INTRODUCTION

In clinic, puerperal infection mainly refers to the reproductive tract infection occurring after delivery, which, as a kind of complication seriously threatening delivery quality and life safety of puerperae, has a certain influence on postpartum recovery and even neonatal feeding. Birth canal injury is caused due to fetal delivery via reproductive tract during the puerperium, and the body’s immunity of pregnant women significantly declines during the puerperium. As a result, pathogenic microorganisms invade the human body, leading to infection, and even septicopyemia and threatening the maternal life. At the same time, the drug resistance of pathogenic bacteria of puerperal infection has significantly increased nowadays, and the incidence rate of puerperal infection caused by uncommon pathogenic bacteria in the past also increases, so the traditional antibacterial drugs, such as penicillin, fail to control the infection effectively in clinical experiential medication.

1 | RESEARCH ARTICLE

Risk factors, changes in serum inflammatory factors, and clinical prevention and control measures for puerperal infection

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Abstract

Background: To investigate the risk factors and changes in serum inflammatory factors in puerperal infection, and propose clinical prevention measures.

Methods: A total of 240 subjects with suspected puerperal infection treated in our hospital from January 2017 to December 2017 were collected, among which puerperal infection was definitely diagnosed in 40 cases, and it was excluded in 40 cases. Levels of interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and high-sensitivity C-reactive protein (hs-CRP) were compared between the two groups, and the change trends of IL-6 and hs-CRP were recorded.

Results: Levels of IL-6, hs-CRP, and TNF-α in puerperal infection group were higher than those in non-infection group (P < .05). Levels of IL-6 and hs-CRP at enrollment and 1-3 days after enrollment in infection group were higher than those in non-infection group (P < .05). The body mass index >25, placenta previa, placenta accreta, postpartum hemorrhage, premature rupture of membrane, gestational diabetes mellitus, and anemia during pregnancy were relevant and independent risk factors for puerperal infection. Puerperal infection occurred in uterine cavity, vagina, pelvic peritoneum, pelvic tissue, incision, urinary system, etc, and gram-negative (G+) bacteria were dominated in pathogens.

Conclusion: The inflammatory response of patients with puerperal infection is significantly enhanced.

Keywords: inflammatory factors, prevention measures, puerperal infection, risk factors
Meanwhile, levels of inflammation-related cytokines in patients with puerperal infection are also significantly increased. Interleukin-6 (IL-6), as the most important inflammation-related cytokine in the body, mainly regulates the cell function and is involved in the body immunity. High-sensitivity C-reactive protein (hs-CRP), as the most widely used inflammation-related cytokine currently, has a definite correlation with the severity of tissue damage and infection, which is an important index in clinical observation in acute infection stage.

In this study, in order to better investigate the occurrence of puerperal infection, the analysis of common pathogenic factors of puerperal infection started with changes in the body’s common inflammatory factors after puerperal infection, and common infection sites and pathogen distribution were explored, hoping to provide corresponding guidance for clinical diagnosis, treatment, and prevention.

2 DATA AND METHODS

2.1 General data

A total of 240 subjects with suspected puerperal infection treated in our hospital from January 2017 to December 2017 were collected. Another 40 subjects without puerperal infection during the same period were selected as control group. Before enrollment, all subjects signed and agreed to be enrolled, and this survey research was approved by the Ethics Committee of hospital. Inclusion criteria: primipara who displayed signs of infection in any part of the body within 48 hours before enrollment, underwent vaginal delivery, and had relevant medical data. Subject who was associated with pain abdomen, malodorous lochia, abdominal distention, uterine tenderness, pelvic abscess, peritonitis, mechanical or foreign body injury. Exclusion criteria: subjects who took antibacterial drugs or immunosuppressors within 48 hours before enrollment, or complicated with malignant tumor, severe dysfunction in the heart, lung, liver, kidney, mental diseases, fever due to medical causes, wound/surgical site infection, mastitis, urinary tract infection or thrombophlebitis.

2.2 Investigation methods

Clinical relevant data of subjects with puerperal infection were analyzed, and all clinical data were collected by obstetricians and related investigators receiving unified training. Patients and their authorizers should be fully cooperated in the collection of investigation data, the investigation was conducted anonymously, the patients’ privacy should be protected during the process, and the question raised by patients was answered. The relevant investigation results obtained should not be disclosed to any organization or individual without the permission of subjects enrolled and their authorizers. At enrollment and 30 days after the first investigation, investigators filled out the same questionnaire and completed the data of subjects, and the correlation coefficients obtained in the two times were set as the stability coefficients. In this study, the reliability coefficient ($\alpha = 0.1$) was used to evaluate the reliability level, and it was 0.921 after calculation. Clinical data obtained were checked alternatively by two people and entered into the Epidata software data analysis system, followed by statistical processing via Statistical Product and Service Solutions (SPSS) 21.0.

2.3 Detection of inflammatory factor levels and standard reference values

IL-6 was detected via enzyme-linked immunosorbent assay, whose standard reference value is 0.37-0.46 ng/L. TNF-α was detected via double-antibody single-step sandwich method, whose standard reference value is 5-100 ng/L, and hs-CRP was detected via latex-enhanced immunoturbidimetry, whose standard reference value is ≤10 mg/L.

2.4 Identification of pathogen species of puerperal infection

Pathogen culture and identification were based on the National Clinical Laboratory Procedures, and all operations were performed in strict accordance with the above operating procedures. Bacteria were cultured using the Kirby-Bauer (K-B) diffusion method, while fungi were cultured using the glucose peptone agar medium. All operations were conducted strictly according to the CLSI 2008-2010 procedures, and data were analyzed using WHONET (version 5.3-5.4). All the above operations were performed by the medical laboratory technicians with working experience in clinical detection for 5 years or above strictly according to the operation procedures and regulations.

2.5 Observation indexes

Levels of inflammatory cytokines (IL-6, TNF-α and hs-CRP) in subjects with and without puerperal infection were compared, and the change trends of IL-6 and hs-CRP in both groups were recorded at enrollment and 1-3 days after enrollment. Univariate and multivariate analyses were performed for relevant clinical data, such as age, body mass index, gestational week, placenta previa, placenta accreta, postpartum hemorrhage, premature rupture of membrane, gestational hypertension, gestational diabetes mellitus, and anemia during pregnancy, and the infection sites and pathogen distribution in subjects with puerperal infection were recorded.

2.6 Statistical analysis

SPSS 21.0 (IBM) statistical software was used. Univariate analysis was performed first for puerperal infection, followed by multivariate logistic regression analysis. Measurement data were presented as mean ± standard deviation ($\bar{x} \pm s$), and chi-square test was used for the intergroup comparison of rate. $P < .05$ suggested that the difference was statistically significant.
3 | RESULTS

3.1 | Comparisons of inflammatory factor levels between the two groups

A total of 240 subjects with suspected puerperal infection treated in our hospital from January 2017 to December 2017 were collected and 40 women with severe maternal sepsis were finally enrolled for the study according to the inclusion and exclusion criteria and result of pathogen culture. They were aged 19-42 years old ([28.5 ± 1.2] years old on average) with the gestational week of 34-41 weeks ([38.1 ± 0.6] weeks on average), including 21 cases receiving lateral episiotomy. Another 40 subjects in control group were aged 19-42 years old ([28.6 ± 1.1] years old on average) with the gestational week of 34-41 weeks ([38.0 ± 0.6] weeks on average), including 20 cases receiving lateral episiotomy. Levels of inflammatory factors (IL-6, hs-CRP and TNF-α) were detected in both groups and the levels in puerperal infection group were significantly higher than those in non-infection group (P < .05; Table 1).

3.2 | Change trends of main inflammatory factor (IL-6) level in the two groups

At enrollment and 1-3 days after enrollment, the IL-6 level was (1.05 ± 0.15) ng/L, (0.89 ± 0.06) ng/L, (0.63 ± 0.05) ng/L, and (0.51 ± 0.03) ng/L, respectively, in infection group, and (0.41 ± 0.03) ng/L, (0.39 ± 0.04) ng/L, (0.32 ± 0.03) ng/L, and (0.29 ± 0.02) ng/L, respectively, in control group.

| TABLE 1 | Comparisons of inflammatory factor levels between the two groups (x ± s) |
|-----------------------------------------------|
|  | IL-6 (ng/L) | hs-CRP (mg/L) | TNF-α (ng/L) |
| Infection group | 1.05 ± 0.15 | 16.5 ± 1.0 | 130.0 ± 7.4 |
| Non-infection group | 0.41 ± 0.03 | 4.1 ± 0.1 | 71.3 ± 4.0 |
| t | 26.461 | 78.035 | 44.134 |
| P | .000 | .000 | .000 |

**FIGURE 1** Levels of inflammatory factors and infection sites. Change trends of main inflammatory factors IL-6 (A) and hs-CRP (B) levels in the two groups by ELISA. C, Main infection sites in patients with puerperal infection include uterine cavity, vagina, pelvic peritoneum, pelvic tissue, incision, and urinary system.
ng/L, (0.39 ± 0.03) ng/L, (0.28 ± 0.02) ng/L, and (0.26 ± 0.02) ng/L, respectively, in non-infection group. Levels of IL-6 in infection group were evidently higher than those in non-infection group at different time points (t = 26.461, 47.140, 41.105, and 43.853, P < .05; Figure 1A).

### 3.3 | Change trends of main inflammatory factor (hs-CRP) level in the two groups

At enrollment and 1-3 days after enrollment, the hs-CRP level was (16.5 ± 1.0) mg/L, (12.5 ± 0.8) mg/L, (11.7 ± 0.6) mg/L, and (9.9 ± 0.3) mg/L, respectively, in infection group, and (4.1 ± 0.1) mg/L, (4.0 ± 0.1) mg/L, and (3.8 ± 0.1) mg/L, respectively, in non-infection group. Levels of hs-CRP in infection group were obviously higher than those in non-infection group at different time points (t = 78.035, 66.679, 82.140, and 118.000, P < .05; Figure 1B).

### 3.4 | Univariate analysis of relevant risk factors in puerperal infection group

According to the univariate analysis, the incidence rate of puerperal infection was significantly increased in subjects with the body mass index >25, placenta previa, placenta accreta, postpartum hemorrhage, premature rupture of membrane, gestational diabetes mellitus, and anemia during pregnancy (P < .05), and they were relevant risk factors for puerperal infection (Table 2).

### 3.5 | Multivariate Logistic regression analysis of relevant risk factors in puerperal infection group

According to the multivariate logistic regression analysis, the body mass index >25, placenta previa, placenta accreta, postpartum hemorrhage, premature rupture of membrane, gestational diabetes mellitus, and anemia during pregnancy were independent risk factors for puerperal infection (Table 3).

### 3.6 | Analysis of main infection sites

Among 40 cases of puerperal infection, there were 14 cases (35.0%) of uterus cavity infection, 8 cases (20.0%) of vaginal infection, 7 cases (17.5%) of pelvic peritoneal infection, 4 cases (10.0%) of pelvic tissue infection, 3 cases (7.5%) of incision infection, 2 cases (5.0%) of urinary system infection, and 2 cases (5.0%) of infection in other sites (Figure 1C).

### 3.7 | Pathogen distribution in subjects with puerperal infection

Among 40 cases of puerperal infection, G− bacteria were detected in 24 cases (60.0%), G+ bacteria in 14 cases (35.0%), and fungi in two cases (5.0%). Specifically, Staphylococcus aureus accounts for 12.5%, Staphylococcus epidermidis 2.5%, Enterococcus 15.0%, Streptococcus 5.0%, Gardnerella vaginalis 12.5%, Escherichia coli 27.5%, Pseudomonas aeruginosa 10.0%, Acinetobacter bauman- nii 5.0%, Klebsiella pneumonia 5.0%, Fungi 5.0%, Candida albicans 2.5%, and Candida tropicalis 2.5%.

### 4 | DISCUSSION

Puerperal infection is a common and frequently occurring disease in clinic, which is also a common postpartum complication in puerperae. Its clinical manifestations mainly include elevated postpartum...
The body mass index >25, placenta previa, placenta accreta, postpartum hemorrhage, premature rupture of membrane, gestational diabetes mellitus, and anemia during pregnancy were relevant and independent risk factors for puerperal infection, suggesting that subjects with the body mass index >25, placenta previa, placenta accreta, postpartum hemorrhage, premature rupture of membrane, gestational diabetes mellitus, and anemia during pregnancy should be paid attention to in clinic, and related measures should be taken to prevent puerperal infection. Finally, the study on puerperal infection sites and pathogenic bacteria manifested that the infection mainly occurred in reproductive tract, such as uterine cavity and vagina, followed by pelvic cavity. Gram-negative bacteria were dominated in the pathogenic bacteria, followed by gram-positive bacteria (about 30%). In terms of antibacterial drugs selected in experiential therapy, therefore, it is recommended that gram-negative bacteria be the main target with consideration to gram-positive bacteria.

Prevention measures of puerperal infection should be taken before pregnancy and during pregnancy, delivery, and puerperium. First, before pregnancy, it is suggested that women of child-bearing age strengthen physical exercise, pay attention to nutritional regulation, actively prevent and control the reproductive system diseases, especially inflammatory diseases, reduce the frequency of uterine curettage, and make good preparation for pregnancy. Therefore, effective measures should be actively taken in clinic to ensure the clinical therapeutic effect once puerperal infection occurs, thereby improving the prognosis of pregnant women, and minimizing the impact of puerperal infection on puerperae and neonates.

In this study, in order to better investigate the occurrence, development, and prevention of puerperal infection, levels of inflammatory factors were compared between subjects with and without puerperal infection. It was found that levels of inflammatory factors (IL-6, hs-CRP, and TNF-α) in puerperal infection group were significantly higher than those in non-infection group, and levels of IL-6 and hs-CRP at enrollment and 1-3 days after enrollment in infection group were also obviously higher than those in non-infection group, indicating that levels of inflammatory cytokines in the body of subjects with puerperal infection are remarkably increased, and the body’s inflammatory response is significant. At the same time, analyses of risk factors for puerperal infection showed that the body mass index >25, placenta previa, placenta accreta, postpartum hemorrhage, premature rupture of membrane, gestational diabetes mellitus, and anemia during pregnancy were relevant and independent risk factors for puerperal infection, suggesting that subjects with the body mass index >25, placenta previa, placenta accreta, postpartum hemorrhage, premature rupture of membrane, gestational diabetes mellitus, and anemia during pregnancy should be paid attention to in clinic, and related measures should be taken to prevent puerperal infection. Finally, the study on puerperal infection sites and pathogenic bacteria manifested that the infection mainly occurred in reproductive tract, such as uterine cavity and vagina, followed by pelvic cavity. Gram-negative bacteria were dominated in

| TABLE 3 Multivariate Logistic regression analysis of relevant risk factors in puerperal infection group |
|-----------------------------------------------|
|                                      | β     | Standard  | W   | OR    | P     | 95% CI          |
|-----------------------------------------------|
| Body mass index                              | 2.34  | 0.46      | 9.92| 12.81 | .01   | 1.21-34.40      |
| Placenta previa                              | 2.92  | 0.54      | 4.46| 6.86  | .04   | 1.59-49.24      |
| Placenta accreta                             | 1.82  | 0.50      | 10.82| 4.81  | .01   | 1.58-14.38      |
| Postpartum hemorrhage                        | 1.83  | 0.57      | 4.82| 1.96  | .04   | 1.03-7.45       |
| Premature rupture of membrane               | 0.89  | 0.53      | 9.47| 2.44  | .00   | 1.38-4.31       |
| Gestational diabetes mellitus                | 1.12  | 15.50     | 6.38| 3.07  | .00   | 1.76-5.34       |
| Anemia during pregnancy                      | 1.71  | 33.60     | 7.11| 5.52  | .00   | 3.10-9.83       |
5 | CONCLUSION

In conclusion, the inflammatory response of patients with puerperal infection is significantly enhanced, with elevation of IL-6 and hs-CRP levels. Subjects with the body mass index >25, placenta previa, placenta accreta, postpartum hemorrhage, premature rupture of membrane, gestational diabetes mellitus, and anemia during pregnancy should be paid attention to, and prevention measures for puerperal infection should be actively taken. In experiential medication, it is recommended that gram-negative bacteria be the main target with consideration to gram-positive bacteria.

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REFERENCES

1. Nenke MA, Zeng A, Meyer EJ, et al. Differential effects of estrogen on corticosteroid-binding globulin forms suggests reduced cleavage in pregnancy. J Endocr Soc. 2017;1:202-210.
2. Bonet M, Ota E, Chibueze CE, Oladapo OT. Routine antibiotic prophylaxis after normal vaginal birth for reducing maternal infectious morbidity. Cochrane Database Syst Rev. 2017;13:21-37.
3. Mascarello KC, Horta BL, Silveira MF. Maternal complications and cesarean section without indication: systematic review and meta-analysis. Rev Saude Publica. 2017;51:116-118.
4. Gudu W, Abdulahi M. Labor, delivery and postpartum complications in nulliparous women with female genital mutilation admitted to karamara hospital. Ethiop Med J. 2017;55:11-17.
5. Bonet M, Ota E, Chibueze CE, Oladapo OT. Antibiotic prophylaxis for episiotomy repair following vaginal birth. Cochrane Database Syst Rev. 2017:2-11-18.
6. Tardieu SC, Schmidt E. Group A streptococcus septic shock after surgical abortion: a case report and review of the literature. Case Rep Obstet Gynecol. 2017;20:63-67.
7. Orazulike NC, Alegbeleye JO, Obiorah CC, Nyengidiki TK, Uzoigwe SA. A 3-year retrospective review of mortality in women of reproductive age in a tertiary health facility in Port Harcourt, Nigeria. Int J Womens Health. 2017;16:769-775.
8. Wu X, Wang C, Li Y, et al. Cervical dilation balloon combined with intravenous drip of oxytocin for induction of term labor: a multicenter clinical trial. Arch Gynecol Obstet. 2018;297:77-83.
9. Rosenbloom JI, Stout MJ, Tuuli MG, et al. New labor management guidelines and changes in cesarean delivery patterns. Am J Obstet Gynecol. 2017;217:689.
10. Gon G, Ali SM, Towriss C, et al. Unpacking the enabling factors for hand, cord and birth-surface hygiene in Zanzibar maternity units. Health Policy Plan. 2017;32:1220-1228.
11. Easter SR, Molina RL, Venkatess KK, Kaimal A, Tuomala R, Riley LE. Clinical risk factors associated with peripartum maternal bacteremia. Obstet Gynecol. 2017;130:710-717.
12. Cobo F, Rodríguez-Granger J, Sampedro A, Navarro-Mari JM. Infected breast cyst due to Prevotella buccae resistant to metronidazole. Anaerobe. 2017;48:177-178.
13. Liabsuetrakul T, Choobun T, Peeyananjarassri K, Islam QM. Antibiotic prophylaxis for operative vaginal delivery. Cochrane Database Syst Rev. 2017;5:8-12.
14. Jena P, Sheela CN, Venkatachala RP, Devarbhavi H. Obstetric outcome in women with chronic liver disease. J Obstet Gynaecol India. 2017;67:263-269.
15. Marwah S, Topden SR, Sharma M, Mohindra R, Mittal P. Severe puerperal sepsis-a simmering menace. J Clin Diagn Res. 2017;11: QC04-QC08.
16. Kulkarni GB, Mirza AM, Ramakrishnan S, Mustare V. Preliminary data on utility of subcutaneous unfractionated heparin in patients with deep cerebral venous thrombosis. J Thromb Thrombolysis. 2017;44:247-253.
17. Cobo F, Rodríguez-Granger J, Sampedro A, Navarro-Mari JM. Breast abscess due to Finegoldia magna in a non-puerperal women. Anaerobe. 2017;47:183-184.
18. Kobayashi N, Ahmed S, Sumi A, Urushibara N, Kawaguchiya M, Aung MS. Collaborative research on puerperal infections in Bangladesh. Nihon Eiseigaku Zasshi. 2017;72:106-111.
19. Subramaniam A, Owen J, Campbell SB, Harper LM, Fitzwater JL, Edwards RK. Maternal body mass index and oxytocin exposure in nulliparous women: is there an interaction associated with maternal and neonatal morbidities? J Matern Fetal Neonatal Med. 2017;6:1-6.
20. Ehrmann Feldman D, Vinet É, Sylvestre MP, et al. Postpartum complications in new mothers with juvenile idiopathic arthriti: a population-based cohort study. Rheumatology (Oxford). 2017;56:1378-1385.

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