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# COMPARATIVE ANALYSIS OF THE EFFECTIVENESS OF NOVEL PROGNOSTIC MARKERS OF POSTPARTUM INFLAMMATORY COMPLICATIONS

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Postpartum inflammatory complications remain a significant medical and social problem and significantly affect maternal morbidity rates. The purpose of this study was to evaluate the effectiveness of Raman spectroscopy as a prognostic marker for inflammatory complications in the postpartum period, compared with traditional laboratory parameters. The study included 300 women in labor (250 women with inflammatory complications and 50 women in the control group). A reliable gradation dependence of the frequency and intensity of spectral peaks on the clinical severity of the inflammatory process has been established. High values of spectral parameters correlated with an increase in C-reactive protein, procalcitonin, IL-6, fibrinogen, neutrophil-lymphocyte ratio, and erythrocyte sedimentation rate ($p<0.001$). The analysis of clinical, laboratory, and spectroscopic data indicates the high diagnostic and prognostic significance of Raman spectroscopy in assessing inflammatory complications of the postpartum period. It was found that changes in the intensity of characteristic spectral bands (Amide I, Amide III, phenylalanine ~1003 $cm^{-1}$, lipid bands 1445 and 2850-2930 $cm^{-1}$) correlate with increased levels of CRP, procalcitonin, IL-6, fibrinogen, as well as with an increase in the NLR index and ESR. The sequential increase in protein and lipid peaks, accompanied by an increase in the frequency of complications, reflects activation of the cytokine cascade, synthesis of acute-phase proteins, and the development of oxidative stress. This confirms Raman spectroscopy's ability to detect molecular changes preceding the clinical manifestation of severe inflammation. Thus, Raman spectroscopy can be considered an effective additional prognostic marker of systemic inflammatory response in the postpartum period and a potential basis for developing rapid diagnostic algorithms for early detection of complications.

**Key words**: postpartum inflammatory complications, Raman spectroscopy, prognostic markers, C-reactive protein, procalcitonin, interleukin-6, neutrophil-lymphocyte ratio, fibrinogen, oxidative stress, early diagnosis.

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# ПОРІВНЯЛЬНИЙ АНАЛІЗ ЕФЕКТИВНОСТІ НОВИХ ПРОГНОСТИЧНИХ МАРКЕРІВ ПОСЛЯПОЛОГОВИХ ЗАПАЛЬНИХ УСКЛАДНЕНЬ

Післяпологові запальні ускладнення залишаються значною медико-соціальною проблемою та суттєво впливають на показники захворюваності матерів. Метою даного дослідження була оцінка ефективності спектроскопії комбінаційного розсіювання як прогностичного маркера запальних ускладнень післяпологового періоду у порівнянні з традиційними лабораторними показниками. До дослідження було включено 300 породіль (250 жінок із запальними ускладненнями та 50 як контрольна група). Встановлено достовірну градаційну залежність частоти та інтенсивності спектральних піків від клінічної вираженості запального процесу. Високі значення спектральних показників корелювали з підвищенням рівня С-реактивного білка, прокальцитоніну, ІЛ-6, фібриногену, нейтрофільно-лімфоцитарного співвідношення та швидкості осідання еритроцитів ($p<0,001$). Таким чином, раман-спектроскопія може розглядатися як ефективний додатковий прогностичний маркер системної запальної реакції в післяпологовому періоді та потенційна основа для розробки експрес-діагностичних алгоритмів раннього виявлення ускладнень.

**Ключові слова:** післяпологові запальні ускладнення, раман-спектроскопія, прогностичні маркери, С-реактивний білок, прокальцитонін, інтерлейкін-6, нейтрофільно-лімфоцитарне співвідношення, фібриноген, оксидативний стрес, рання діагностика.

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A modern urgent task of obstetrics is the careful management of pregnancy and its final stage – the birth act [4, 6]. It is known that the peculiarities of the course of labor largely determine the perinatal outcomes for the mother and fetus [3, 8].

Early prognostic assessment of postpartum inflammatory complications, identification of effective predictors, and the introduction of modern diagnostic methods and rapid tests are of great clinical importance [8, 13]. The definition of prognostic criteria, the development of effective algorithms, and the development of prognostic scales are essential for the identification of risk factors and

the timely prevention of postpartum inflammatory complications [9, 12].

Thus, the search for highly effective and prognostically significant diagnostic methods to determine the likelihood of inflammatory complications in maternity patients remains an urgent medical and social task [2, 7]. In this regard, the use of Raman spectroscopy seems promising, as it can provide a comprehensive picture of processes occurring in the uterus during the postpartum period [10, 14]. The method is based on Raman scattering, in which the spectrum of back-reflected laser radiation is analyzed [10].

**The purpose** of the study was to determine the effectiveness of Raman spectroscopy as a prognostic marker for postpartum complications compared with other inflammatory markers.

**Materials and methods.** The study was conducted in 2017–2019 at the Scientific Research Institute of Obstetrics and Gynecology of the Ministry of Health of the Republic of Azerbaijan (Baku city). To solve these tasks, 250 pregnant women aged 17 to 45 years with postpartum inflammatory complications (postpartum endometritis and endomyometritis) were included in the study. The control group consisted of 50 women with a physiological course of the postpartum period.

Criteria for excluding patients from the study: women in labor with inflammatory conditions in the postpartum period associated with extragenital diseases (acute respiratory viral infections, pyelonephritis exacerbation); women with increased body temperature associated with lactostasis; HIV-infected women.

During the clinical study, Raman spectroscopy was used to analyze blood samples obtained from participants in both study groups. The relevant biological materials taken from the participants were sent to the Institute of Physics of the National Academy of Sciences of Azerbaijan, where they were studied using Raman spectroscopy. The study was performed on a Nanofinder 30 instrument (Tokyo Instruments, Japan). The materials were irradiated at a wavelength of 532 nm. The obtained results were substantiated by a comparative analysis of phonon characteristics on spectrograms.

A biochemical blood test was performed in the women included in the study to determine the following parameters: C-reactive protein (CRP), leukocyte formula, procalcitonin (PCT) as a specific marker of bacterial inflammation, interleukin-6 (IL-6) as an early cytokine response, tumor necrosis factor-α (TNF-α) as a pro-inflammatory mediator, fibrinogen as an acute phase protein, erythrocyte sedimentation rate (ESR), as well as calculated indices – NLR (ratio of neutrophils to lymphocytes) and PLR (ratio of platelets to lymphocytes).

The statistical analysis in the study was conducted in accordance with a generally accepted methodological sequence. For indicators with a normal distribution, intergroup comparisons were performed using univariate analysis of variance (ANOVA); for those with an abnormal distribution, the Kruskal-Wallis test was used. Spearman's correlation methods were used to evaluate the relationships between biochemical markers. The level of statistical significance was set at $p<0.05$ [5].

According to the Ethics Committee decision dated March 3, 2026, No. 3-28-10/2-248/2026, the protocol for this study complies with the current ethical standards and principles of the Helsinki Declaration. All participants in the study were previously properly informed about the study's objectives and methods and signed a written informed consent form to participate.

**Results of the study and their discussion.** An analysis of Raman spectroscopic parameters in the blood serum of 300 maternity patients revealed differences in the frequencies and intensities of spectral peaks. In the control group (practically healthy women in labor), these indicators were significantly lower. Variability in values was observed in the main group, enabling the identification of subgroups with high, medium, and low peak frequency and intensity. 48 (19.2 %) women had high-frequency, high-intensity spectral peaks; 95 (38 %) had average-frequency peaks; and 107 (42.8 %) had low-frequency peaks. Low frequency and intensity values were also detected in the control group.

The average frequency of spectral peaks in the group with high severity was 1581.7124±2.404 $cm^{-1}$ (n=48). The differences between this group and the average frequency group were statistically significant ($p<0.001$). Significant differences were also found in the group with an average frequency (1471.8071±23.36 $cm^{-1}$; n=95) compared with the low frequency group ($p<0.001$).

In the group with a low peak frequency (1370.342±22.77 $cm^{-1}$; n=107), the differences compared with the control group (1362.1774±37.280 $cm^{-1}$; n=50) were not statistically significant ($p=0.27093$), which indicates the absence of pronounced spectral changes in this category of patients compared with the physiological postpartum condition.

A similar pattern was revealed when analyzing the intensity of spectral peaks. The differences between the high and medium intensity groups were statistically significant ($p<0.001$), as well as between the medium and low intensity groups. However, there were no significant differences between the low-intensity group and the control group ($p=0.44828$).

The high-intensity spectral peaks exceeded the average level by 2014.774 mW/cm2 and the low-intensity spectral peaks by 2513.644 $mW/cm^2$, reflecting a pronounced molecular restructuring during the development of inflammatory complications.

Thus, the revealed gradation dependence of the frequency and intensity of spectral peaks on the clinical severity of the inflammatory process confirms the diagnostic and prognostic value of Raman spectroscopy.

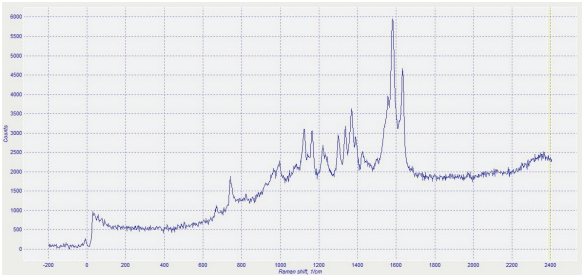

Fig. 1. Raman spectrum of blood serum of A.V. maternity hospital.

A peak of about 1003 $cm^{-1}$ corresponds to phenylalanine and reflects changes in protein metabolism. Its enhancement indicates an increase in serum protein concentration and activation of catabolic processes characteristic of the inflammatory response.

The range of 1240–1270 $cm^{-1}$ (Amide III) is associated with the structural components of proteins. An increase in the intensity of this peak indicates an increase in the concentration of inflammatory proteins and a reorganization of their secondary structure under systemic inflammation.

The peak of 1445 $cm^{-1}$ (lipid $CH_2$) reflects changes in lipid composition and increased lipid peroxidation processes. Its increase is associated with damage to cell membranes and the development of oxidative stress. The 1650 $cm^{-1}$ band (Amide I) is a marker of protein structures, primarily alpha helices and beta structures. Clinically, an increase in this peak correlates with higher levels of CRP and fibrinogen, the main acute-phase proteins.

The range of 2850–2930 $cm^{-1}$ corresponds to the valence fluctuations of C–H bonds in lipids and proteins. An increase in intensity in this zone indicates pronounced oxidative stress and metabolic restructuring of tissues.

Thus, the totality of these spectral changes reflects the complex activation of the inflammatory cascade, increased acute-phase protein synthesis, and the development of oxidative damage, confirming the diagnostic and prognostic significance of Raman spectroscopy in assessing the systemic inflammatory process. The presented data demonstrate a clear gradation in the levels of inflammatory markers with respect to the clinical incidence of complications (Table 1).

Table 1

**Comparative characteristics of indicators of CRP, PCT and IL-6**

| Group | CRP (mg/l) | PCT (ng/ml) | IL -6 (pg/ml) |
|---|---|---|---|
| High frequency (n=48) | 5.904±0.76 | 1.82±0.21 | 38.6±3.2 |
| Average frequency (n=95) | 4.41±0.903 | 1.14±0.18 | 24.3±2.7 |
| Low frequency (n=107) | 1.72±0.66 | 0.62±0.11 | 12.8±1.9 |
| The control group (n=50) | 0.37±0.123 | 0.08±0.02 | 4.6±0.8 |

In the high-frequency group (n=48), the maximum values for all indicators were observed: CRP – 5.904±0.76 mg/l, PCT – 1.82±0.21 ng/ml, IL-6 – 38.6±3.2 pg/ml. Compared with the control group, CRP levels increased by more than 15 times, PCT by about 22 times, and IL-6 by more than 8 times. This pattern indicates a pronounced systemic inflammatory reaction, with activation of the acute-phase cytokine cascade and protein synthesis.

In the medium–frequency group (n=95), there was a significant decrease in the indicators compared with the high–frequency group, but they remained significantly higher than the control values: CRP – 4.41±0.903 mg/l, PCT – 1.14±0.18 ng/ml, IL-6 – 24.3±2.7 pg/ml. This indicates the persistence of moderate-intensity systemic inflammation.

In the low–frequency group (n=107), the inflammation indices were lower, but still exceeded the control: CRP – 1.72±0.66 mg/l, PCT – 0.62±0.11 ng/ml, IL-6 – 12.8±1.9 pg/ml. These values reflect a less pronounced but persistent activation of the inflammatory response.

In the control group (n=50), the indicators were at minimum levels (CRP: -0.37±0.123 mg/l; PCT: 0.08±0.02 ng/ml; IL-6: 4.6±0.8 pg/ml), corresponding to the physiological postpartum state without signs of severe inflammation.

The presented data demonstrate a clear dependence of leukocyte formula indicators and the NLR index on the frequency of inflammatory complications. (Table 2).

Table 2

**Comparative characteristics of leukocytes, NLR index, Fibrinogen, and ESR**

| Group | White blood cells ($\times 10^3$/l) | Neutrophils (%) | Lymphocytes (%) | NLR | Fibrinogen (g/l) | ESR (mm/hr) |
|---|---|---|---|---|---|---|
| High frequency | 17.891±0.99 | 82±3 | 11±2 | 7.4±0.6 | 5.6±0.4 | 38±5 |
| Average frequency | 14.541±0.935 | 76±2 | 16±2 | 4.7±0.4 | 4.7±0.3 | 29±4 |
| Low frequency | 11.344±0.87 | 69±3 | 22±3 | 3.1±0.3 | 3.9±0.2 | 18±3 |
| The control group | 7.46±1.521 | 58±2 | 32±2 | 1.8±0.2 | 2.8±0.2 | 9±2 |

In the high–frequency group, the maximum leukocyte count was 17.891±0.99×103/l, more than 2 times higher than in the control group ($7.46±1.521×10^3$/l). At the same time, pronounced neutrophilosis (82±3 %) and a significant decrease in the proportion of lymphocytes (11±2 %) were observed. The NLR index reaches 7.4±0.6, indicating a pronounced systemic inflammatory response and dominance of the innate immune response.

In the medium–frequency group, there is a decrease in indicators compared with the high–frequency group: leukocytes – 14.541 $±0.935×10^3$/l, neutrophils – 76±2 %, lymphocytes -16±2 %, NLR – 4.7±0.4. Nevertheless, these values remain significantly higher than the control values, indicating the persistence of a moderate degree of active inflammation. In the low–frequency group, the indicators continue to decrease: leukocytes – $11.344±0.87×10^3$/l, neutrophils – 69±3 %, lymphocytes – 22±3 %, NLR – 3.1±0.3. Despite a decrease in inflammation severity, the values still exceed control levels. In the control group, leukocytes were $7.46±1.521×10^3$/l, neutrophils were 58±2 %, lymphocytes were 32±2 %, and NLR was 1.8±0.2, which corresponded to the physiological postpartum state without signs of pronounced systemic inflammation.

A pronounced dependence of fibrinogen and ESR levels on the frequency of inflammatory complications in the postpartum period was revealed. In the high-frequency group, the maximum fibrinogen level was 5.6±0.4 g/l, almost 2 times higher than in the control group (2.8±0.2 g/l). ESR is also significantly increased, at 38±5 mm/hour versus 9±2 mm/hour in the control. These values reflect the pronounced activation of acute-phase proteins and an intense systemic inflammatory process.

In the medium–frequency group, fibrinogen decreases to 4.7±0.3 g/l and ESR to 29±4 mm/hr, but both remain significantly higher than the control values. This indicates the persistence of a moderate inflammatory reaction.

In the low–frequency group, there is a further decrease in indicators: fibrinogen – 3.9±0.2 g /l, ESR – 18±3 mm/ hr. Despite the trend towards normalization, the values still exceed the control level, indicating a residual inflammatory response.

In the control group, the indicators correspond to the physiological values of the postpartum period: fibrinogen – 2.8±0.2 g /l, ESR – 9±2 mm/hr.

In general, fibrinogen and ESR levels increase consistently as the incidence of complications rises. An increase in fibrinogen, an acute-phase protein, is directly related to increased synthesis under the influence of proinflammatory cytokines (in particular, IL-6), whereas an increase in ESR reflects changes in plasma protein composition and increased red blood cell aggregation. The results confirm the diagnostic significance of these indicators for assessing the severity of the systemic inflammatory response in the postpartum period.

The results confirm the position outlined in the introduction regarding the high prognostic significance of laboratory markers of inflammation in postpartum infectious complications. A systematic review by Oben A.G. et al. showed that interleukin-6, C-reactive protein, and procalcitonin are among the most informative biomarkers of maternal infection [9]. In our study, these indicators consistently increased with the frequency and intensity of spectral peaks, indicating a close relationship between spectroscopically detectable molecular changes and the severity of the systemic inflammatory response. An additional increase in fibrinogen, ESR, and the NLR index confirms the multicomponent nature of the inflammatory response and shows that Raman spectroscopy reflects not one single marker, but a set of biochemical shifts.

The relevance of the early prognosis is also confirmed by clinical and epidemiological data. The GLOSS study emphasized that timely detection of maternal infection and prompt initiation of treatment are key conditions for preventing severe outcomes [13]. Liu L.Y. et al. established a link between postpartum septic readmissions with an unfavorable course and the need for more intensive monitoring [8]. The work of Wen Y. et al. also showed that even simple models based on inflammatory parameters and clinical risk factors can be useful for early patient stratification [12]. Our data support these positions, as they demonstrate the possibility of supplementing standard laboratory tests with an integrated spectroscopic approach capable of detecting pathological changes before a detailed clinical picture is formed.

From a molecular biological point of view, the revealed amplification of the bands Amide I, Amide III, zone 1445 $cm^{-1}$and range 2850–2930 $cm^{-1}$corresponds to the data presented in the review by M. Paraskevaidi et al., where it was shown that infrared and Raman spectroscopy are sensitive to changes in the protein and lipid profile in infectious and inflammatory conditions [10].

A similar principle for the diagnostic interpretation of spectra is described in the work of Zhang J. et al., demonstrating the high accuracy of Raman spectroscopy in differentiating pathologically altered tissues from normal ones [14]. Although this study was conducted in a different clinical field, its results confirm the method's general analytical ability to detect subtle molecular rearrangements. Therefore, our data do not contradict the literature and indicate the potential to include Raman spectroscopy in a comprehensive algorithm for the early prediction of postpartum inflammatory complications.

Unlike individual laboratory markers, Raman spectroscopy provides an integrated assessment of

metabolic and structural changes in biological environments, which increases its prognostic value. The method is non-invasive, fast, and does not require complex sample preparation, which makes it a promising tool for early risk stratification of postpartum inflammatory complications [1].

**Limitations.** The limitations of the study include a limited sample size, a single-center design, and a relatively short follow-up period. This does not allow us to fully assess the long-term prognostic value of the identified changes and extend the results to the entire maternity population.

## Conclusion

The analysis of clinical, laboratory, and spectroscopic data indicates the high diagnostic and prognostic significance of Raman spectroscopy in assessing inflammatory complications of the postpartum period. It was found that changes in the intensity of characteristic spectral bands (Amide I, Amide III, phenylalanine ~1003 $cm^{-1}$, lipid bands 1445 and 2850-2930 $cm^{-1}$) correlate with increased levels of CRP, procalcitonin, IL-6, fibrinogen, as well as with an increase in the NLR index and ESR.

The sequential increase in protein and lipid peaks, accompanied by an increase in the frequency of complications, reflects activation of the cytokine cascade, synthesis of acute-phase proteins, and the development of oxidative stress. This confirms Raman spectroscopy's ability to detect molecular changes preceding the clinical manifestation of severe inflammation.

Thus, Raman spectroscopy can be considered an effective additional prognostic marker of systemic inflammatory response in the postpartum period and a potential basis for developing rapid diagnostic algorithms for early detection of complications.

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