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O.V. Bulavenko, L.R. Ostapiuk, V.O. Rud, A.S. Voloshinovskii, T.S. Malyi Modern methods of the diagnostic of pathology of pregnancy and the postpartum period

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Postpartum purulent-inflammatory diseases are currently a serious problem.

Purpose — to develop and implement of a new modern method of the diagnosis, monitoring and assessment of health of women during pregnancy, before childbirth and in the postpartum period — the method of fluorescence spectroscopy — to ensure the provision of highly qualified medical care, including the effective treatment.

Materials and methods. The research material consisted of blood serum samples of 265 patients. There were 40 pregnant women (the Group 1), 40 women with an uncomplicated postpartum period (the Group 2), 170 — with postpartum purulent-inflammatory diseases (the Group 3), 15 patients with sepsis (the Group 4). Diagnostic methods: clinical, laboratory, instrumental, method of fluorescence spectroscopy, statistical (logistic regression and ROC analysis methods).

Results. In the Group 1 there is an increase in the intensity of fluorescence to 1.3 r.u. For the Group 2 the intensity of fluorescence was within 0.86–1.0 r.u. For the Group 3, the decrease in fluorescence intensity from 1 to 0.35 r.u. was recorded. For the Group 4 in addition to decreasing the fluorescence intensity, a noticeable shift of the fluorescence spectra of blood serum into the long-wave range was recorded.

Conclusions. A reliable prognostic model of the development of postpartum purulent-inflammatory diseases was created. The modern approach for the diagnosis and effective control of treatment within the framework of the method of fluorescent spectroscopy and biomarkers using infusions of donor albumin solutions is proposed.

The research was carried out in accordance with the principles of the Helsinki Declaration. The study protocol was approved by the Local Ethics Committee of participating institution. The informed consent of the patient was obtained for conducting the studies.

No conflict of interest was declared by the authors.

Keywords: postpartum purulent-inflammatory diseases, the method of fluorescence spectroscopy, albumin, the pathogenetic concept, the prognostic model.

Сучасні методи діагностики патології вагітності та післяпологового періоду

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Післяпологові гнійно-запальні захворювання залишаються серйозною проблемою.

Мета — розробити і впровадити новий сучасний метод діагностики, моніторингу та оцінки стану здоров'я жінок під час вагітності, перед пологами та в післяпологовому періоді — метод флуоресцентної спектроскопії — для забезпечення надання їм висококваліфікованої медичної допомоги, у тому числі ефективного лікування.

Матеріали та методи. Матеріал дослідження становили зразки сироватки крові 265 осіб. З них було 40 вагітних жінок (1-ша група), 40 породілей із неускладненим перебігом післяпологового періоду (2-га група), 170 породілей із післяпологовими гнійно-запальними захворюваннями (3-тя група), 15 хворих на сепсис осіб (4-та група). Методи діагностики: клінічні, лабораторні, інструментальні, метод флуоресцентної спектроскопії, статистичні (методи логістичної регресії та ROC-аналізу).

Результати. Алгоритм проведення дослідження ґрунтувався на розробленій нами модифікованій патогенетичній концепції. У пацієнток 1-ї групи спостерігалось зростання інтенсивності флуоресценції до 1,3 в.о. У пацієнток 2-ї групи інтенсивність флуоресценції знаходилася в межах 0,86–1,0 в.о. У пацієнток 3-ї групи відмічалось зниження інтенсивності флуоресценції в межах 1–0,35 в.о. В осіб 4-ї групи, окрім зниження інтенсивності флуоресценції, фіксувався помітний зсув спектрів флуоресценції сироватки крові в довгохвильову ділянку.

Висновки. Побудовано достовірну прогностичну модель розвитку післяпологових гнійно-запальних захворювань. Запропоновано сучасний підхід для діагностики та ефективного контролю лікування в рамках методу флуоресцентної спектроскопії та біомаркерів із використанням інфузій розчинами донорського альбуміну.

Дослідження виконано відповідно до принципів Гельсінської декларації. Протокол дослідження ухвалено Локальним етичним комітетом зазначеної в роботі установи. На проведення досліджень отримано інформовану згоду пацієнток.

Автори заявляють про відсутність конфлікту інтересів.

Ключові слова: післяпологові гнійно-запальні захворювання, метод флуоресцентної спектроскопії, альбумін, патогенетична концепція, прогностична модель.

Introduction

The issue of women's reproductive health is the urgent problem of the modern medicine. Many different factors, including chronic stress, affect negatively the reproductive health of women and lead to impaired fertility. In the recent years, the level of stress in the modern Ukrainian

society is extremely high. Stress is the emotional state that arises as the response to all kinds of the extreme influences. Stress is the feeling that a person feels when s/he believes that s/he cannot cope effectively with the situation that has arisen. This concept was introduced by Hans Selye (Canadian biologist and endocrinologist, founder

of the theory of stress, 1907–1982) in order to denote a non-specific reaction of the body to any adverse effect. About 70% of our experiences are about events that exist only in our imagination. The golden rule is: if the stressful situation depends on us, it is necessary to focus our efforts more rationally on changing it. And if the situation does not depend on us, we need to come to terms with it and change our perception and attitude towards this situation. Since 2020, many new objective reasons for stress in society have emerged. In 2020–2021, the problem of the COVID-19 pandemic caused a high level of stress in the world, including Ukraine. And on February 24, 2022, after the beginning of the full-scale invasion of the Russian Federation troops on the territory of Ukraine, the level of stress in Ukrainian society became critically high.

The link between stress and infertility has been debated for years. Women with infertility report about the increased levels of the anxiety and depression, so infertility obviously causes stress. However, understanding, if stress causes infertility, is less clear [23]. In the study [11], 40% of the 122 women before their first visit to the infertility clinic, were found to have anxiety, and 9.4% of women even reported to have suicidal thoughts or attempts. 25–60% of the infertile individuals had psychiatric symptoms, which exceeded significantly the corresponding figures for individuals in the control group. So, it is quite difficult to confirm the theory that stress prevents the implementation of the reproductive function.

Along with the problem of fertility, the issue of the course of pregnancy and the postpartum period is also very relevant. Approximately 810 women in the world die every day from causes related to pregnancy and childbirth, and almost one third of them occur in South Asia [26]. In 60% of them, maternal death occurred directly during the childbirth or in the postpartum period [19]. In Pakistan, a death occurs every 40 minutes due to the complications of pregnancy or childbirth [27]. Even in well-income countries, there is a tendency towards the increase in the frequency of postpartum purulent-inflammatory diseases, despite the extremely high level of medical care. According to the foreign studies, the frequency of severe sepsis with fatal consequences increases by 10% during the year. At the same time, the main risk factors are: late age of mothers, obesity, and pregnancy against the background of chronic diseases, the use of assisted reproductive technologies, multiple pregnancies and the high frequency of cae-

sarean sections. The risk of developing of the postpartum purulent-septic complications increases by 5–20 times after the operative delivery [7,14].

A non-invasive tool was developed, that can identify sepsis in women in the postpartum period [6]. The purpose of the study was to develop the model based on the risk factors and clinical signs and symptoms that may facilitate the early identification of women with postpartum sepsis. In this study, the significant risk factors for developing the postpartum sepsis were the number of antenatal visits, place of delivery, presence of preterm birth, gestational diabetes, lower abdominal pain, vaginal discharge, SPO₂ and blood glucose.

Over the past 30 years, the definition of sepsis and approaches to its effective diagnosis have changed three times. This indicates the high relevance of this problem in the world. A comparison of the main approaches to this issue deserves special attention from medical scientists. Sepsis defined by The Sequential Organ Failure Assessment (SOFA) may be a good alternative diagnostic tool because it well reflects the severity of sepsis by survival analysis. Systemic inflammatory response syndrome (SIRS) showed higher sensitivity and lower specificity, while qSOFA and bSIRS showed higher specificity and lower sensitivity for the diagnosis of sepsis; therefore, according to data [29], they are not adequate for the diagnosis of sepsis.

Sepsis continues to be the leading cause of death and disability worldwide. In the USA, more than a quarter of a million adults are hospitalized with the diagnosis of sepsis and die each year. The algorithm for managing patients with sepsis includes obtaining a blood culture, measuring lactate, and administering broad-spectrum antibiotics within 3 hours after establishing the patient's compliance with sepsis criteria. Also, for these patients, it is advisable to administer at least 30 ml/kg of intravenous crystalloids to correct hypotension or hyperlactatemia and recheck lactate and start using vasopressors within 6 hours [29]. Currently, there is no gold standard for the diagnosis of sepsis. Each hour of treatment delay is associated with the increase in mortality from sepsis by 7–10% [1].

Among the new markers for the diagnosis of sepsis, the monocyte distribution width (MDW) [4,5] and the sepsis index, which is calculated using the MDW indicators and the average volume of monocytes by a mathematical method using the formula, are considered. According to the authors [2,3], it showed better efficiency than individual biomarkers, reaching a level of sensitivi-

ty and specificity of 80% and 91%, respectively, for the detection of sepsis. Red blood cell distribution width (RDW), which indicates red blood cell anisocytosis, is another possible promising biomarker of sepsis. RDW, which indicates red blood cell anisocytosis, is another possible promising biomarker of sepsis. K.-Y. Hung et al. have showed that blood glucose levels measured on the first day of hospitalization may also indicate mortality risk stratification in critically ill patients with sepsis [18]. Diagnostic and prognostic value of pentraxin-3 (PTX3) in patients with sepsis and septic shock who were hospitalized in the intensive care unit was evaluated. E. Yagmur et al. investigated for the first time the possible role of clusterin as a prognostic biomarker in critically ill patients hospitalized in the intensive care unit, with or without sepsis [28]. It is interesting that A. Kyriakoudi et al. evaluated the possible role of IL-18 and its binding to IL-18BP protein as a biomarker of patients with sepsis [21]. Programmed death protein (PD-1) is another inflammatory marker proposed as a diagnostic and prognostic tool of sepsis [24]. The interesting field of the research is also the study of non-coding RNA, including long non-coding RNA (lncRNA), circular RNA (circRNA) and microRNA (miRNA). Sepsis is a very heterogeneous disease, and thus there is still a long way to go before identifying the ideal biomarker. So, the search for such a biomarker is a priority task of the modern medical science.

Attention should be paid to the importance of physical research methods in medical practice, in particular method of fluorescence spectroscopy (MFS). During the last 20 years, starting from 2001 in Lviv (Ukraine) on the initiative of Ihor Herych, systematic studies of blood serum BS of patients with purulent-inflammatory diseases and sepsis within the framework of MFS began [15]. This method is the most versatile method in the biological spectroscopy. Further studies within the framework of the MFS were devoted to the problems of purulent-inflammatory complications and sepsis. In this research, the main attention will be paid to the discussion and analysis of the results of the scientific studies we received, which relate to the development of purulent-inflammatory diseases in obstetrics and gynaecology with the aim of improving significantly the treatment process in order to prevent septic complications.

The **purpose** of the research is the development and implementation of the new modern method of the diagnostic, monitoring and assessment of the

women's health during the pregnancy, before childbirth and in the postpartum period — the MFS — to ensure the provision of highly qualified medical care, including the effective treatment.

Materials and methods of the research

The research was conducted in the Department of Gynaecology No. 2 of Vinnytsia Council's Clinical Hospital No. 2. The luminescent laboratory of the Department of Experimental Physics, the Ivan Franko National University of Lviv, was an experimental research centre. The research study took place in 2015–2020. The research methods are as following: clinical, laboratory (general blood and urine analysis, biochemical blood analysis, immunoenzymatic analysis for TORCH infection, bacterioscopic examination of smears from the vagina and cervix), instrumental one (ultrasonographic examination of the pelvic organs, and for women with postpartum purulent-inflammatory diseases also histological examination of metro aspirate) and methods of statistical data processing using logistic regression and ROC analysis. In addition to standard examinations, we also used MFS. The research material consisted of serum samples (BS) of 265 patients. Their fluorescence spectra (FS) were investigated. Among them there were 40 pregnant women (the Group 1), 40 women with uncomplicated course of postpartum period (the Group 2), 170 women with postpartum purulent-inflammatory diseases (the Group 3) and 15 patients with sepsis (the Group 4).

The research was carried out in accordance with the principles of the Helsinki Declaration. The study protocol was approved by the Local Ethics Committee of participating institution. The informed consent of the patient was obtained for conducting the studies.

Results of the research and discussion

Unquestionably, taking into the account the seriousness and urgency of the problem of sepsis, a comprehensive approach should be used for its diagnosis and various possible available methods should be combined. The sensitive biomarkers of systemic inflammation are cytokines (interleukins: IL-1, IL-6, IL-8, IL-10, IL-12), tumour necrosis factor (TNF- α), platelet activation factor (PAF), transforming growth factor-b (TGF- β), presepsin (PSP), lactate, as well as C-reactive protein (CRP) and procalcitonin (PCT). TNF- α is the first triggering pro-inflammatory cytokine, and IL-10-important anti-inflammatory [13]. The

results of the search will be considered successful if the discovery of biomarkers is available for the routine clinical use. The biomarker, which possesses all these requirements, has not been identified yet [12]. The diagnosis of sepsis should include the following characteristics: rapid detection, minimal invasiveness, high sensitivity and specificity for immediate initiation of antibiotics in the case of symptoms of systemic inflammation. At the same time, for a long-time insufficient attention was paid to the microscopic processes occurring in the bodies of patients with this condition. Consequently, traditional schemes were used in the treatment. The excessive attachment to monitoring the external signs of the clinical picture of patients with sepsis does not provide an opportunity to analyze the changes in their BS at the molecular level in detail. So, it did not lead to the improvement of the traditional treatment regimens. Nevertheless, in a biochemical blood analysis with the determination of protein fractions and the level of albumin, it was impossible to detect the real changes in its structure. The most widely studied biomarkers do not predict effectively sepsis in patients with burn injury. Procalcitonin was moderately sensitive (73%) and specific (75%) for sepsis in patients with burn injury. C-reactive protein was highly sensitive (86%), but not specific (54%). Leukocyte count had low sensitivity (47%) and moderate specificity (65%) [25].

In patients with sepsis, endogenous intoxication (EI) deepens significantly. At the same time, the albumin molecules in their blood turn into the partially blocked system. The albumin molecules perform transport, detoxification, antioxidant and ligand-binding functions. This is a complex mechanism. It is necessary to find the ways to preserve the vital activity of the body with such pathological changes. The pathogenesis of the development of this phenomenon has not been analyzed and described. A deep understanding of the above-mentioned processes led to the creation of the pathogenetic concept and a reasonable approach to solving an important problem: if full-fledged albumin in patient with sepsis becomes less and less, it is advisable to carry out exogenous albumin infusions in order to replenish its reserves in human blood. At the same time, it is necessary to continue traditional treatment: operative, etiotropic and symptomatic. Besides, albumin infusion allows us to provide the pathogenetic therapy by replenishing the amount of albumin capable of performing detoxification and transport functions. At first glance,

it seems that this is too simple, although an understandable solution. But how was it obtained?

In the framework of the conducted research, MFS was used for the diagnosis of purulent-inflammatory diseases and sepsis. The research algorithm is based on the scientific approach, on the modified pathogenetic concept developed by us. The basis of the concept is that in patients with diseases accompanied by EI, part of the albumin molecules are blocked by toxins. As a result, there are two types of albumin molecules in their blood: normal (concentration (X)) and blocked (concentration (1-X)). Blocked albumin molecules lose their ability to perform their main functions, namely transport and detoxification. This allows us to understand better the processes of genesis during the course of sepsis in patients' bodies. So, the use of infusion therapy with albumin solutions is the effective pathogenetic component of the treatment of purulent-inflammatory diseases and sepsis.

The creation of the above-mentioned modified pathogenetic concept was preceded by a number of «*in vitro*» and «*in vivo*» studies. The research included several stages. On the first of them, the «*in vitro*» study was carried out, which included dilution of blood serum with distilled water (DW), a 20% solution of donor albumin, sugar broth (SB), centrifuged (CC) and non-centrifuged (NCC) cultures of bacterial cultures of *Staphylococcus aureus*. For this aim, regular solutions with a step interval of 10% were created. The finding of BS changes during their dilution during further «*in vivo*» studies allowed the interpretation of the obtained results. In particular, the dilution of BS with distilled water helped us to explain the changes in the blood serum during physiological hypoproteinemia, which occurs during pregnancy and during massive infusion therapy. The dilution of the BS with sugar broth makes it possible to conduct the in-depth study of the BS of patients with diabetes. The dilution of BS with CC and NCC of bacteria are especially relevant when studying BS of patients with purulent-inflammatory diseases and sepsis.

When breeding BS with 20% solution of albumin fluorescence intensity (I_F) in this case does not change practically, but there is a gradual long-wave shift of the fluorescence band of the solution; position of the fluorescence maximum (λ_{max}) of the fluorescence band in a solution of 90% BS reaches the highest value, remaining a constant value with further reduction of BS in the solution. Spectral-fluorescence characteristics of 20% donor

albumin are very close to the similar characteristics of BS. In this regard, we used a 20% solution of albumin as a standard when conducting studies of BS of patients in medical practice.

Studies have proven that due to an increase in the concentration of BS in the solution up to 12%, I_F increases by 25%. This phenomenon, is most likely associated with the decrease in the concentration quenching of fluorescence spectra (FS) of BS, associated with the effects of interaction between protein molecules. Following the further increase in the concentration of sugar broth in the solution, I_F gradually decreases and acquires the characteristics of the sugar broth. The position of the fluorescence band does not change practically and, only starting from 75% of the sugar broth in the solution, its gradual monotonous long-wave shift is noted.

When diluting BS with DW, the position of the fluorescence bands (λ_{max}) does not change. But at the same time, a clear dependence was revealed between I_F and concentration ratio of BS and DW in the studied solutions. A gradual increase of I_F was recorded, which reached a maximum at the concentration (C) $\approx 2.5\%$ of BS in the solution. Changes of I_F were connected with the effect of concentration quenching of fluorescent characteristics of the solutions. Thus, after the decrease of BS in the prepared solutions, there is a gradual decrease in the number of albumin molecules in them and, accordingly, a weakening of the concentration quenching of BS fluorescence. But the growth of I_F occurs up to the certain limit which corresponds to the $\approx 2.5\%$ of BS in the solution. When the content of BS in DW is further reduced, there is a sharp decrease of the I_F of BS until its complete extinction. These changes are specific and depend on the concentration of various types of diluted substances in the BS.

The spectral-fluorescence characteristics of the dilutions of the BS with CC and NCC were studied (the 6-day inoculation of *Staphylococcus aureus* on the sugar broth) with the aim of simulating of BS changes in patients with sepsis *in vitro*. In this regard, we further focused our attention on the detection of the spectral-fluorescence signs of

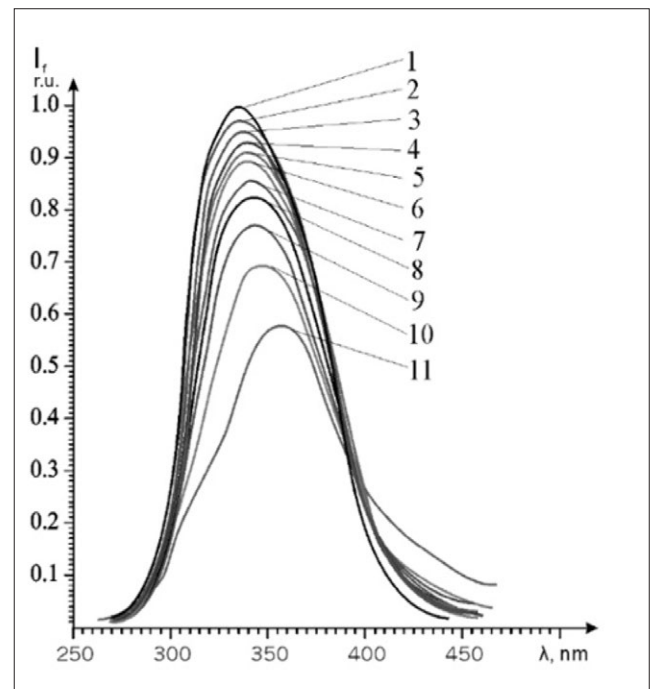


Fig. 1. Effect of dilution centrifuged (CC) culture on fluorescence spectra of donor BS (1 — BS, 2 — 90% BS, 3 — 80% BS, 4 — 70% BS, 5 — 60% BS, 6 — 50% BS, 7 — 40% BS, 8 — 30% BS, 9 — 20% BS, 10 — 10% BS, 11 — CF crops). $\lambda_{excitation} = 280 \text{ nm}$

the pathognomonic for the patients with sepsis the pathological constellation of blood serum + bacteria — the phenomenon of bacteremia. When diluting the BS with CC and NCC of bacteria I_F gradually decreases with the increase of the content of the bacterial culture in the solution. At the same time, a long-wavelength shift of the fluorescence bands of dilutions (λ_{max}) is also noted.

The detected effect of changing the spectral-fluorescence characteristics of BS dilutions with bacterial NCC and CC is connected with the effect of bacteria and the products of their metabolism on the fluorescence characteristics of BS. The changes of the FS of BS when diluting the BS with CC (Fig. 1, Table 1) and NCC are specific and form the basis for the development of the fluorescent method for the early diagnosis of sepsis by modelling the changes of BS in patients with sepsis *in vivo* [9,20].

The main purpose of the *in vitro* research stage was to study the behaviour of the spectral-fluorescence characteristics of BS in normal conditions and in the case of presence of the purulent-inflammatory diseases of various degrees of severity

Table 1

The effect of dilution by centrifuged cultures of bacteria on the spectral-fluorescence characteristics of blood serum

Curves	1	2	3	4	5	6	7	8	9	10	11
$\lambda_{max} \text{ nm}$	335	335	337	340	340	340	341	343	343	347	357
$I_F \text{ r.u.}$	1.00	0.97	0.95	0.93	0.91	0.89	0.86	0.82	0.77	0.69	0.58

ОРИГІНАЛЬНІ ДОСЛІДЖЕННЯ

in vivo, in order to clarify the main laws of their behaviour, to learn how to interpret correctly and also to explain their changes during the treatment. The need for MFS approbation to study the behaviour of the spectral-fluorescence characteristics of patients' BS is associated with the significant prevalence of severe forms of purulent-inflammatory diseases in these patients and the prospect of its widespread use in medical practice.

When BS is excited by the light with a wavelength of 280 nm, the luminescence of human serum albumin molecules is observed. At the same time, we register FS and measure quantitative indicators — I_F and the λ_{max} . In the case of presence of the purulent-septic conditions in patients, the products of bacterial metabolism interact with albumin molecules in their BS. This leads to the decrease of I_F . In particularly severe cases, a long-wave shift is observed and a fluorescence peak is formed in the long-wave region. In the case of presence of purulent-septic conditions in patients, the products of bacterial metabolism interact with albumin molecules in their BS.

In our previous studies, it was established that on the basis of the difference of FS of BS, it is possible to carry out the early diagnosis of sepsis (the patent of Ukraine No. 76953) [16] and postpartum purulent-inflammatory diseases (the patent of Ukraine No. 133472) [10]. This is due to the fact that the spectral-fluorescence characteristics, typical for sepsis, appear 24–48 hours before the appearance of obvious clinical manifestations [17]. In connection with changes of albumin molecules in patients with purulent-septic conditions, in the complex pathogenetic treatment of patients with postpartum purulent-inflammatory complications,

we recommend the use the albumin solution infusions [22].

The comprehensive results of the study of the FS of BS of healthy pregnant women, women with the uncomplicated postpartum period, and women with postpartum purulent-inflammatory diseases are presented in Fig. 2 and in Table 2.

In healthy people, FS has the form of a λ -shaped curve with a fluorescence peak in the region of 330.1–335.1 nm. The fluorescence intensity of their BS was in the range from 0.86 to 1.0 r.u. In pregnant women (the Group 1), there is the normal increase in the fluorescence intensity up to 1.3 r.u., which is associated with the physiological increase in the volume of circulating blood and hypoalbuminemia and is consistent with the results of the study of BS dilutions with distilled water during the *in vitro* research (Fig. 2, curves 12, 13, 16) [9]. In particular, a clear dependence between the I_F and the concentration ratio of BS and DW in the studied solutions was revealed. A gradual increase in I_F was recorded, which reached a maximum at a concentration of 2.5% BS in the solution. Thus, with the decrease of the BS content in the prepared solutions, there is a gradual decrease in the number of albumin molecules in them and, accordingly, a weakening of the concentration quenching of the BS fluorescence. Due to the further decrease of the BS content in the DW, there is a sharp decrease in the I_F of the BS up to its complete extinction. The case when the I_F is proportional directly to the BS concentration in the solution corresponds to the condition when the optical density of the solution $D \leq 0.1$.

For the patients with an uncomplicated course of the postpartum period (the Group 2), there was no noticeable shift of the I_{max} (the value of this indicator ranged from 330 nm to 337 nm). The intensity of fluorescence was in the range of 0.86–1.0 r.u. compared to the I_F of the 20% donor albumin, the spectral-fluorescence characteristics of which were taken as a standard during the measurements (Fig. 2, curves 1, 2, 3).

The decrease in the fluorescence intensity from 1 to 0.35 r.u. for the 170 women with postpartum purulent-inflammatory diseases (the Group 3) was recorded (Fig. 2, curves 69, 70). These changes are qualitatively consistent with the results of the study of BS in patients with sepsis and the results of *in vitro* research of the dilution of BS of bacterial NCC and CC. In particularly severe cases, a noticeable shift of the FS of BS into the long-wave range was recorded (curves 1', 3', 4' —

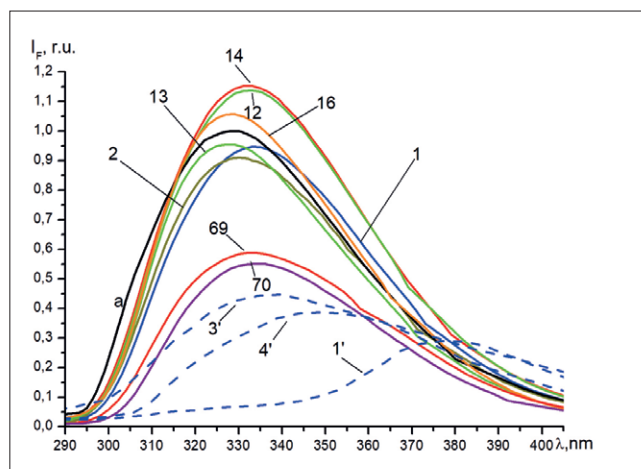


Fig. 2. Fluorescence spectra of blood serum of a 20% albumin solution, the Group 1 (curves 12, 13, 14, 16), the Group 2 (curves 1, 2), the Group 3 (curves 69, 70), the Group 4 in dynamics (curves 1', 3', 4'). $\lambda_{excitation} = 280$ nm.

Spectral-fluorescence characteristics of women of the Group 1 (curves 12, 13, 14, 16), the Group 2 (curves 1, 2), the Group 3 (curves 69, 70) the Group 4 (curves 1', 3', 4')

Table 2

Curves	Albumin	1	2	12	13	14	16	69	70	1'	3'	4'
λ_{\max} , nm	330.1	333.1	330.1	333.1	327	333.1	329	334.1	334.1	376.8	339.8	349.5
I _F r.u.	1	0.947	0.91	1.137	0.955	1.153	1.056	0.589	0.552	0.289	0.447	0.388

Diagnostic value of the mathematical model for predicting postpartum purulent-inflammatory diseases in the Group 3

Table 3

Value	the Group 2	the Group 3	In total
Calculated value <0.78	39 (97.5%)	6 (3.53%)	45
Calculated value ≥0.78	1 (2.5%)	164 (96.47%)	165
In total	40	170	210

patient with sepsis). Changes in the spectral-fluorescence characteristics are dynamic indicators that change quite quickly during the treatment against the background of recovery.

During the development of personal medicine now, it is fundamentally important to assess the risk of postpartum purulent-inflammatory diseases and to create individual approach to all patients, management of each clinical case in accordance with the principles of case management. For this purpose, it is important to conduct a primary measurement of FS of BS during pregnancy. In our research, these measurements were performed at 29–31 weeks of gestation.

Let us summarize the obtained results. Pregnant women are characterized by a certain increase in I_F of BS up to 1.3 r.u., which is associated with a physiological increase in the volume of circulating blood and hypoalbuminemia during the pregnancy. In the postpartum period, the normal I_F of BS is 0.86–1.0 r.u. After reducing I_F of BS below 0.86 r.u., such patients require close monitoring and follow-up and are at increased risk of developing postpartum purulent-inflammatory diseases. The minimum value of I_F of BS was 0.35 r.u. Due to further reduction of I_F of BS, the appearance of septic conditions is possible.

The timely diagnosis and effective treatment of postpartum endometritis are necessary for these patients. At the same time, in order to carry out an independent objective assessment of the role of MFS and other factors in predicting the occurrence of postpartum purulent-inflammatory diseases within the framework of this study, we studied and analysed in the Group 3 and the Group 2 40 factors that included clinical and anamnestic data, features of the course of pregnancy and childbirth, results of laboratory examinations (general blood and urine analysis, biochemical blood analysis, enzyme immunoassay for TORCH infection,

bacterioscopic examination of smears from the vagina and cervix), results of instrumental methods examination (ultrasonographic examination of the pelvic organs, histological examination of metro aspirate, MFS and statistical data processing using the method of logistic regression and ROC analysis).

Based on these results, we developed the mathematical model for predicting the risk of developing of postpartum purulent-inflammatory diseases. MFS was used to optimize the management of patients with postpartum purulent-inflammatory diseases. On the basis of the conducted research, 13 main factors for predicting the development of postpartum purulent-inflammatory diseases were established (extragenital pathology, gynaecological diseases, the threat of abortion, the presence of operative treatment, TORCH infections, colpitis, the duration of labour more than 12 hours, the presence of labour abnormalities, I_{max} of blood serum, fluorescence intensity ≤0.845 r.u., age, number of bed days, presence of foetal distress). Based on these results, we created the prognostic model for the development of postpartum purulent-inflammatory diseases. The proposed model is reliable, along with a probability of more than 99% (p<0,001; $\chi^2=174.74$; df=13) [8]. It was established that all 13 factors have a provoking effect on the likelihood of postpartum purulent-inflammatory diseases, but their influence is manifested to varying degrees. The greatest diagnostic value for assessing the risk of postpartum purulent-inflammatory diseases, including endometritis, in the main group is the value of serum fluorescence intensity ≤0.845 r.u., which increases significantly the risk of this complication. Thus, as a result of the research, it was established that only 6 (3.53%) patients of the Group 3 (Table 3) had no risk of postpartum purulent-inflammatory diseases according to the proposed prognostic model.

Conclusions

The significant improvement of the results of diagnosis of the purulent-inflammatory diseases and sepsis is still a fundamental problem of medical science. Unfortunately, most modern diagnostic methods are representative against the background of already manifesting manifestations of pathological processes. Basic research during the last decades has demonstrated that MFS is the most versatile method of biological spectroscopy. High sensitivity, accuracy, simplicity of fluorescent characteristics cause the special interest to the fluorescent analysis as an important method of modern, and especially early diagnosis of purulent-septic complications.

The special attention within the framework of the MFS was paid to the study of spectral-fluorescence characteristics of BS of pregnant wo-

men and patients with postpartum purulent-inflammatory diseases. The reliable prognostic model of the development of postpartum purulent-inflammatory diseases was created with a probability of more than 99% ($p < 0.001$; $\chi^2 = 174.74$; $df = 13$). At the same time, in order to overcome EI in patients with a severe course of diseases, the effectiveness of the treatment of infusions with solutions of donor albumin was proven. An important condition for the effectiveness of the treatment process is the constant monitoring within the framework of the MFS until its completion. A modern approach for diagnosis and effective control of treatment within the framework of MFS and biomarkers by using infusions of donor albumin solutions is proposed.

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