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Received by the editorial office: 22.01.2025 / Accepted for publication: 09.04.2026



DOI 10.25789/YMJ.2026.94.02

UDC 616-053.31:618.5-089.888]:616.8-001.8

Criteria for early diagnosis of neonatal neurological abnormalities by mode of delivery

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Abstract. The article presents an analysis of the impact of cesarean section (CS) on the health of newborns, driven by the high (28.5%) and continuously growing rate of operative delivery in the Russian Federation. The aim of the work was to develop an algorithm for the early detection of hypoxic, metabolic, and neurological disorders in children. The study included a retrospective analysis of 6629 births and a prospective observation of 104 full-term newborns (after vaginal delivery, planned, and emergency CS). It was established that CS, especially emergency CS, is associated with a higher frequency of neurological abnormalities (62-67% versus 18% in vaginal delivery), metabolic stress (lactate level 4.4 mmol/L), and problems with breastfeeding. Independent predictors of neonatal disorders were identified. Based on the obtained data, a two-stage monitoring algorithm (in the maternity hospital and outpatient setting) was developed for the timely diagnosis and prevention of pathologies in children born by CS.

Keywords: newborns, cesarean section, umbilical cord blood lactate, neurosonography, neurological disorders, prognostic factors

Funding. The study had no sponsorship. The material of the article was collected as part of writing a dissertation for the degree of Candidate of Medical Sciences.

For citation: Kulik A.A., Rzyankina M.F. Criteria for early diagnosis of neonatal neurological abnormalities by mode of delivery. Yakut Medical Journal, 2026. 94(2): 9-14. <https://doi.org/10.25789/YMJ.2026.94.02>

Introduction. The current demographic situation in the Russian Federation is marked not only by a steady decline in the birth rate but also by a progressive increase in the proportion of operative deliveries. According to data for 2022, the frequency of cesarean sections reached 28.5%, and in large perinatal centers, this figure often exceeds 60% [1, 2]. Such figures significantly deviate from the optimal range of 10-15% recommended by the World Health Organization [3]. It is known that birth via CS is associated for the child with an increased probability of developing a number of complications, including respiratory distress syndrome, hypoxic-ischemic lesions of the central nervous system, as well as metabolic and neurocognitive disorders [3, 4, 5]. Among the key pathogenetic mechanisms considered are the absence of physiological stress impact during vaginal delivery and

the induction of oxidative stress [6, 7]. A particular challenge is the management of pregnancy and delivery when meconium is detected in the amniotic fluid, which significantly increases the risks of both surgical intervention and neonatal asphyxia [8, 9]. The concentration of lactate in umbilical cord blood is recognized as an informative marker of the fetal metabolic state; however, its routine determination in the clinical practice of maternity facilities is not established [10, 11]. Despite numerous studies on perinatal outcomes, aspects related to oxidative stress, metabolic acidosis, and nervous system dysfunction in children born by CS require deeper and more systematic investigation.

The aim of this work was to develop, based on a detailed assessment of neonatal health in the neonatal period, considering the method of delivery, a clear

algorithm of actions aimed at the early detection of hypoxic, metabolic, and neurological abnormalities.

Materials and Methods. During the period 2022-2025, a study dedicated to the comparative analysis of the influence of different delivery methods on the condition of newborns was conducted at the Department of Polyclinic Pediatrics of FESMU. Data from 6629 births in Khabarovsk facilities for 2015-2023 were retrospectively analyzed. The prospective study included 104 full-term newborns after vaginal delivery (n=34), planned (PCS, n=34), and emergency cesarean section (ECS, n=36), performed using the modified M. Stark technique under spinal-epidural anesthesia.

Newborns underwent a standard set of examinations, including analysis of medical records, Apgar score assessment, physical examination (including

neurological status assessment), anthropometric measurements using INTERGROWTH-21st standards, laboratory tests (determination of lactate level in umbilical cord blood, assessment of redox balance using the induced chemiluminescence method), and neurosonography (with Dopplerography if necessary).

To identify relationships between variables, the quadratic regression method was used. Prediction of binary outcomes was performed using binary logistic regression. Diagnostic accuracy was assessed using ROC analysis. In all cases, the critical significance level was set at $p < 0.05$ with the Bonferroni correction applied to control the rate of false-positive results.

Ethical Review. The Local Ethics Committee of the FGBOU VO "Far Eastern State Medical University" of the Ministry of Health of the Russian Federation granted permission to conduct this study. The corresponding approval is reflected in the minutes of the committee meeting No. 2 dated January 28, 2021, which provided a positive assessment of the ethics of the presented work (FGBOU VO FESMU of the Ministry of Health of Russia, 2021).

Results and Discussion. Analysis of obstetric care indicators in Khabarovsk over a nine-year period revealed a steady negative trend. The total number of births in three level II facilities decreased from 6629 to 2993, corresponding to a decline of 54.84% (Fig. 1). The most frequent maternal factors determining the need for cesarean section were the presence of a uterine scar (422 episodes per year), disorders during labor (233 episodes), and cephalopelvic disproportion (222 episodes) (Fig. 2). Concerning the fetus, the main reasons for operative delivery were signs of hypoxia (144 episodes, with a 3.5-fold increase over the period under review) and breech presentation (109 episodes) (Fig. 3).

A comparative characterization of the condition of newborns from different groups showed that macrosomia was diagnosed statistically significantly more often in children after planned CS (20.4% of cases) (Tab. 1). Pathological weight loss exceeding 10% of birth weight was most frequently recorded in the emergency CS group (17%) compared to the planned CS group (8.8%) and physiological birth group (5.9%) (Fig. 4). Data analysis demonstrated that the Apgar score at the 1st minute was statistically significantly lower in newborns after elective cesarean section. By the 5th minute of life, indicators in all compared groups normalized, reaching 8-10 points (Fig.

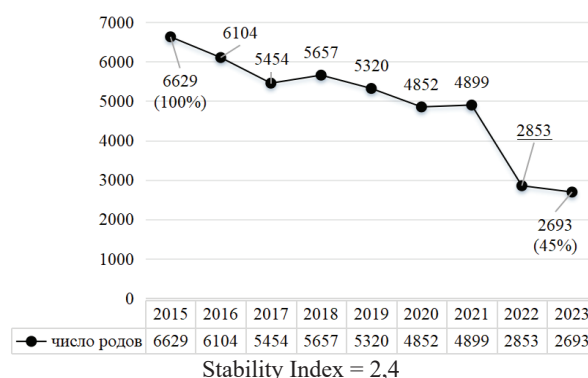


Fig. 1. Number of births in the city of Khabarovsk across three institutions

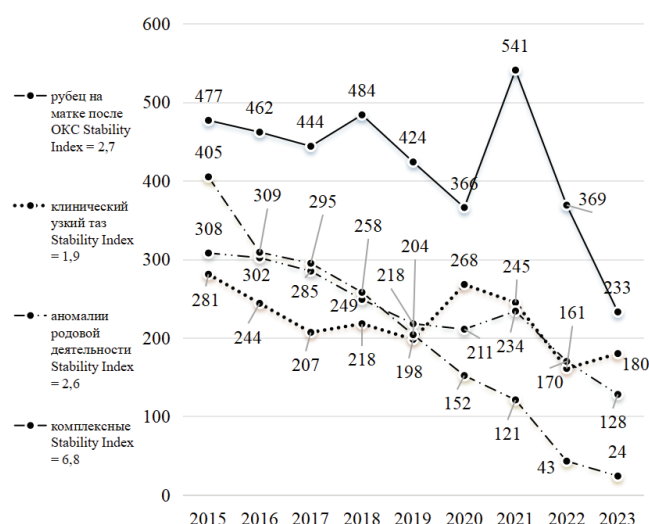


Fig. 2. Maternal indications for cesarean section

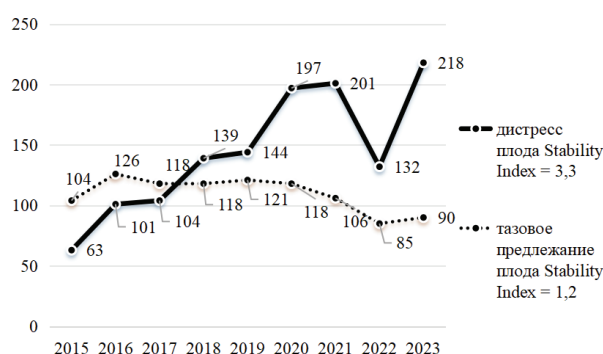


Fig. 3. Fetal indications for cesarean section

Table 1

Comparative characteristics of the physical development of newborns

Indicator	Me [LQ; UQ] (N=34) Childbirth	Me [LQ; UQ] (N=34) Planned cesarean section	Me [LQ; UQ] (N=36) Urgent cesarean section	Level P (df=2)
Birth weight	3 760.0 [3 307.5; 3 901.2]	3 650.0 [3 345.0; 4 063.8]	3 567.5 [3 226.2; 3 845.0]	0.5813
Z-score (weight)	1.0 [0.0; 1.2]	0.9 [0.2; 1.4]	0.6 [-0.3; 1.1]	0.4359
Percentile (weight)	83.5 [51.6; 88.9]	80.6 [59.0; 92.5]	71.6 [39.6; 86.8]	0.4097

5;6). Furthermore, a significant difference was found in the frequency of successful breastfeeding initiation: in the vaginal delivery group it was 88.2%, whereas after ECS it was only 44.4% (Fig. 7).

The results of neurosonography performed before discharge from the maternity hospital indicated a significantly higher frequency of pathological changes in children born operatively. After planned CS, abnormalities were detected in 62% of newborns, after emergency CS in 67%, while in the vaginal delivery group this figure was only 18% ($p < 0.001$). In the structure of findings after vaginal delivery, signs of venous hypertension with discirculation (6%) and grade I intraventricular hemorrhages (6%) predominated. In the planned CS group, analysis of neurosonography data revealed characteristic patterns of structural changes in the brain in the studied groups. The most common findings in the overall cohort were dilation of the interhemispheric fissure combined with vasoparesis (18% of cases) and enlargement of the occipital horns of the lateral ventricles (9%). For newborns born by emergency operative delivery (cesarean section), a distinct ultrasound picture was established. In this group, intraventricular hemorrhages associated with dilation of the anterior horns of the lateral ventricles (20%) and isolated dilation of the interhemispheric fissure (18%) predominated (Fig. 8).

The study of biochemical parameters revealed significant intergroup differences in umbilical cord blood lactate levels ($p < 0.0001$). Median values were 3.6 [3.2; 3.7] mmol/L in vaginal delivery, 2.2 [1.7; 2.8] mmol/L in planned CS, and 4.4 [2.8; 4.7] mmol/L in emergency CS. The reduced lactate level in planned surgery may reflect insufficient activation of the sympathoadrenal system in the absence of labor stress, while its increase in emergency intervention serves as an indicator of pronounced metabolic stress and the development of pre-acidosis. In newborns exposed to meconium-stained amniotic fluid, the lactate concentration was 1.6 times higher than in the comparison group (3.90 [3.40; 4.68] mmol/L vs. 2.85 [2.00; 3.80] mmol/L, $p = 0.0006$) (Fig. 9; 10).

During follow-up observation in the first month of life, abnormalities in health status were recorded in 37% of children ($n = 38$). The lowest frequency of disorders was noted in the vaginal delivery group (17.6%), the highest after emergency CS (52.7%). Among newborns born operatively, the proportion of diagnosed encephalopathy was high (36.10% after

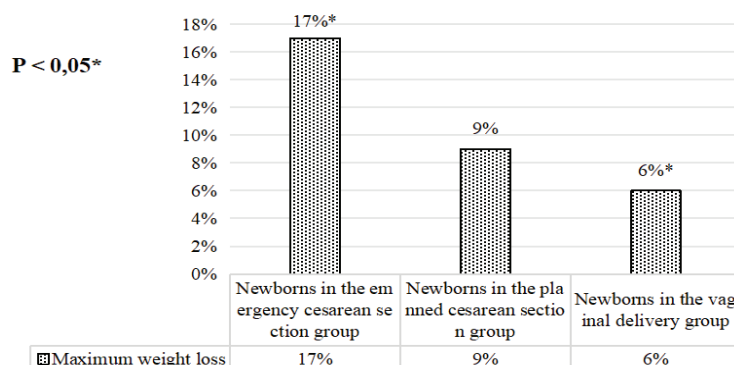


Fig. 4. Pathological loss of body weight in newborns

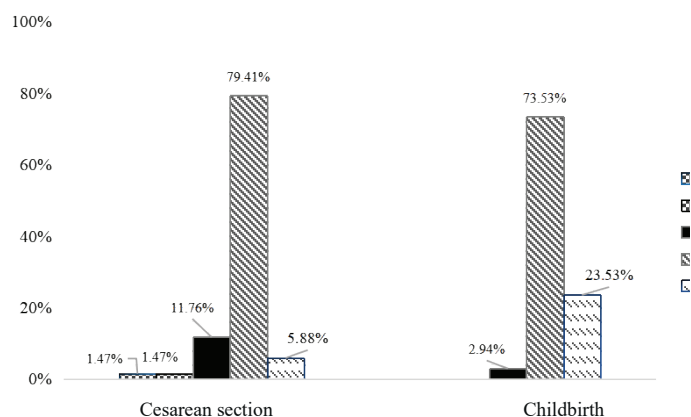


Fig. 5. Apgar score at the first minute of life

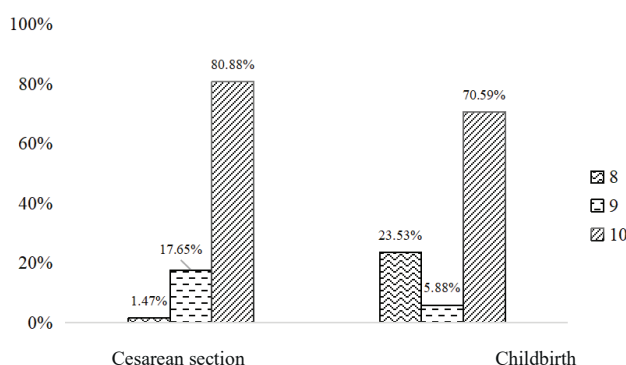


Fig. 6. Apgar score at the fifth minute of life

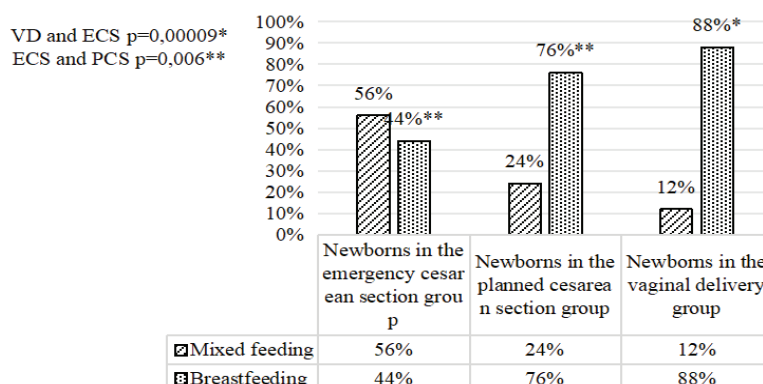


Fig. 7. Breastfeeding in the early neonatal period

planned CS and 41.10% after emergency CS) (Tab. 2). Control neurosonography data at 1 month of age confirmed a threefold higher frequency of pathological changes in the ECS group compared to the vaginal birth group (44% vs. 15%). The findings were predominantly subependymal pseudocysts (19% of cases) and cerebrospinal fluid dynamics disorders (14%) (Fig. 11).

Multivariate regression analysis allowed the identification of independent predictors of neurological disorders in the neonatal period. These include: presence of maternal uterine or adnexal tumors (OR=34.19; 95% CI [3.84-304.15]), pathological changes on neurosonography in the form of cerebral ventricular dilation (OR=29.09; 95% CI [5.67-149.21]), the very fact of delivery by cesarean section (OR = 6.56; 95% CI [1.97-21.89]; $p < 0.05$), and prolonged (≥ 12 hours) rupture of membranes (OR = 4.27; 95% CI [1.34-13.59]; $p < 0.05$). Meanwhile, an Apgar score below 8 at the fifth minute of life was also an independent factor, however demonstrating a protective effect (OR = 0.284; 95% CI [0.10-0.79]; $p < 0.05$) (Tab. 3).

The predictive model including these variables was statistically highly significant ($\chi^2=43.464$; $df=6$; $p<0.0001$) and demonstrated a sensitivity of 87.2% with a specificity of 63.1% (area under the ROC curve AUC=0.814) (Fig. 12).

Based on the totality of the obtained data, a two-stage monitoring algorithm for newborns after operative delivery was developed. At the maternity hospital stage, it mandates the determination of lactate in umbilical cord blood, an in-depth assessment of neurological status, and neurosonography. At the outpatient polyclinic stage, the following are recommended: early pediatric follow-up — observation includes a mandatory examination of the newborn within the first 72 hours after discharge, as well as at least two repeated examinations at scheduled times before the end of the neonatal period. Upon identification of the recognized risk factors, a planned consultation with a pediatric neurologist, including neurosonography at one month of age, was included in the protocol. The main objective of the algorithm is to ensure timely detection and secondary prevention of neurological pathology in this category of patients.

Conclusions.

1. The dynamics of obstetric care in Khabarovsk for 2015-2023 are characterized by a significant (55%) reduction in the total number of births, concurrently with an increase in the frequency of

VD and ECS $p < 0.001^*$

PCS and VD $p < 0.001^{**}$

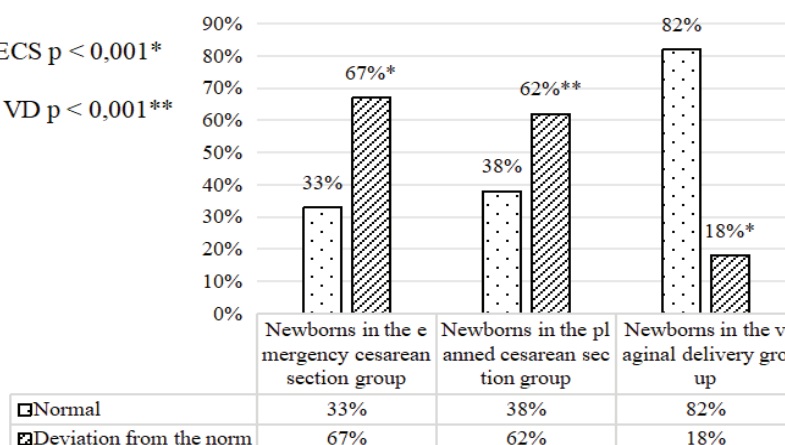


Fig. 8. Comparative analysis of changes in newborns at the time of hospital discharge based on neurosonography data depending on the mode of delivery

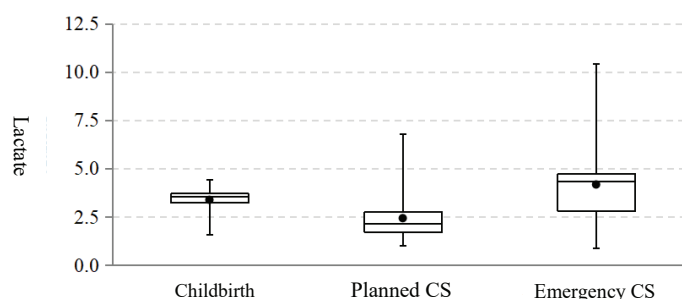


Fig. 9. Level of lactate in arterial umbilical cord blood depending on the mode of delivery

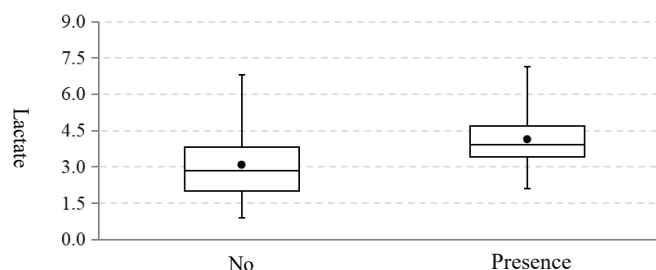


Fig. 10. Level of lactate in arterial umbilical cord blood depending on the presence/absence of meconium in the amniotic fluid

Table 2

Follow-up observation during the first month of life

Neurologist's conclusion	Children born via VD (n=34)	Children born via ECS (n=36)	Children born via PCS (n=34)
G93.4 Unspecified encephalopathy	15	39	41
P12.0 Bilateral parietal cephalohematomas	3	0	0
G96.8 Other specified disorders of the central nervous system	0	8	3
Q68.0 Abnormal head posture / Pathological head position	0	6	0

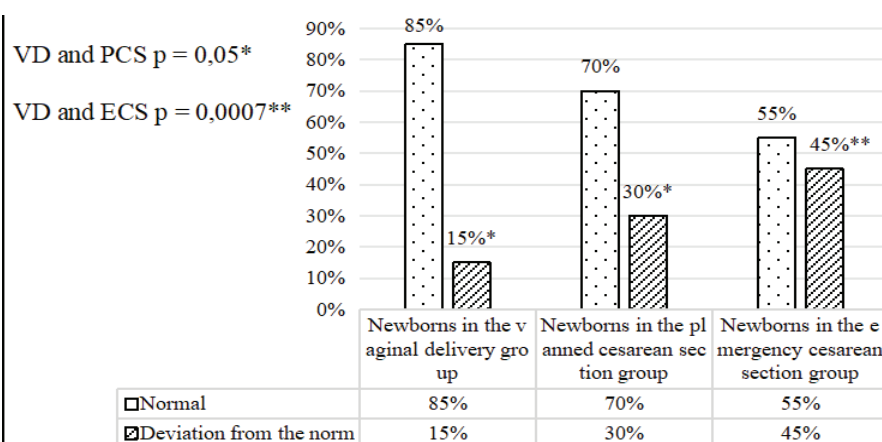


Fig. 11. Follow-up neurosonography at the age of 1 month

Table 3

Multivariate regression analysis

Indicator	Multivariate analysis	
	OR (95%)	p
Cesarean section	6.559 (1.613 – 26.673)	0.0086
Tumors of the uterus and/or adnexa	34.190 (2.794 – 418.334)	0.0057
Dilation of the MPT with symmetrical dilation of the anterior horns of the lateral ventricles	29.091 (1.837 – 460.610)	0.0168
Premature rupture of membranes (12 hours or more)	4.267 (1.154 – 15.770)	0.0296

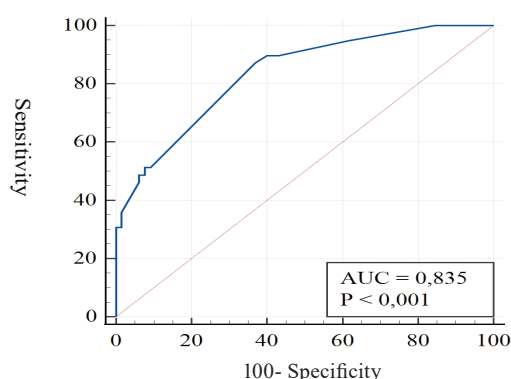


Fig. 12. ROC curve describing the association of the regression function value with the probability of neurological abnormalities in newborns

cesarean section use from 21.08% to 34.42%.

2. Newborns delivered by cesarean section, especially performed on an emergency basis, constitute a high-risk group for the development of macrosomia, significant weight loss, neurological dysfunctions, and structural changes in the brain according to neurosonography data.

3. Lactate level in umbilical arterial blood is an informative biochemical marker. Its decrease in planned CS may indicate insufficiency of the adaptive stress response, while its increase in emergency CS and with meconium staining of the fluid indicates pronounced metabolic stress and the risk of hypoxic lesions.

4. A set of independent predictors associated with the occurrence of neurolog-

ical disorders in the neonatal period has been established: maternal uterine and adnexal tumor pathology, dilation of the cerebral ventricles on neurosonography, the fact of operative delivery, prolonged rupture of membranes, and low Apgar score at the 5th minute of life.

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The authors declare no conflicts of interest.

Authors' contributions: Kulik A.A. – development of the concept and design of the study, collection and processing of clinical material,

statistical analysis, preparation of the initial version of the manuscript; Rzyankina M.F. – scientific supervision of the work, methodological support, critical analysis and editing of the text of the article, approval of the final version for publication.

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Received by the editorial office: 22.01.2026 / Accepted for publication: 11.02.2026



DOI 10.25789/YMJ.2026.94.03

UDC 616.72

Laboratory assessment of bone metabolism parameters by determining serum C-terminal type I collagen telopeptides in patients with rheumatoid arthritis

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Abstract. The aim of the study was to investigate the relationship between the serum level of C-terminal telopeptides of type I collagen and clinical and laboratory features of rheumatoid arthritis in elderly female patients.

Materials and methods. We observed 87 female patients with a confirmed diagnosis of RA. The average age of the patients was 67.4±6.9 (61.7-73.4) years. The duration of RA ranged from 0.2 to 33 years (9 [4-16]). The DAS28 index was used to assess activity; the study predominantly included individuals with stage II activity. X-ray stage I was diagnosed in 6 (6.89%) patients, II – in 33 (37.93%), III – in 44 (50.57%), and IV – in 4 (4.60%) patients. RF was detected in 63 (72.4%) patients, and ACPA – in 58 (66.6%). The background therapy of patients with RA complied with generally accepted clinical guidelines. The study included 36 patients with a diagnosis of osteoporosis (OP), and 51 patients did not have a diagnosis of OP.

Results. The average β -Cross Laps level in RA patients was 0.684 [0.40-0.78] ng/ml, with the upper limit of normal being increased in 28 (32.2%) patients. No significant correlation was found between β -Cross Laps levels and age, height, weight, and BMI of the patients. A correlation was found between β -Cross Laps concentration and disease activity (K-W $\chi^2=3.318$, $p=0.042$), radiographic stage (K-W $\chi^2=2.960$, $p=0.036$), functional class (K-W $\chi^2=3.639$, $p=0.030$), and CRP level ($p=3.1907$; $p=0.037$).

Findings. Elevated β -Cross Laps levels may predict a high risk of bone tissue destruction in patients with RA, including the elderly. Therefore, β -CTX is a promising marker for assessing bone turnover in geriatric patients with RA.

Keywords: C-telopeptides of type I collagen; β -Cross laps; CTX-1; rheumatoid arthritis, osteoporosis.

Funding. The study had no sponsorship.

For citation: Akhverdyan Y.R., Zavovovsky B.V., Papichev E.V., Polyakova Y.V., Sivordova L.E. Laboratory assessment of bone metabolism parameters by determining serum C-terminal type I collagen telopeptides in patients with rheumatoid arthritis. Yakut Medical Journal, 2026. 94(2): 14-17. <https://doi.org/10.25789/YMJ.2026.94.03>

Introduction. Bone remodeling markers play an important role in studying the pathogenesis and prognosis of rheumatic diseases. In the study of rheumatoid arthritis (RA), the diagnosis of osteoporosis (OP), a secondary metabolic osteopathy, is of particular importance [1]. OP is characterized by impaired bone remodeling processes, leading to a progressive decrease in bone mineral density. Bone remodeling results from osteoclastic resorption and osteoblastic formation. This process is regulated by many factors, both local and systemic [2, 3]. As is known, the C-telopeptide of type I collagen (β -Cross laps, CTX-1, β -CTX) is a classic marker of bone resorption. Literature

data on the relationship between RA activity and CTX-I levels are extremely contradictory. A number of researchers conclude that β -CTX levels are elevated in patients with active RA, especially with a high concentration of proinflammatory cytokines (TNF- α , IL-6) [4]. Other authors obtained the following results: a direct correlation was found, no significant correlation was found after adjusting for age, and a correlation was found only at CRP levels above 10 mg/L (evidence levels 2b, 3b, and 2a) [5, 6].

An important current trend is the search for a personalized approach based on the clinical and laboratory characteristics of the disease, its severity, and risk profiles in elderly patients with RA.

It is generally accepted that RA in elderly patients is currently under-controlled, and treatment should be more individualized [7].

The aim of this study was to investigate the possible relationship between serum levels of C-terminal telopeptides of type I collagen and clinical and laboratory characteristics of rheumatoid arthritis in elderly female patients.

Materials and methods. The study was conducted at the A.B. Zborovsky Research Institute of Clinical and Experimental Rheumatology in Volgograd. We observed 87 female patients with a confirmed diagnosis of RA. The diagnosis is based on the ACR/EULAR 2010 diagnostic criteria. The inclusion criteria