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Evaluation of the effectiveness of using leucocyte indices in the differential diagnosis of acute abdominal pain in children in the first 6 years of life

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ABSTRACT. Introduction. Evaluation of diagnostic efficiency of leukocyte indices in differential diagnostics of acute abdominal pain in children under 6 years of age, with identification of the most informative indicators, is a highly relevant task of modern pediatrics. The solution to this problem can significantly improve the accuracy of diagnostics, reduce the incidence of complications and optimize patient management tactics. **The aim** – to evaluate the efficiency of integral leukocyte indices in differential diagnostics of acute abdominal pain in children of the first 6 years of life. **Materials and methods.** A retrospective cohort study of 130 children was conducted (acute appendicitis n=35; functional bowel disorders: n=40; control: n=55). Based on the general blood test data, 13 integral leukocyte indices were calculated. Statistical analysis was performed using nonparametric methods. **Results.** High differential potential was revealed for the following indices: erythrocyte loading coefficient (0.88 ± 0.76 conventional units for acute appendicitis, compared with 0.53 ± 0.33 conventional units for functional bowel disorders; $p=0.006$), immunolymphocytic potential (147.41 ± 177.87 conventional units for acute appendicitis, compared with 287.21 ± 272.83 conventional units for functional bowel disorders; $p < 0.001$), leukocyte intoxication index (4.84 ± 5.58 conventional units for acute appendicitis, compared with 0.86 ± 1.29 conventional units for functional bowel disorders; $p < 0.0001$), modified leukocyte intoxication index (4.32 ± 3.24 conventional units for acute appendicitis, compared with 3.27 ± 2.57 conventional units for functional bowel disorders; $p < 0.01$), reactive neutrophil response (15.54 ± 13.07 conventional units in acute appendicitis compared to 9.21 ± 15.36 conventional units in functional bowel disorders; $p > 0.05$), body resistance index (5.82 ± 9.69 conventional units in acute appendicitis, compared to 33.59 ± 13.66 conventional units in functional bowel disorders; $p < 0.001$), lymphocyte-granulocyte index (2.45 ± 3.31 conventional units in acute appendicitis, compared to 5.72 ± 7.98 in functional bowel disorders; $p < 0.05$). Moderate value was noted for blood leukocyte shift index and Krebs index, but with limitations. Low significance was revealed for cell-phagocytic potential, leukocyte ratio and erythrocyte sedimentation rate, nuclear index of endotoxemia – no significant differences, for allergic predisposition of the body – nonspecificity. **Conclusions.** The combination of erythrocyte loading coefficient, immunolymphocytic potential, leukocyte intoxication index, modified leukocyte intoxication index, body resistance index, blood leukocyte shift index, lymphocyte-granulocyte index demonstrated the greatest potential for differential diagnosis of acute appendicitis and functional bowel disorders in children under 6 years of age. Validation on an independent cohort and clarification of threshold values are necessary for implementation in clinical practice.

KEYWORDS: acute abdominal pain, differential diagnosis, leukocyte indices, children

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Оригинальная статья

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Оценка эффективности применения лейкоцитарных индексов при дифференциальной диагностике острой боли в животе у детей первых 6 лет жизни

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РЕЗЮМЕ. Введение. Оценка диагностической эффективности лейкоцитарных индексов при дифференциальной диагностике острой абдоминальной боли у детей в возрасте до 6 лет с выявлением наиболее информативных показателей — высокоактуальная задача современной педиатрии. Решение этой проблемы может существенно повысить точность диагностики, снизить частоту осложнений и оптимизировать тактику ведения пациентов. **Цель** — оценить эффективность интегральных лейкоцитарных индексов при дифференциальной диагностике острой боли в животе у детей первых 6 лет жизни. **Материалы и методы.** Проведено ретроспективное когортное исследование 130 детей (острый аппендицит: $n=35$; функциональные нарушения кишечника: $n=40$; контроль: $n=55$). На основе данных общего анализа крови рассчитаны 13 интегральных лейкоцитарных индексов. Статистический анализ выполнен с использованием непараметрических методов. **Результаты.** Высокий дифференциальный потенциал выявлен у следующих индексов: нагрузочный эритроцитарный коэффициент ($0,88 \pm 0,76$ усл. ед. при остром аппендиците в сравнении с $0,53 \pm 0,33$ усл. ед. при функциональных нарушениях кишечника; $p=0,006$), иммунолимфоцитарный потенциал ($147,41 \pm 177,87$ усл. ед. при остром аппендиците в сравнении с $287,21 \pm 272,83$ усл. ед. при функциональных нарушениях кишечника; $p < 0,001$), лейкоцитарный индекс интоксикации ($4,84 \pm 5,58$ усл. ед. при остром аппендиците в сравнении с $0,86 \pm 1,29$ усл. ед. при функциональных нарушениях кишечника; $p < 0,0001$), лейкоцитарный индекс интоксикации модифицированный ($4,32 \pm 3,24$ усл. ед. при остром аппендиците в сравнении с $3,27 \pm 2,57$ усл. ед. при функциональных нарушениях кишечника; $p < 0,01$), реактивный ответ нейтрофилов ($15,54 \pm 13,07$ усл. ед. при остром аппендиците в сравнении с $9,21 \pm 15,36$ усл. ед. при функциональных нарушениях кишечника; $p > 0,05$), индекс резистентности организма ($5,82 \pm 9,69$ усл. ед. при остром аппендиците в сравнении с $33,59 \pm 13,66$ усл. ед. при функциональных нарушениях кишечника; $p < 0,001$), индекс лимфоцитарно-гранулоцитарный ($2,45 \pm 3,31$ усл. ед. при остром аппендиците в сравнении с $5,72 \pm 7,98$ усл. ед. при функциональных нарушениях кишечника; $p < 0,05$). Умеренная ценность отмечена у индекса сдвига лейкоцитов крови и индекса Кребса, но с ограничениями. Низкая значимость выявлена у клеточно-фагоцитарного потенциала, индекса соотношения лейкоцитов и скорости оседания эритроцитов, у ядерного индекса эндотоксикоза — отсутствие значимых различий, у аллергической настроенности организма — неспецифичность. **Выводы.** Комбинация нагрузочного эритроцитарного коэффициента, иммунолимфоцитарного потенциала, лейкоцитарного индекса интоксикации, лейкоцитарного индекса интоксикации модифицированного, реактивного ответа нейтрофилов, индекса резистентности организма, индекса сдвига лейкоцитов крови, индекса лимфоцитарно-гранулоцитарного продемонстрировала наибольший потенциал для дифференциальной диагностики острого аппендицита и функциональных нарушений кишечника у детей до 6 лет. Для внедрения в клиническую практику необходима валидация на независимой когорте и уточнение пороговых значений.

КЛЮЧЕВЫЕ СЛОВА: острая абдоминальная боль, дифференциальная диагностика, лейкоцитарные индексы, дети

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

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INTRODUCTION

Acute abdominal pain (AAP) is the most common reason for referral to a pediatric surgeon in children under 6 years of age [1, 2]. Between 10% and 25% of children experience recurrent episodes of abdominal pain over the course of a year, yet only 2% to 4% of them seek medical care [1–3]. In the breakdown of emergency surgical procedures on abdominal organs, appendectomy accounts for 80%, diagnostic laparoscopy for 11%, acute gynecological pathology for 5%, abdominal trauma for 2%, other conditions – 2%, of which 1% is intestinal obstruction [1–3]. Overall, complaints of abdominal pain in children rank second in frequency after infectious diseases in pediatric practice [2, 3]. This symptom serves as a nonspecific marker for a wide range of conditions – from transient functional disorders to life-threatening surgical pathologies – with up to 60% of episodes of acute abdominal pain remaining etiologically unrecognized at the initial stage [4, 5, 7].

The key diagnostic challenge is to distinguish conditions requiring urgent surgical intervention – such as acute appendicitis (AA), intussusception, and peritonitis – from conditions that can be managed conservatively or do not require active treatment (functional bowel disorders (FBD), gastroenteritis, mesadenitis) [6]. Delayed detection of surgical pathology or unwarranted surgical intervention is associated with high risks of complications and an unjustified burden on the child and the healthcare system [2, 4, 7].

The differential diagnosis of acute abdominal pain is particularly challenging in preschool-aged children (≤ 6 years) for the following reasons:

- the nonspecific nature of the clinical presentation (symptoms of AAP and other acute surgical conditions – such as pain, vomiting, fever, refusal to eat) are virtually indistinguishable from the manifestations of common viral infections, gastroenteritis, and functional abdominal pain) [8, 9];
- limited communication (a young child cannot accurately describe the nature, location, and intensity of pain) [8, 9];
- difficulties with physical examination (assessment of the abdomen is often hampered by the child's fear, restlessness, and muscle guarding, which reduces the informative value of physical findings, including signs of peritoneal irritation) [9, 10];
- high frequency of complications (due to diagnostic difficulties, children under 6 years of age with acute appendicitis are admitted to the hospital at the stage of perforation in 43–72% of cases, with the development of peritonitis and sepsis) [7];
- the standard diagnostic algorithm includes a clinical evaluation and a complete blood count (CBC), with a focus on leukocytosis; however, it has extremely low specificity [11]. Leukocytosis is observed in bacterial infections, viral diseases, stress reactions, and many non-surgical causes of AAP. Its level does not allow for reliable differentiation of AA from FBD or other inflammatory non-surgical conditions. The lack of accessible, rapid, and objective laboratory tests to distinguish between surgical and non-surgical causes of AAP in preschoolers remains one of the key unresolved problems, leading to delays in vital surgery or to unnecessary surgical interventions [9, 12].

In this context, the use of calculated leukocyte indices (LI) derived from standard CBC data appears to be a promising approach. These composite indices (such as the leukocyte shift index, leukocyte intoxication index, neutrophil-to-lymphocyte ratio, etc.) combine information about various leukocyte subpopulations and their ratios. In theory, they are capable of reflecting the degree and nature of the systemic inflammatory response (bacterial and viral, acute and chronic) and the severity of endogenous intoxication more accurately than isolated leukocytosis. Assessing the body's immunoreactivity allows for predicting the course of the process and evaluating the risk of postoperative complications [8–10].

Their advantages lie in their objectivity, accessibility, speed of results, and potentially higher specificity due to the simultaneous consideration of multiple parameters, which reduces the influence of individual variations [8–10]. LI make it possible to detect endogenous intoxication even in cases where standard CBC levels fall within the reference range. The use of LI should be viewed not as a replacement for existing comprehensive diagnostic algorithms, but as a valuable supplement to them in the early stages. Integrating LI into established assessment scales (e.g., the Alvarado scale) can enhance their objectivity and informative value, particularly in borderline cases or when diagnostic resources are limited [8–10].

A critical barrier to incorporating LI into the differential diagnosis algorithm for AAP in young children is the lack of evidence specifically for this population. Their actual diagnostic effectiveness and differential diagnostic significance have not been studied specifically for distinguishing between surgical (AA) and nonsurgical (FBD) causes of AAP in this complex group of patients [8–10].

Thus, evaluating the diagnostic effectiveness of LI for the differential diagnosis of AAP, particularly the distinction between AA and FBD, in children under 6 years of age – including the determination of reference values and the identification of the most informative indicators – is a highly relevant task in modern pediatrics and pediatric surgery. Resolving this issue could significantly improve diagnostic accuracy, reduce the incidence of complications, and optimize patient management strategies.

AIM

To evaluate the effectiveness of comprehensive leukocyte indices in the differential diagnosis of acute abdominal pain in children under 6 years of age.

MATERIALS AND METHODS

A cohort, comparative, retrospective study was conducted involving 75 children with AAP (AA, n=35; FBD, n=40), aged 1 month to 6 years. The children were hospitalized within 1–72 hours of the onset of initial symptoms. Healthy children of the same age constituted the control group (CG) (n=55).

Inclusion criteria: clinical diagnosis of AA or FBD (at discharge from the hospital), hospitalized for elective surgical treatment of a pathological condition, age ranging from 1 month to 6 years, consent of parents or guardians to participate in the study.

Exclusion criteria: failure to meet inclusion criteria, congenital malformations and abdominal neoplasms, HIV infection.

Complete blood count (CBC) parameters were analyzed (performed within 1 hour of admission). Based on the complete blood count data, integral leukocyte indices (ILI) were calculated [9, 10]. In practice, calculating ILI data does not require special software and can be performed by a physician

using Microsoft Excel (or similar software), as well as manually.

The data were analyzed using STATISTICA 13.3 with nonparametric methods. Continuous variables are expressed as medians (Me) with confidence intervals (95% CI) or means (M) and standard deviations. The Mann–Whitney U test was used to compare two independent samples in the absence of evidence of a normal distribution of the data. Differences were considered statistically significant at a p-value of less than 0.05.

RESULTS AND DISCUSSION

In CG patients ILI was studied, and reference values were established for children under 6 years of age. The status of the overall reactive potential was assessed based on the calculation of integral indices [9, 10].

Erythrocyte Load Coefficient (ELC). This indicator indirectly reflects the degree of endogenous intoxication and inflammatory processes in the body. It is based on the ability of erythrocyte membranes to adsorb toxic metabolites, inflammatory mediators, and tissue breakdown products on their surface. An increase in ELC indicates increased absorption of pathological substances on erythrocytes, which is a marker of toxic exposure [9, 10].

Cellular-Phagocytic Potential (CPP). This indicator reflects the overall ability of blood immune cells (primarily neutrophils and monocytes) to perform phagocytosis. The higher the CPP level, the greater the body's protective capacity [9, 10].

Immunolymphocytic Potential (ILP). This indicator reflects the functional activity and reserve capacity of lymphocytes. A decrease in ILP directly indicates functional insufficiency of the lymphocytic component [9, 10].

Allergic Predisposition of the Body (APB). This indicator is primarily based on the eosinophil level. It serves as an indirect marker of the presence and activity of an inflammatory process (parasitic, autoimmune) in the body. A decrease in APB indicates infectious inflammatory phenomena, while an increase in APB indicates an autoimmune or allergic process [9, 10].

The degree of endogenous intoxication was assessed according to the calculation of integral indices.

Leukocyte Intoxication Index (LII). This indicator takes into account changes in the leukocyte

formula, the ratio of different types of leukocytes, and the appearance of immature and degenerative forms of neutrophils. An increase in LII is associated with an increase in toxic burden and severity of the condition [9, 10].

Modified Leukocyte Intoxication Index (MLII).

This is an improved formula for assessing the severity of endogenous intoxication and the inflammatory process, calculated on the basis of the blood leukocyte formula. Its calculation also includes eosinophils and plasma cells, with correction for zero values [9, 10].

Neutrophil Reactive Response (NRR). This indicator reflects the intensity of the neutrophil response to inflammation or intoxication. Unlike LII, it focuses only on the neutrophilic component [9, 10].

Body Resistance Index (BRI). This indicator assesses the ability of the immune system for emergency mobilization during acute inflammation or intoxication. An increase in BRI indicates immune hyperreactivity (acute bacterial process, pronounced intoxication), while a decrease in BRI indicates depletion of reserves (severe sepsis, viral infections, immunodeficiency) [9, 10].

Blood Leukocyte Shift Index (BLSI). This index reflects the presence of immature forms of the neutrophilic component in response to inflammation or intoxication. An increase in BLSI indicates an acute bacterial process and the release of immature neutrophils from the bone marrow into the bloodstream, while a decrease in BLSI is observed in viral infections or depletion of the granulocytic lineage [9, 10].

Lymphocyte-Granulocyte Index (LGI). This indicator reflects the balance between lymphocytes and neutrophils, and the immune response in the hemogram. An increase in LGI indicates predominance of the lymphocytic component (typical of viral infections and autoimmune processes), while a decrease in LGI indicates dominance of the neutrophilic response (typical of acute bacterial infections and pronounced intoxication) [9, 10].

Garkavi Index (GI). This indicator reflects the relationship between two components of immunity—cellular and humoral. Its key essence is the assessment of the adaptive tension of the body during inflammation, intoxication, or stress. A decrease in GI indicates dominance of the neutrophilic component, characteristic

of acute bacterial infections. An increase in GI indicates predominance of the lymphocytic response, typical of viral infections, chronic inflammation, and autoimmune processes. It is also observed in depletion of the neutrophilic lineage [9, 10].

Leukocyte-to-Erythrocyte Sedimentation Rate Ratio Index (LESRI). This indicator assesses the relationship between the cellular and humoral components of the inflammatory response. An increase in LESRI indicates predominance of an acute cellular response, where leukocytosis rises faster than ESR. A decrease in LESRI indicates dominance of the humoral immune response, where ESR is elevated despite normal or reduced leukocyte levels [9, 10].

Krebs Index (KI). This indicator reflects the ratio between neutrophils and lymphocytes in peripheral blood. An increase in KI indicates acute bacterial infections and stress conditions, while a decrease in KI is interpreted as a manifestation of viral infection or depletion of the neutrophilic component [9, 10].

Nuclear Endotoxiosis Index (NEI). This indicator assesses the degree of toxic damage to neutrophils during severe intoxication. An increase in NEI is associated with the severity of endotoxiosis and reflects the accumulation of toxins that damage blood cells [9, 10].

Comparing the groups of children with FBD and AA according to the above-mentioned ILI, the following results were obtained.

The ELC in the group of children with FBD was 0.53 ± 0.33 conventional units, $Me = 0.43$ (95% CI 0.28–0.41), which was significantly higher than in the CG (0.43 ± 0.24 conventional units, $p < 0.05$) and indicated the presence of a moderate inflammatory process and intoxication. In the group of patients with AA, the ELC was 0.88 ± 0.76 conventional units, $Me = 0.59$ (95% CI 0.62–1.01), which sharply and significantly exceeded both the CG values and the values of the FBD group ($p < 0.01$) (Fig. 1). This indicates a pronounced inflammatory process and severe intoxication in AA. Objective confirmation of significant inflammation in the vermiform appendix in all patients with AA confirms the diagnostic value of ELC for this pathology in this age group.

The CPP in the group of children with FBD was 685.64 ± 287.79 conventional units, $Me = 652.54$ (95% CI 237.29–365.78), which was slightly higher than in the CG (604.10 ± 238.14 conventional



Fig. 1. Erythrocyte loading coefficient (ELC) levels in the study groups: OA — acute appendicitis; FBD — functional bowel disorders (here and further in the figures) (the figure is prepared by the authors)

Рис. 1. Уровень нагрузочного эритроцитарного коэффициента (НЭК) в исследуемых группах: ОА — острый аппендицит; ФНК — функциональные нарушения кишечника (здесь и далее на рисунках) (рисунок подготовлен авторами)



Fig. 2. Cell-phagocytic potential (CPP) levels in the study groups (the figure is prepared by the authors)

Рис. 2. Уровень клеточно-фагоцитарного потенциала (КФП) в исследуемых группах (рисунок подготовлен авторами)



Fig. 3. Immunolymphocytic potential (ILP) levels in the study groups (the figure is prepared by the authors)

Рис. 3. Уровень иммунолимфоцитарного потенциала (ИЛП) в исследуемых группах (рисунок подготовлен авторами)

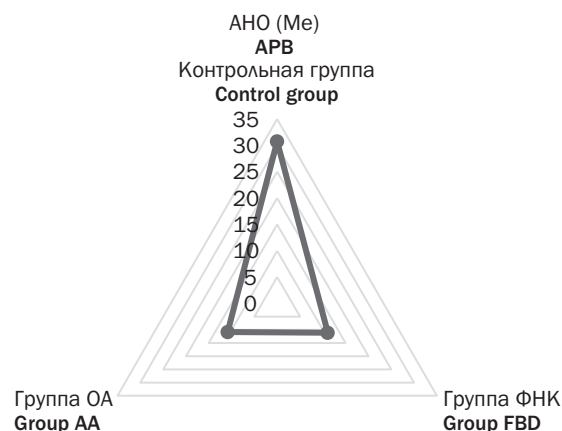


Fig. 4. Allergic predisposition of the body (APB) levels in the study groups (the figure is prepared by the authors)

Рис. 4. Уровень аллергической настроенности организма (АНО) в исследуемых группах (рисунок подготовлен авторами)

units, $p > 0.05$) and indicated activation of nonspecific defense mechanisms in response to a moderate inflammatory process in FBD. In the group of patients with AA, the index was 641.7 ± 195.6 conventional units, $Me = 601.45$ (95% CI 159.85–252.09). These index values were slightly higher than in the CG but showed marked differences compared with the FBD group ($p > 0.05$) (Fig. 2). These values may reflect either insufficient activation of phagocytosis to control acute inflammation (which contributed to the development of AA) or depletion of protective capacities (decom-

pensation) against the background of a severe inflammatory process.

The ILP in the group of children with FBD was 287.21 ± 272.83 conventional units, $Me = 201.92$ (95% CI 224.96–346.77), which was significantly lower than in the CG (646.99 ± 265.64 conventional units, $p < 0.001$). In the group of patients with AA, the index was 147.41 ± 177.87 conventional units, $Me = 116.79$ (95% CI 145.37–229.24), and was even more significantly reduced compared with both the CG ($p < 0.001$) and FBD ($p < 0.01$) (Fig. 3). Since ILP reflects the activity of the

lymphocytic component (specific immunity), a pronounced decrease in both groups, especially in AA, is characteristic of inflammatory processes of bacterial origin, where redistribution of immune resources and/or suppression of lymphopoiesis occurs.

The APB in the group of children with FBD was 16.02 ± 12.11 conventional units, $Me=11.10$ (95% CI 8.62–19.25), which was significantly lower than in the CG (38.15 ± 32.72 conventional units, $p < 0.001$). In the group of patients with AA, the index was 15.17 ± 11.25 conventional units, $Me=10.86$ (95% CI 6.29–17.69), which was also lower than in the CG (Fig. 4). Compared with the CG, both groups demonstrated more than a two-

fold decrease in the index ($p=0.01$), which may be interpreted as an acute inflammatory process. The index values between the study groups differed insignificantly ($p \geq 0.05$).

The LII in the group of children with FBD was 0.86 ± 1.29 conventional units, $Me=0.44$ (95% CI 1.08–1.60), which was slightly higher than in the CG (0.33 ± 0.59 conventional units, $p < 0.01$). In the group of patients with AA, the index was 4.84 ± 5.58 conventional units, $Me=1.96$ (95% CI 4.56–7.19), thus sharply and significantly exceeding both the CG and the FBD group values ($p < 0.001$) (Fig. 5). This clearly demonstrates the severity of endogenous intoxication and inflammatory changes in AA compared with FBD.

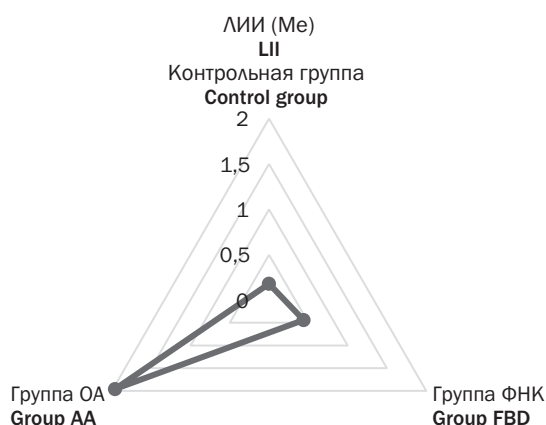


Fig. 5. Leukocyte intoxication index (LII) levels in the study groups (the figure is prepared by the authors)

Рис. 5. Уровень лейкоцитарного индекса интоксикации (ЛИИ) в исследуемых группах (рисунок подготовлен авторами)



Fig. 6. Modified leukocyte intoxication index (LIIm) levels in the study groups (the figure is prepared by the authors)

Рис. 6. Уровень лейкоцитарного индекса интоксикации модифицированного (ЛИИм) в исследуемых группах (рисунок подготовлен авторами)



Fig. 7. Reactive neutrophil response (RNR) levels in the study groups (the figure is prepared by the authors)

Рис. 7. Уровень реактивного ответа нейтрофилов (РОН) в исследуемых группах (рисунок подготовлен авторами)



Fig. 8. Body resistance index (BRI) levels in the study groups (the figure is prepared by the authors)

Рис. 8. Уровень индекса резистентности организма (ИРО) в исследуемых группах (рисунок подготовлен авторами)

The modified LII in the group of children with FBD was 3.27 ± 2.57 conventional units, $Me = 2.57$ (95% CI 1.78–3.76), which was slightly higher than in the CG (0.88 ± 0.68 conventional units, $p < 0.001$). In the group of patients with AA, the index was 4.32 ± 3.24 conventional units, $Me = 3.29$ (95% CI 2.92–5.25; $p < 0.001$) (Fig. 6). Considering the differences in the obtained values, this index quite accurately ($p < 0.001$) reflects the severity of the inflammatory process.

The NRR in the group of children with FBD was 9.21 ± 15.36 conventional units, $Me = 3.13$ (95% CI 12.19–20.78), which was significantly higher than in the CG (0.88 ± 1.29 conventional units, $p < 0.001$). In the group of patients with AA, the index was 15.54 ± 13.07 conventional units, $Me = 13.43$ (95% CI 9.81–19.59), which was also significantly higher than in the CG ($p < 0.001$) and in the FBD group ($p < 0.05$) (Fig. 7). As a modification of LII, NRR confirms the pattern: the severity of inflammatory changes and intoxication is maximal in AA, moderate in FBD, and minimal in the CG. A correlation was found between increased NRR and the severity of the process.

The BRI in the group of children with FBD was 33.59 ± 13.66 conventional units, $Me = 6.32$ (95% CI 105.14–156.19), and was significantly higher than in the CG (19.52 ± 25.53 conventional units, $p < 0.05$). This may be regarded as an adequate response of the body's defense systems to moderate inflammation in FBD. In the group of patients

with AA, the index was 5.82 ± 9.69 conventional units, $Me = 1.16$ (95% CI 7.90–12.54), and was significantly lower than in the CG ($p < 0.001$) (Fig. 8). Such a sharp decrease in BRI indicates suppression of the body's resistance in AA, reflecting the severity of the condition and decompensation of defense mechanisms.

The BLSI in the group of children with FBD was 3.02 ± 2.57 conventional units, $Me = 2.33$ (95% CI 2.15–3.19), and was significantly higher than in the CG (1.01 ± 0.78 conventional units, $p < 0.001$). In the group of patients with AA, the index was 4.51 ± 2.88 conventional units, $Me = 3.76$ (95% CI 2.36–3.72), exceeding the values in both the CG ($p < 0.001$) and the FBD group ($p < 0.05$) (Fig. 9). The obtained data confirm the presence of an inflammatory process in both groups, with greater severity in AA. However, the difference between FBD and AA is less pronounced than their difference from the CG, which may indicate relatively low specificity of BLSI for differentiating these two pathologies compared with other indices (e.g., ILP, LII, NRR).

The LGI in the group of children with FBD was 5.72 ± 7.98 conventional units, $Me = 3.19$ (95% CI 6.67–9.92), which was lower than in the CG (14.19 ± 11.09 conventional units, $p < 0.001$). In the group of patients with AA, the index was 2.45 ± 3.31 conventional units, $Me = 1.84$ (95% CI 2.71–4.27), which was significantly lower than in both the CG and the FBD group ($p < 0.001$) (Fig. 10). A significant decrease in LGI in the



Fig. 9. Blood leukocyte shift index (BLSI) levels in the study groups (the figure is prepared by the authors)

Рис. 9. Уровень индекса сдвига лейкоцитов крови (ИСКЛ) в исследуемых группах (рисунок подготовлен авторами)



Fig. 10. Lymphocytic granulocytic index (ILG) levels in the study groups (the figure is prepared by the authors)

Рис. 10. Уровень индекса лимфоцитарно-гранулоцитарного (ИЛГ) в исследуемых группах (рисунок подготовлен авторами)



Fig. 11. Harkavi index (IH) levels in the study groups (the figure is prepared by the authors)

Рис. 11. Уровень индекса Гаркави (ИГ) в исследуемых группах (рисунок подготовлен авторами)



Fig. 12. Leukocyte ratio and ESR index (LRESR) levels in the study groups (the figure is prepared by the authors)

Рис. 12. Уровень индекса соотношения лейкоцитов и СОЭ (ИЛСОЭ) в исследуемых группах (рисунок подготовлен авторами)



Fig. 13. Krebs index (IK) levels in the study groups (the figure is prepared by the authors)

Рис. 13. Уровень индекса Кребса (ИК) в исследуемых группах (рисунок подготовлен авторами)



Fig. 14. Nuclear index of endotoxemia (NIE) levels in the study groups (the figure is prepared by the authors)

Рис. 14. Уровень ядерного индекса эндотоксикоза (ЯИЭ) в исследуемых группах (рисунок подготовлен авторами)

pathological groups (especially in AA) compared with the CG indicates intoxication by autolysis products.

The GI in the group of children with FBD was 0.39 ± 0.34 conventional units, $Me = 0.32$ (95% CI 0.05–1.42), which was lower than in the CG (1.65 ± 1.36 conventional units, $p < 0.001$). In the group of patients with AA, the index was 0.29 ± 0.41 conventional units, $Me = 0.20$ (95% CI 0.09–0.56) (Fig. 11). The results in both groups were significantly lower than in the CG ($p < 0.001$), indicating a reduced immune response to the inflammatory process (typical of acute bacterial infections); however, the difference between the FBD and AA groups was small ($p > 0.05$).

The L/ESR ratio in the group of children with FBD was 202.41 ± 106.51 conventional units, $Me = 168.29$ (95% CI 88.66–133.41), which was slightly higher than in the CG (196.28 ± 97.88 conventional units, $p > 0.05$). In the group of patients with AA, the index was 188.66 ± 111.88 conventional units, $Me = 162.85$ (95% CI 90.50–146.59), which was slightly lower than in the CG. The differences between the FBD and AA groups were statistically insignificant ($p > 0.05$) (Fig. 12). The observed fluctuations relative to the CG values do not provide a clear picture for differentiating the infectious nature of inflammation (where an increase would be expected) from the autoimmune nature (where a decrease would be expected) in

either group. The results appear questionable. It is possible that studying a larger number of observations would reveal more significant patterns.

The KI in the group of children with FBD was 4.49 ± 4.75 conventional units, $Me = 3.04$ (95% CI 3.97–5.90), which was significantly higher than in the CG (1.09 ± 0.91 conventional units, $p < 0.001$). In the group of patients with AA, the index was 6.06 ± 3.25 conventional units, $Me = 5.43$ (95% CI 2.66–4.19), which was also significantly higher than in the CG ($p < 0.001$) (Fig. 13). Exceeding the reference values in both groups indicates the presence of a certain degree of endogenous intoxication. Higher index values in AA compared with FBD ($p > 0.05$) indicate greater severity of intoxication.

The NEI in the group of children with FBD was 0.22 ± 0.16 conventional units, $Me = 0.16$ (95% CI 0.13–0.19), which was slightly lower than in the CG (0.25 ± 0.17 conventional units, $p > 0.05$). In the group of patients with AA, the index was 0.19 ± 0.14 conventional units, $Me = 0.14$ (95% CI 0.11–0.18), which was also slightly lower than in the CG ($p > 0.01$) (Fig. 14). The differences between the FBD and AA groups were statistically insignificant ($p > 0.05$). The obtained results (a decrease relative to the CG in both groups)

contradict the expected increase in the index in endotoxiosis. This may indicate either insufficient sensitivity of NEI in the studied processes or an insufficient sample size for evaluating this parameter.

A COMPARATIVE ANALYSIS OF THE DIAGNOSTIC EFFECTIVENESS OF THE LEUKOCYTE INDEX

For a comprehensive assessment of the diagnostic value of the ILI, a three-stage comparison was performed. The pathology groups (FBD, AA) and the control group (CG) were compared to assess sensitivity to inflammatory changes. The AA and FBD groups were compared with each other to evaluate differential diagnostic potential.

ELC in the FBD group (0.53 ± 0.33 conventional units) did not differ statistically significantly from the CG (0.43 ± 0.24 conventional units, $p < 0.05$) (Fig. 15). In the AA group, a significant increase in the parameter to 0.88 ± 0.77 conventional units was recorded. Differences compared with the CG ($p < 0.01$) and the FBD group ($p < 0.01$) were statistically significant, confirming the differential diagnostic potential of ELC for distinguishing these pathological conditions. The value in the

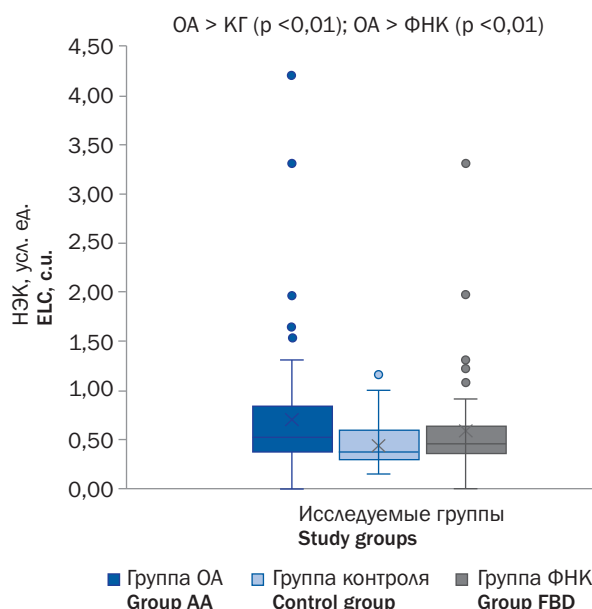


Fig. 15. Comparative characteristics of the erythrocyte loading coefficient (ELC) level in the studied groups (the figure is prepared by the authors)

Рис. 15. Сравнительная характеристика уровня нагрузочного эритроцитарного коэффициента (НЭК) в исследуемых группах (рисунок подготовлен авторами)

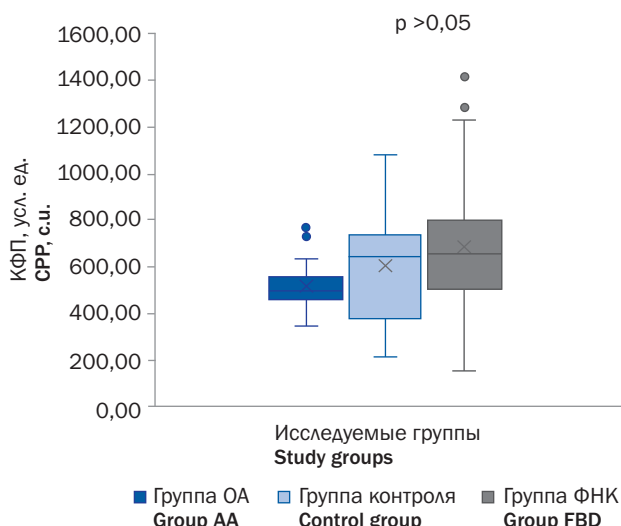


Fig. 16. Comparative characteristics of the cell-phagocytic potential (CPP) level in the studied groups (the figure is prepared by the authors)

Рис. 16. Сравнительная характеристика уровня клеточно-фагоцитарного потенциала (КФП) в исследуемых группах (рисунок подготовлен авторами)

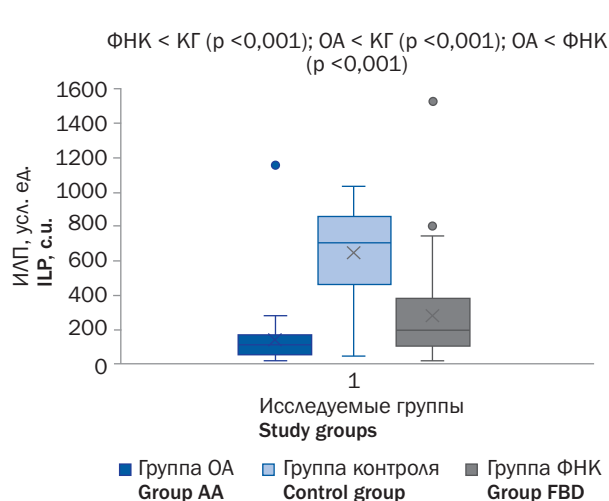


Fig. 17. Comparative characteristics of the immunolymphocytic potential (ILP) level in the studied groups (the figure is prepared by the authors)

Рис. 17. Сравнительная характеристика уровня иммунолимфоцитарного потенциала (ИЛП) в исследуемых группах (рисунок подготовлен авторами)

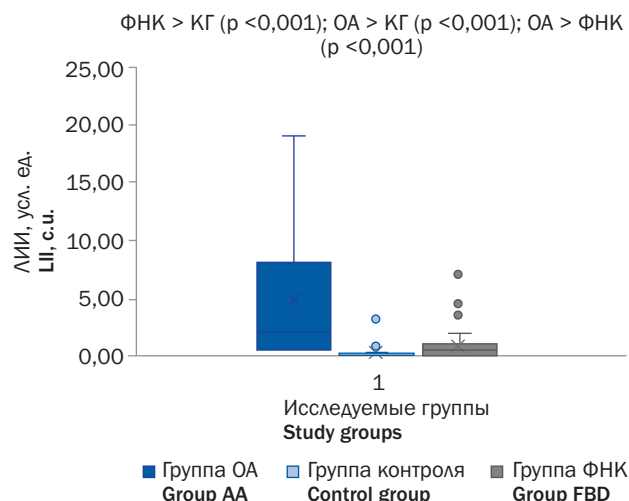


Fig. 18. Comparative characteristics of the leukocyte intoxication index (LII) level in the studied groups (the figure is prepared by the authors)

Рис. 18. Сравнительная характеристика уровня лейкоцитарного индекса интоксикации (ЛИИ) в исследуемых группах (рисунок подготовлен авторами)

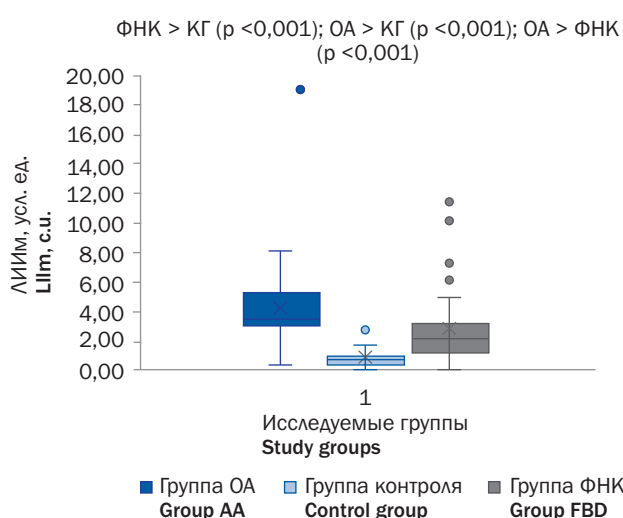


Fig. 19. Comparative characteristics of the leukocyte intoxication index (LIIIm) level in the studied groups (the figure is prepared by the authors)

Рис. 19. Сравнительная характеристика уровня лейкоцитарного индекса интоксикации модифицированного (ЛИИм) в исследуемых группах (рисунок подготовлен авторами)

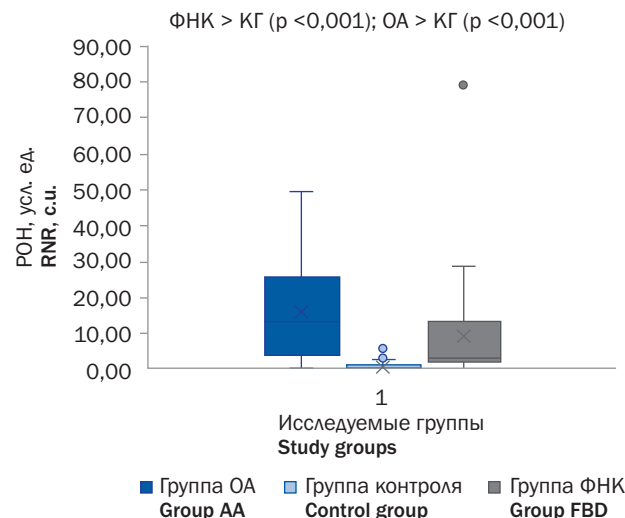


Fig. 20. Comparative characteristics of the reactive neutrophil response (RNR) level in the studied groups (the figure is prepared by the authors)

Рис. 20. Сравнительная характеристика уровня реактивного ответа нейтрофилов (РОН) в исследуемых группах (рисунок подготовлен авторами)

AA group exceeded the ELC in the CG by more than two standard deviations. These findings suggest that ELC may be considered a promising marker for differentiating surgical (AA) and functional (FBD) pathology. The statistically significant increase in ELC in the AA group compared

with the FBD group is consistent with its potential role as an indicator of destructive processes.

СРР in the FBD group (685.64 ± 287.79 conventional units) did not differ statistically significantly from the CG (604.11 ± 238.14 conventional units, $p > 0.05$) (Fig. 16). In the AA group

(641.70±195.60 conventional units), the CPP level also showed no statistically significant difference compared with the CG ($p > 0.05$). No statistically significant differences were observed between the groups either. At this stage of the study, these findings call into question the clinical utility of CPP as a diagnostic marker for differentiating the presented pathological conditions.

ILP in the FBD group (287.21±272.83 conventional units) was significantly lower than in the CG (646.99±265.64 conventional units, $p < 0.001$) (Fig. 17). In the AA group, a pronounced decrease in the parameter was recorded (147.41±177.88 conventional units), statistically significant compared with both the CG ($p < 0.001$) and the FBD group ($p < 0.01$), corresponding to severe lymphopenia. The observed marked decrease in ILP in the AA group indicates its potential as a marker of immunosuppression in this pathology, consistent with the assumption that the degree of ILP reduction correlates with disease severity.

LII in the FBD group (0.86±1.29 conventional units) was statistically significantly higher than in the CG (0.33±0.59 conventional units, $p < 0.01$), corresponding to a moderate increase (Fig. 18). In the AA group, a pronounced increase in the parameter was observed (4.84±5.58 conven-

tional units), statistically significant compared with both the CG ($p < 0.001$) and the FBD group ($p < 0.01$), with a mean value exceeding the control by 14.4 times. These findings confirm the role of LII as an important indicator of intoxication severity, while its marked elevation in the AA group supports its potential value for identifying purulent-destructive forms.

Modified LII in the FBD group (2.88±2.42 conventional units) was statistically significantly higher than in the CG (0.88±0.68 conventional units, $p < 0.001$) (Fig. 19). In the AA group, a pronounced increase in the parameter was recorded (4.37±2.92 conventional units), statistically significant compared with both the CG ($p < 0.001$) and the FBD group ($p < 0.01$). The observed marked elevation of modified LII in the AA group compared with both the CG and the FBD group is consistent with its potential role as a marker of inflammatory severity and endotoxemia characteristic of AA. The high variability of this parameter in the studied groups (standard deviation comparable to the mean value) should be taken into account when interpreting individual measurements.

NRR in the FBD group (9.21±15.36 conventional units) was statistically significantly higher than in the CG (0.88±1.29 conventional units, $p < 0.001$) (Fig. 20). In the AA group, a pronounced increase

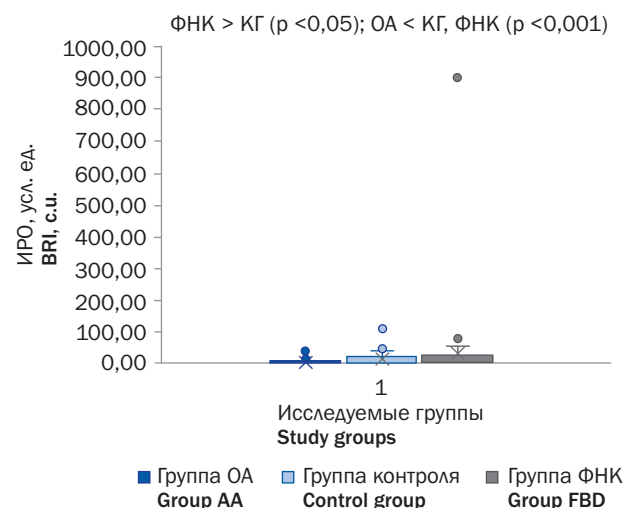


Fig. 21. Comparative characteristics of the body resistance index (BRI) level in the studied groups (the figure is prepared by the authors)

Рис. 21. Сравнительная характеристика уровня индекса резистентности организма (ИРО) в исследуемых группах (рисунок подготовлен авторами)

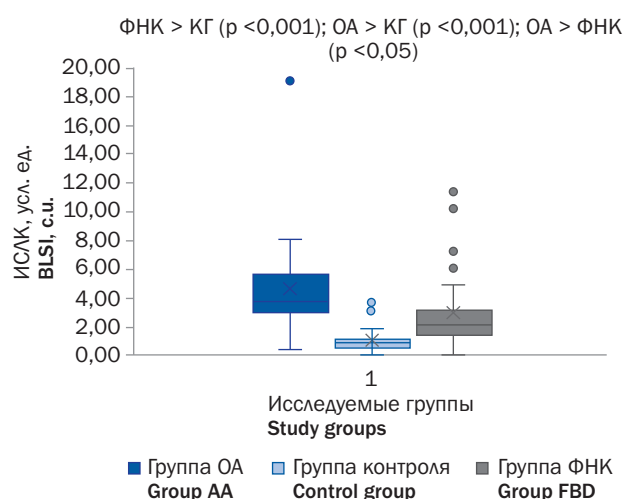


Fig. 22. Comparative characteristics of the blood leukocyte shift index (BLSI) level in the studied groups (the figure is prepared by the authors)

Рис. 22. Сравнительная характеристика уровня индекса сдвига лейкоцитов крови (ИСЛК) в исследуемых группах (рисунок подготовлен авторами)

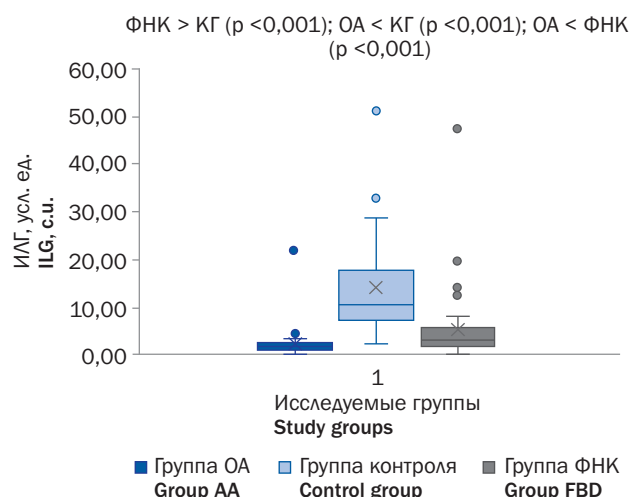


Fig. 23. Comparative characteristics of the lymphocytic granulocytic index (ILG) level in the studied groups (the figure is prepared by the authors)

Рис. 23. Сравнительная характеристика уровня индекса лимфоцитарно-гранулоцитарного (ИЛГ) в исследуемых группах (рисунок подготовлен авторами)

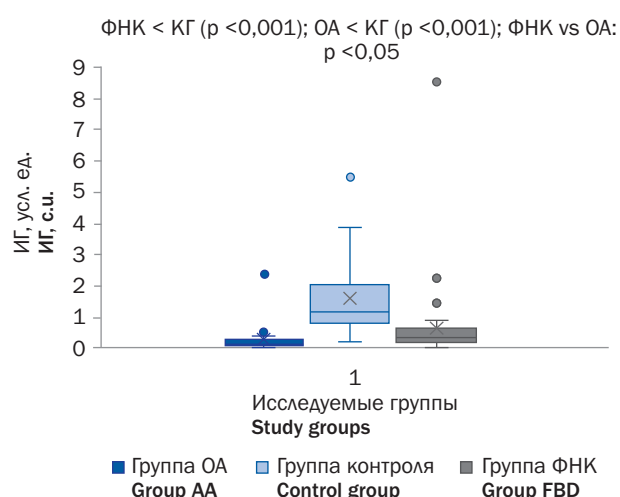


Fig. 24. Comparative characteristics of the Harkavi index (IH) level in the studied groups (the figure is prepared by the authors)

Рис. 24. Сравнительная характеристика уровня индекса Гаркави (ИГ) в исследуемых группах (рисунок подготовлен авторами)

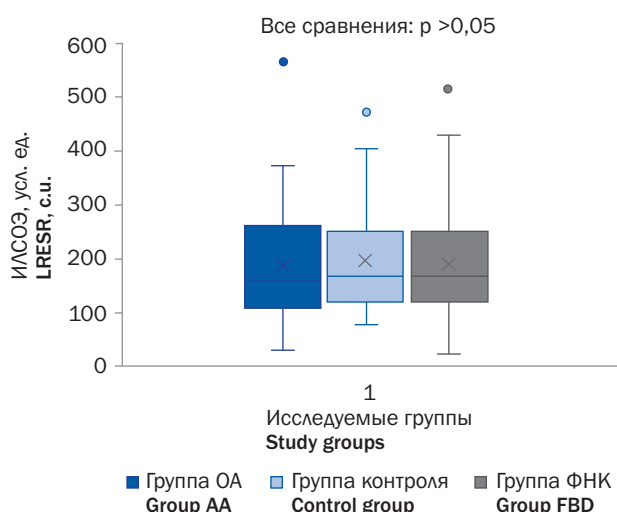


Fig. 25. Comparative characteristics of the leukocyte ratio and ESR index (LRESR) level in the studied groups (the figure is prepared by the authors)

Рис. 25. Сравнительная характеристика уровня индекса соотношения лейкоцитов и СОЭ (ИЛСОЭ) в исследуемых группах (рисунок подготовлен авторами)

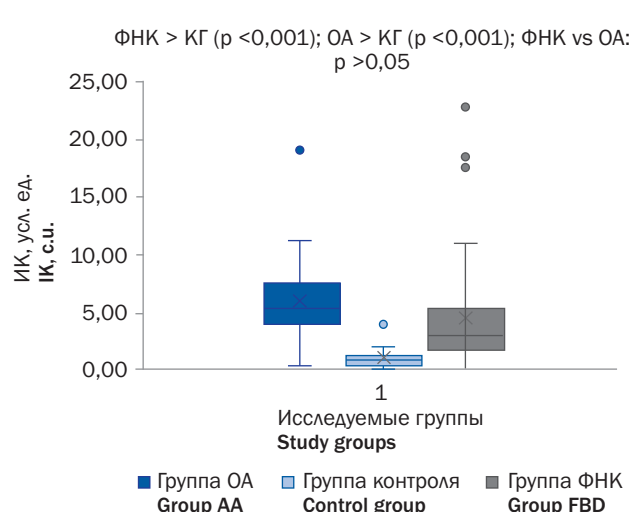


Fig. 26. Comparative characteristics of the Krebs index (IK) level in the studied groups (the figure is prepared by the authors)

Рис. 26. Сравнительная характеристика уровня индекса Кребса (ИК) в исследуемых группах (рисунок подготовлен авторами)

in the parameter was recorded (15.54 ± 13.07 conventional units), statistically significant compared with the CG ($p < 0.001$). Despite the significant increase in pathological conditions, the high variability of the parameter, with a standard deviation exceeding 100% of the mean value in both the FBD and AA groups, substantially reduces the diagnostic reliability of NRR in single measure-

ments, suggesting its potential value mainly for dynamic monitoring.

BRI in the FBD group (33.59 ± 12.66 conventional units) was slightly but statistically significantly higher than in the CG (19.52 ± 25.53 conventional units, $p < 0.05$) (Fig. 21). In the AA group, a significant decrease in the parameter was observed (5.82 ± 9.69 conventional units),

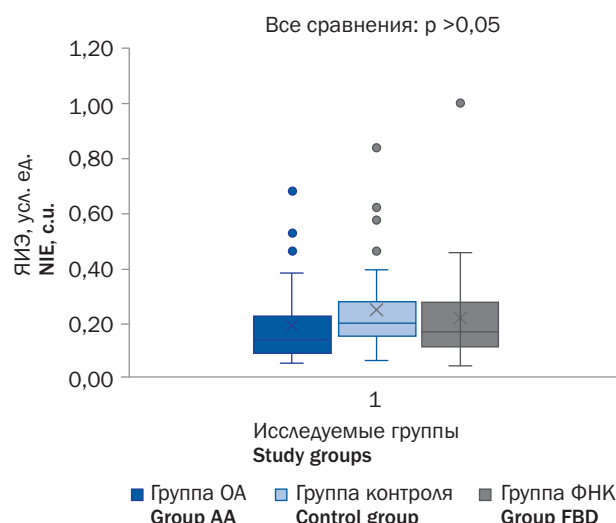


Fig. 27. Comparative characteristics of the nuclear index of endotoxemia (NIE) level in the studied groups (the figure is prepared by the authors)

Рис. 27. Сравнительная характеристика уровня ядерного индекса эндотоксикоза (ЯИЭ) в исследуемых группах (рисунок подготовлен авторами)

statistically significant compared with both the CG and the FBD group ($p < 0.001$). These findings reflect decreased body resistance in AA; however, the difference from FBD may be influenced by the high variability of the parameter in the FBD group, which limits the specificity of this index.

BLSI in the FBD group (3.02 ± 2.57 conventional units) was statistically significantly higher than in the CG (1.01 ± 0.78 conventional units, $p < 0.001$) (Fig. 22). In the AA group, a pronounced increase in the parameter was recorded (4.51 ± 2.88 conventional units), statistically significant compared with both the CG ($p < 0.001$) and the FBD group ($p < 0.05$). BLSI demonstrates the ability to reflect the intensity of the inflammatory process; however, overlapping values between the FBD ($Me=2.33$) and AA ($Me=3.76$) groups limit its specificity for differential diagnosis, suggesting that it is more appropriate when used in combination with other markers.

LGI in the FBD group (5.72 ± 7.98 conventional units) was statistically significantly lower than in the CG (14.19 ± 11.09 conventional units, $p < 0.001$) (Fig. 23). In the AA group, a pronounced decrease in the parameter was recorded (2.45 ± 3.31 conventional units), statistically significant compared with both the CG ($p < 0.001$) and the FBD group ($p < 0.001$). The observed marked decrease in LGI under pathological conditions contradicts the theoretical expectation of its increase during

infectious-inflammatory processes, indicating the need to revise the interpretative criteria and methodological aspects of its application for this pathology within the present study.

GI in the FBD group (0.39 ± 0.34 conventional units) was statistically significantly lower than in the CG (1.65 ± 1.36 conventional units, $p < 0.001$) (Fig. 24). In the AA group, a comparable decrease was observed (0.29 ± 0.41 conventional units), also statistically significant compared with the CG ($p < 0.001$), but without significant differences compared with the FBD group ($p > 0.05$), making this index of limited value for differential diagnosis of these conditions.

L/ESR Index in the FBD group (202.41 ± 106.51 conventional units) did not differ statistically significantly from the CG (196.28 ± 97.88 conventional units, $p > 0.05$) (Fig. 25). In the AA group, the parameter (188.66 ± 111.89 conventional units) also did not differ significantly from the CG ($p > 0.05$) or from the FBD group ($p > 0.05$). The absence of significant changes in the studied groups indicates that the L/ESR Index cannot be used for differential diagnosis of abdominal syndrome in children.

KI in the FBD group (4.49 ± 4.75 conventional units) was statistically significantly higher than in the CG (1.09 ± 0.91 conventional units, $p < 0.001$) (Fig. 26). In the AA group, a pronounced increase in the parameter was observed (6.06 ± 3.26 conventional units), statistically significant compared with both the CG and the FBD group ($p < 0.001$). The statistically significant increase in KI confirms its sensitivity as a marker of endotoxemia; however, the absence of a significant difference between the FBD and AA groups ($p > 0.05$) indicates limited differential diagnostic potential for distinguishing these conditions at this stage.

NEI in the FBD group (0.22 ± 0.16 conventional units) did not differ statistically significantly from the CG (0.250 ± 0.170 conventional units, $p > 0.05$) (Fig. 27). In the AA group (0.189 ± 0.139 conventional units), no significant differences were also observed compared with either the CG ($p > 0.05$) or the FBD group ($p > 0.05$). These results indicate that NEI is not an informative marker for these pathologies.

CONCLUSION

The conducted study revealed a high differential diagnostic potential of the combination of the indices ELC, ILP, LII, modified LII, NRR, BRI,

BLSI, and LGI for distinguishing acute appendicitis and functional bowel disorders in children. Statistically significant differences in these markers between the acute appendicitis and functional bowel disorder groups, as well as characteristic dynamics (in acute appendicitis: a pronounced increase in ELC, LII, modified LII, NRR, and BLSI; a significant decrease in ILP, BRI, and LGI), indicate the promise of their combined use. Our findings require validation in an independent patient cohort, i.e., under the conditions of a new prospective study conducted prior to establishing a final diagnosis, followed by analysis of the new results.

ADDITIONAL INFORMATION

Authors' contribution. R.F. Makhmutov – formulation and development of the idea, research objectives, final editing; G.A. Novikov – preparation, writing of the initial draft of the manuscript.

All authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

Consent for publication. Written consent was obtained from legal representatives of the patients for publication of relevant medical information within the manuscript.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Р.Ф. Махмутов – формулирование и развитие идеи, цели исследования, финальное редактирование; Г.А. Новиков – подготовка, написание первоначального черновика рукописи.

Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Информированное согласие на публикацию. Авторы получили письменное согласие законных представителей пациентов на публикацию медицинских данных.

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