



Prediction and Early Diagnosis of Postpartum Purulent-Septic Complications

Negmatullaeva Mastura Nurullaevna¹, Kenjaeva Zarnigor Olimovna²

^{1,2} Bukhara State Medical Institute

Abstract: Currently, the problem of early diagnosis of purulent-inflammatory postpartum diseases and the prediction of possible septic complications is extremely relevant. However, due to the predominance of abortive and erased clinical forms, timely diagnosis of this pathology remains difficult. In this regard, an important task is to search for highly informative markers of the inflammatory response, which allow determining the prognosis of the course in the shortest possible time and prescribing etiotropic therapy in time.

Keywords: postpartum endometritis, postpartum purulent-inflammatory complications, sepsis, inflammation, interleukins, fluorescence spectroscopy.

Currently, postpartum purulent-inflammatory diseases continue to occupy a leading position in the structure of maternal mortality, while septic complications (according to the Siberian Federal District) are third in frequency and in 2020 amounted to 12%, second only to extragenital diseases (48%) and amniotic fluid embolism (20%). However, early diagnosis and prognosis of these complications are still difficult. The current situation is exacerbated by an increase in the age of puerperas, associated with an increase in the percentage of somatic pathology, an increase in the virulent properties and antibiotic resistance of microbial pathogens, which dictates the need to optimize the prevention and treatment of purulent-inflammatory postpartum diseases (PID) [1-4].

It should be noted that there are not enough statistical data on the topic of CVD and septic complications, supported by systematic reviews and meta-analyses, to date. So, we structured the data of foreign articles from the Medline, EMBASE, Global Health databases from 2005 to 2019. [5-10]. It was noted that the incidence of wound infection in the postpartum period ranged from 0 to 10.9%, with a mean value of 2.1% (95% CI 1.2–3.2%). At the same time, the overall rate was highest in East and Southeast Asia (6.2%), and the lowest in the USA and Europe (0.9%) [5-13]. The incidence of sepsis in the postpartum period, combining systemic inflammatory response syndrome (SIRS) and severe sepsis, ranged from 0 to 3.8%, with an overall incidence of 0.1% (95% CI 0.04-0.21%) [5-14].

The incidence of postpartum endometritis (PE) ranges from 0 to 16.2% with an average incidence of 1.4% (95% CI 0.9-1.9%), with the most common (2.4-2.5 %) endometritis has been reported in the United States [8, 9] and Argentina [10].

PE, according to the Cochrane Collaboration (2015), was diagnosed on average from 1 to 3% after vaginal delivery and up to 27% after caesarean section [11], with a long anhydrous gap and multiple vaginal examinations during childbirth also appear to increase the risk of its development.

Clinically, PE presents with fever, pelvic tenderness, and a foul-smelling, purulent vaginal discharge after childbirth. This can lead to serious complications such as pelvic abscesses, blood clots, peritonitis and sepsis [12, 13].

It should be noted that after abdominal delivery, a predominantly severe form of PE is observed [12],

however, even with a mild form of PE, rapid generalization of infection with the development of septic complications is possible [13].

In relation to the prediction of septic complications in the postpartum period, first of all, it is necessary to pay attention to the clinical manifestations and symptoms of SIRS and multiple organ failure syndrome (MOS). Interesting data obtained as a result of a retrospective analysis of clinical and laboratory data based on forensic medical examinations of cases of severe maternal outcomes resulting from sepsis, including in "near miss" and dead patients (maternal mortality) are cited by V.F. Bezhenar et al. [fourteen]. The symptoms that make it possible to reliably predict a high degree of probability of developing obstetric sepsis, the authors include: the appearance before the end of pregnancy of hyperthermia $> 38.0^{\circ}\text{C}$ or hypothermia $< 36.0^{\circ}\text{C}$, hectic fever, leukocytosis $> 12 \times 10^9/\text{l}$ and/or leukopenia $< 4 \times 10^9/\text{l}$; after the end of pregnancy - persistent subfebrile condition, febrile condition, hypothermia, hectic fever, PON, as well as early local signs of hysterogenic infection - subinvolution of the uterus and pathological discharge from the genital tract [14].

However, according to modern data, the course of sepsis can take on blurred forms, and various manifestations of PON require timely differential diagnosis with other pathologies. Undoubtedly, a favorable outcome of the treatment of an infectious process is determined by its early diagnosis and adequate therapeutic measures, and with the development of generalized forms, the question arises of immediate surgical sanitation of the focus of infection, which determines the patient's survival [15-17].

Thus, undoubtedly, timely diagnosis and effective treatment of localized forms of postpartum infection, primarily PE, are controllable factors in reducing the frequency of generalized forms of this pathology and, ultimately, can reduce maternal mortality and morbidity in the development of purulent -septic complications after natural childbirth and caesarean section [16, 17].

Due to the great importance of the problem of sepsis, world congresses were devoted to it. In 1991, at a meeting on the classification of sepsis in Chicago, a classification was proposed based on the systemic inflammatory response syndrome to any inflammatory or non-inflammatory injury. The following definition of sepsis was discussed in 2001 [18-12], with the presence of SIRS and suspected or proven infection being the basis for the diagnosis [1, 2]. These criteria for the clinical diagnosis of sepsis and its classification proposed by the American College of Chest Physicians and the Society of Critical Care Medicine (ACCP/SCCM) are still the basis for today's experts [13-16].

However, given the accumulated clinical data in recent years, at the 45th Critical Care Congress in Orlando in 2016, the Society for Critical Care Medicine and the European Society for Critical Care Medicine organized a working group of 19 experts who gave a new concept of sepsis, "Sepsis-3" [17]. According to them, sepsis is a life-threatening organ dysfunction caused by dysregulation of the body's response to infection. The purpose of these changes was to speed up the diagnosis and improve the treatment of sepsis. In particular, the clinical signs of sepsis are infection and functional organ failure due to exposure to a microbial agent. PON is determined by the qSOFA scale, which includes impaired consciousness, systolic blood pressure < 100 mm Hg. Art. and respiratory rate > 22 per minute. The key provisions of the new terminology and definition are presented in the table [10].

However, the problem of sepsis still remains relevant and has not been fully resolved: simple qSOFA criteria only help to identify patients with suspected sepsis, but they do not allow timely diagnosis of this pathology (including at the preclinical level), and also dynamically monitor the effectiveness of the therapy [1].

For a long time, up to the present day, the most accessible method for diagnosing inflammatory diseases is the analysis of blood serum. However, the results of a number of studies [17, 18] indicate that the indicators of the number of leukocytes and the leukocyte formula do not reliably reflect the severity of the inflammatory response and do not play a significant role in the appointment of antibiotic therapy. In addition, there was no statistically significant correlation between bacterial infection and the characteristics of the leukocyte formula as a whole.

To date, the most studied and used in clinical practice markers of the inflammatory process are C-

reactive protein (CRP) and procalcitonin (PCT) [40-42]. At the same time, CRP is considered the gold standard in the diagnosis of inflammatory processes, and can also be determined in blood serum as a marker of inflammation during pregnancy, premature rupture of the membranes and purulent postpartum complications.

An increase in PCT is observed during systemic inflammation in complex bacterial infections or sepsis. It is important to emphasize that PCT reaches its peak values much earlier than CRP. However, there is an opinion that a change in PCT values does not necessarily indicate an infection or an inflammatory process, especially in the presence of hemodynamic instability [15, 4]. At the same time, severe bacterial infections and sepsis contribute to an increase in the concentration of PCT in the blood serum as a result of extrathyroid synthesis occurring in leukocytes, neuroendocrine cells of the lungs and liver (under the influence of pro-inflammatory stimulants). The combination of PCT and other clinical and physical data is considered a diagnostic marker of sepsis, inflammatory reactions, and severity of sepsis in the most clinically difficult patients [16].

PCT and CRP, as acute phase proteins, are most often used to diagnose bacterial sepsis, as well as to monitor the effectiveness of antibiotic therapy. At the same time, the limitations associated with their use are that their level can increase in various inflammatory conditions, while a highly sensitive and specific biomarker is needed to diagnose and predict bacterial infections and sepsis [18]. Such a marker is presepsin (PSP), a circulating protein whose concentration increases with the development of systemic infections, sepsis, and septic shock. According to international studies, including multicenter studies, it has been proven that the mechanism of increasing the level of PSP is fundamentally different from the mechanism of increasing such pro-inflammatory markers as tumor necrosis factor- α (TNF- α), interleukins (IL-6, IL-10), CRP etc. The production of this protein involves immune mechanisms aimed at activating phagocytosis, which is how it differs from traditional markers of sepsis [4]. In addition, during the induction of systemic inflammation, the increase in PSP occurs faster than other markers of sepsis [5]. Due to the short half-life (about 0.5-1.0 h), PSP reflects not only more accurately, but also "in real time" the effectiveness of antibiotic therapy [12]. At the same time, the PSP level not only helps to differentiate between sepsis and SIRS, but also acts as a prognostic tool in bacterial sepsis [17].

Currently, the following immunomodulatory responses are considered in response to exposure to an infectious agent: initially, a local immune response develops, with an increase in the level of pro-inflammatory cytokines at the site of inflammation, then a compensatory increase in the concentration of anti-inflammatory agents [18]. In addition, if local damage is sufficiently pronounced, there is a significant increase in pro-inflammatory factors and their dissemination into the blood. At the level of the whole organism, pro-inflammatory cytokines mobilize the action of all organs to fight infection, activating the production of non-specific anti-inflammatory drugs.

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