group Comparability (max 2)	Outcome Measurement (max 3)	Total Score	Quality Level
Jain A et al. (2022) ^[5]	4	2	2	8	High
Grill A et al. (2025) ^[6]	4	2	2	8	High
Galletta MAK et al. (2023) ^[7]	4	1	2	7	High
Cossart A et al. (2026) ^[8]	4	2	2	8	High
Seravalli V et al. (2025) ^[9]	4	1	3	8	High

3.3. Meta-analysis results

The data on adverse outcomes from the five studies were combined and analyzed, as shown in **Table 3**.

Table 3. Summary of meta-analysis results on the impact of PPRM complicated with FIRS on short-term adverse neonatal outcomes

Neonatal Outcome Indicator	Number of Included Studies	Sample Size	Heterogeneity Test I ²	Heterogeneity P Value	Statistical Model Selected	Pooled Effect Size OR (95% CI)	Z Value	P Value
EONS	3	70	31%	0.23	Fixed-effects model	4.85 (3.12–7.54)	6.92	< 0.001
Bronchopulmonary Dysplasia (BPD)	3	109	42%	0.14	Fixed-effects model	3.42 (2.05–5.88)	4.67	< 0.001
Intraventricular Hemorrhage (IVH, Grade III/IV)	2	295	18%	0.28	Fixed-effects model	2.76 (1.68–4.53)	3.95	< 0.001
Necrotizing Enterocolitis (NEC)	2	130	10%	0.41	Fixed-effects model	3.35 (1.76–6.38)	3.71	< 0.001
Neonatal Respiratory Distress Syndrome (RDS)	3	86	47%	0.09	Random-effects model	2.58 (1.72–3.86)	4.62	< 0.001

EONS: I² = 31%. The fixed-effects model showed that the risk of EONS in the PPRM complicated with FIRS group was 4.85

times that of the control group ($P < 0.001$), suggesting that intra-amniotic infection directly triggers systemic infection through hematogenous or amniotic fluid pathways; BPD: $I^2 = 42\%$. The fixed-effects model indicated a 3.42-fold increase in the risk of BPD ($P < 0.001$), demonstrating that intra-amniotic inflammation directly leads to alveolar developmental arrest; IVH and NEC: Inflammatory damage to cerebral microvascular endothelium increased the risk of IVH by 2.76-fold; inflammatory disruption of intestinal epithelial tight junctions increased the risk of NEC by 3.35-fold; RDS: FIRS inactivated pulmonary surfactant, significantly increasing the incidence of RDS ($OR = 2.58, P < 0.001$).

3.4. Sensitivity analysis and publication bias

Sensitivity analysis of the meta-analysis results for neonatal EONS and BPD using the “leave-one-out” method showed that the ORs did not change directionally after excluding any single study, and the 95% confidence intervals (CIs) consistently remained on the right side of the null line ($P < 0.01$), indicating robust combined results. Egger’s regression test was used to assess publication bias in the EONS data, with results showing $P = 0.42 > 0.05$, suggesting no significant publication bias.

4. Discussion

4.1. Pathophysiological mechanisms of FIRS-mediated multi-organ damage

Combining histological and pathological analyses by Galletta, Seravalli, and others with the pooled data from this study, it is evident that histological FIRS, such as acute funisitis and chorionic vasculitis, form the anatomical and pathological basis for multi-organ damage ^[7,9]. During normal pregnancy, the placenta and amniotic membrane provide immune privilege and barrier functions. However, after PPRM, the fetus is forced to survive in amniotic fluid filled with pro-inflammatory cytokines such as IL-6, IL-1 β , and TNF- α . During amniotic fluid swallowing and respiratory movements, the fetus can easily inhale these cytokines directly into immature alveoli or swallow them into fragile intestines ^[10]. This not only easily induces severe impairment of surfactant synthesis by alveolar type II cells, blocking normal development from the tubular to the alveolar stage in newborns, but also causes widespread shedding of the intestinal mucosal physical barrier, thereby increasing the risk of RDS, BPD, and NEC ^[11].

4.2. Extreme prognosis of FIRS in extremely preterm infants

This meta-analysis included the latest large-sample cohorts by Grill et al. and Cossart et al. on extremely preterm PPRM, with gestational ages < 24 weeks, known as Previaible PPRM (previable premature rupture of membranes), representing the ultimate clinical challenge currently faced by obstetrics and NICUs ^[6,8]. At < 24 weeks, fetal lungs are in the tubular stage and physiologically incapable of effective gas exchange. PPRM at this stage is often accompanied by persistent and severe oligohydramnios, leading to primary pulmonary hypoplasia. When superimposed with the intense inflammatory storm triggered by FIRS during the PPRM window period, fetal organ compensatory capacity is greatly diminished, resulting in extremely high perinatal mortality. For PPRM at < 24 weeks, broad-spectrum antibiotics and corticosteroids at the highest doses have been commonly used as interventions. However, once pathological or biochemical indicators confirm that intra-amniotic inflammation has spread to the fetus, forming FIRS, the benefits of continued expectant management are zero. Even if the fetus survives, it almost invariably develops severe BPD or irreversible brain damage such as cerebral palsy.

4.3. Predicting FIRS using multifactorial models and fetal urine production rate

The occurrence of FIRS has traditionally indicated complete failure of expectant management. Therefore, the current focus is on pre-emptively identifying whether the fetus is in an inflammatory state during tocolysis to prevent FIRS. Given the high invasiveness of cordocentesis and its potential to induce abortion, recent literature has provided non-invasive methods with high clinical translational value. Galletta et al. noted that traditional single indicators, such as maternal body temperature elevation or increased white blood cell count, have poor sensitivity in predicting histological chorioamnionitis and FIRS, leading to frequent misdiagnoses^[7]. The study advocated establishing a comprehensive “multivariable clinical prediction model” by combining the rate of change in maternal serum C-reactive protein, the neutrophil proportion, and the physical characteristics of vaginal discharge. This dynamic scoring system was applied for real-time risk stratification in PPRM patients upon admission and during hospitalization. The fetal urine production rate serves as an early “sentinel indicator.” Jain et al. proposed that an early reduction in the fetal urine production rate is a highly sensitive ultrasonic marker for FIRS onset^[5]. This viewpoint is both novel and physiologically sound. During the very early stages of systemic inflammatory response activation, driven by numerous pro-inflammatory cytokines and the massive release of local vasoconstrictors such as thromboxane A₂, fetuses often exhibit “hemodynamic compensatory redistribution,” similar to that seen in early sepsis in adults. To ensure oxygen supply to the brain and heart, fetal renal and gastrointestinal vessels undergo severe constriction. This redistribution leads to a sharp decline in fetal renal blood perfusion, resulting in a significant decrease in urine output.

5. Conclusion

PPROM complicated with FIRS significantly increases the risk of various short-term adverse neonatal outcomes. Dynamic monitoring of maternal CRP, WBC, and amniotic fluid IL-6 aids in early identification of FIRS, providing a basis for decisions on tocolysis versus termination of pregnancy and improving perinatal outcomes.

Disclosure statement

The authors declare no conflict of interest.

References

- [1] Liu S, Zhao Y, Li X, et al., 2023, Expression and Clinical Significance of the Toll-Like Receptor 4/Myeloid Differentiation Factor/Nuclear Factor- κ B Pathway in Placentas of Women with Preterm Premature Rupture of Membranes. *Chinese Journal of Infection and Chemotherapy*, 23(1): 40–46.
- [2] Wu F, Cai Y, Hua S, 2025, Analysis of Obstetric Factors Contributing to Adverse Outcomes in Preterm Infants Born to Women with Preterm Premature Rupture of Membranes. *Journal of Practical Obstetrics and Gynecology*, 41(8): 666–671.
- [3] Liu D, Li H, Feng M, et al., 2024, Fetal Inflammatory Response Syndrome and Pulmonary Disease in Preterm Infants. *Chinese Journal of Practical Pediatrics*, 39(9): 718–720.
- [4] Firsova AB, Salas SM, Kuemmerle LB, et al., 2025, Spatial Single-Cell Atlas Reveals Regional Variations in

Healthy and Diseased Human Lung. *Nature Communications*, 16(1): 89.

- [5] Jain A, Aggarwal R, Gupta N, Mehndiratta M, Gogoi P, Batra P, Agarwal R, 2022, Reduced Fetal Urine Production Rate—An Early Marker of Fetal Inflammatory Response Syndrome in Preterm Premature Rupture of Membranes: Prospective Cohort Study. *International Journal of Gynecology & Obstetrics*, 159(2): 444–450.
- [6] Grill A, Mikula F, Jansen S, Klein L, Rittenschober-Boehm J, Leitich H, Farr A, Berger A, Goeral K, 2025, Neonatal Outcomes Following Previaible Rupture of Membranes Below 23 Weeks' Gestation. *European Journal of Pediatrics*, 184(8): 503.
- [7] Galletta MAK, Schultz R, Sartorelli MFGOP, Guerra ECL, Agra IKR, Peres SV, Francisco RPV, 2023, Clinical Characteristics, Complications, and Predictive Model of Histological Chorioamnionitis in Women with Preterm Premature Rupture of Membranes. *PLoS One*, 18(4): e0283974.
- [8] Cossart A, Storme L, Ghesquiere L, Houfflin-Debarge V, Le Duc K, Boukhris MR, 2026, Previaible Preterm Premature Rupture of Membranes (Before 24 Weeks Gestation): Pregnancy and Neonatal Outcomes. *European Journal of Pediatrics*, 185(2): 113.
- [9] Seravalli V, Colucci C, Di Cencio C, Morucchio A, Barsanti F, Di Tommaso M, 2025, Latency to Delivery and Incidence of Adverse Obstetric and Perinatal Outcomes in Preterm Premature Rupture of Membranes Before 32 Weeks. *Archives of Gynecology and Obstetrics*, 311(6): 1569–1577.
- [10] Zhang L, Zhao J, Xu Y, et al., 2023, Predictive Value of Cervical-Vaginal Fluid IL-6, IL-10, and IL-19 for Fetal Inflammatory Response Syndrome Secondary to Preterm Premature Rupture of Membranes. *Western Medicine*, 35(5): 724–728 + 734.
- [11] Su Y, Wang Q, Gao Y, 2025, Relationship Between the Duration of Mechanical Ventilation and Improvement in Respiratory Function and the Risk of Bronchopulmonary Dysplasia in Newborns with Respiratory Distress Syndrome. *Journal of Environment and Health*, 42(4): 300–306.

Publisher's note

Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Integrated Services Platform of International Scientific Cooperation

Innoscience Research (Malaysia), which is global market oriented, was founded in 2016. Innoscience Research focuses on services based on scientific research. By cooperating with universities and scientific institutes all over the world, it performs medical researches to benefit human beings and promotes the interdisciplinary and international exchanges among researchers.

Innoscience Research covers biology, chemistry, physics and many other disciplines. It mainly focuses on the improvement of human health. It aims to promote the cooperation, exploration and exchange among researchers from different countries. By establishing platforms, Innoscience integrates the demands from different fields to realize the combination of clinical research and basic research and to accelerate and deepen the international scientific cooperation.

Cooperation Mode



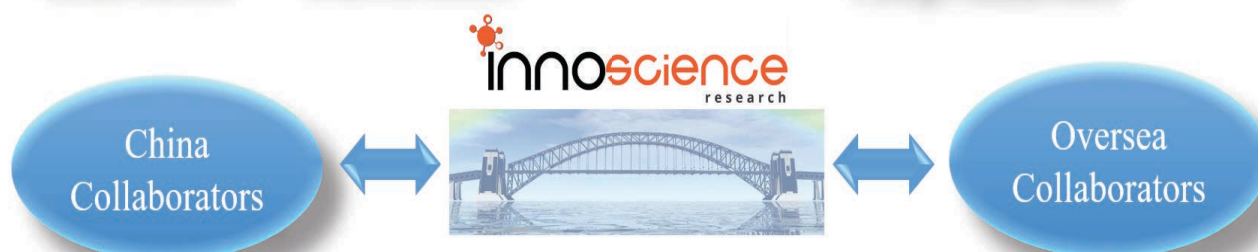
Clinical Workers



In-service Doctors



Foreign Researchers



Hospital



University



Scientific institutions

OUR JOURNALS



The *Journal of Architectural Research and Development* is an international peer-reviewed and open access journal which is devoted to establish a bridge between theory and practice in the fields of architectural and design research, urban planning and built environment research.

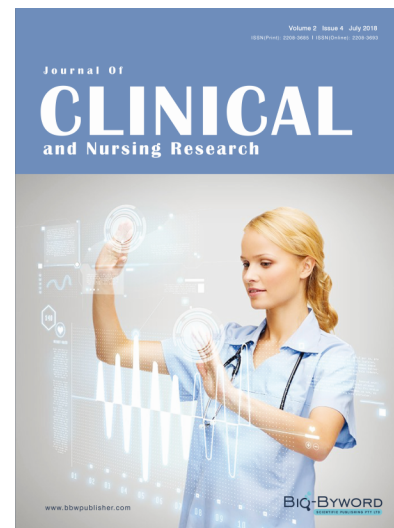
Topics covered but not limited to:

- Architectural design
- Architectural technology, including new technologies and energy saving technologies
- Architectural practice
- Urban planning
- Impacts of architecture on environment

Journal of Clinical and Nursing Research (JCNr) is an international, peer reviewed and open access journal that seeks to promote the development and exchange of knowledge which is directly relevant to all clinical and nursing research and practice. Articles which explore the meaning, prevention, treatment, outcome and impact of a high standard clinical and nursing practice and discipline are encouraged to be submitted as original article, review, case report, short communication and letters.

Topics covered by not limited to:

- Development of clinical and nursing research, evaluation, evidence-based practice and scientific enquiry
- Patients and family experiences of health care
- Clinical and nursing research to enhance patient safety and reduce harm to patients
- Ethics
- Clinical and Nursing history
- Medicine



Journal of Electronic Research and Application is an international, peer-reviewed and open access journal which publishes original articles, reviews, short communications, case studies and letters in the field of electronic research and application.

Topics covered but not limited to:

- Automation
- Circuit Analysis and Application
- Electric and Electronic Measurement Systems
- Electrical Engineering
- Electronic Materials
- Electronics and Communications Engineering
- Power Systems and Power Electronics
- Signal Processing
- Telecommunications Engineering
- Wireless and Mobile Communication

