REPUBLIC OF AZERBAIJAN

On the rights of the manuscript

ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

METABOLIC STATUS AND ION HOMEOSTASIS IN NEWBORNS WITH PERINATAL ASPHYXIA

Specialty: 3220.01 – Pediatry

Field of science: Medicine

Applicant: **Shovket Azer Sadigova**

BAKU – 2025

The work was perfopmed at the "I Children diseases" department of Azerbaijan Medical University.

Scientific supervisor: Doctor of Medical Sciences, Professor
Safikhan Shamil Hasanov

Official opponents: Doctor of Medical Sciences
Raksana Yusif Mammadova

Doctor of Medical Sciences,
Associate Professor
Naila Calil Rahimova

Doctor of Medical Sciences,
Associate Professor
Gunduz Ahmad Ahmadov

Dissertation council ED 2.27 of Supreme Attestation Commission under the President of the Republic of Azerbaijan operating at the Azerbaijan Medical University

Chairman of the Dissertation Council: Doctor of Medical Sciences, professor
Vasadat Ali Azizov

Scientific Secretary of the Dissertation Council: Doctor of Philosophy of Medical Sciences, Associate Professor
Tora Akif Sadigova

Chairman of the scientific seminar: Honored Scientist, Doctor of Medical Sciences, professor
Ibrahim İsa İsayev

İMZANI TƏSDİQ EDİRƏM
Azərbaycan Tibb Universitetinin
ELMİ KATİBİ
Tibb üzrə fəlsəfə doktoru, dosent
Rəşad Şəmsəddin oğlu Talışınskiy
"03" 03 2025 il

GENERAL DESCRİPTİON OF THE WORK

Relevance of the research. Perinatal asphyxia remains one of the leading causes of neonatal morbidity and mortality worldwide[1,2]. Neonatal asphyxia is recognized as one of the preventable causes of neonatal mortality worldwide, and its incidence can be reduced through timely preventive and early diagnostic measures. Organ failure and hypoxic-ischemic encephalopathy (HIE) following perinatal asphyxia are considered responsible for 25% of all postnatal deaths[3].

Globally, the majority of neonatal deaths (78%) occur within the first week of life, with nearly 1 million newborns dying within the first 24 hours[4].

Among affected infants, 15–20% die during the neonatal period, while approximately 25% of survivors live with permanent neurological impairments[5].

However, making a long-term prognosis for these children is very difficult. Surviving infants often experience mild to severe neurological disorders and may also succumb to aspiration or systemic infections.

---

1. Hacıyeva, S.A. Perinatal asfiksiya keçirmiş yenidoğulanlarda poliorqan zədələnmələrinin erkən diaqnostikası və gedişinin proqnozlaşdırılması // Bakı: Sağlamlıq jurnalı, -2017. №6, -s.93-97.
2. Usman, F. Newborn Mortality in Sub-Saharan Africa: Why is Perinatal Asphyxia Still a Major Cause? / F.Usman, A.Imam, ZL.Farouk [et al] // Ann Glob Heal, -2019. Aug;8. 85(1),-p.112.
3. Dathe, AK. Early Prediction of Mortality after Birth Asphyxia with the nSOFA / AK.Dathe, A.Stein, N.Bruns, [et al] // J Clin Med, -2023. Jun;27. 12(13), -p.4322.
4. WHO Newborn Mortality: https://www.who.int/news-room/fact-sheets/detail/newborn-mortality, -2024. Mar;14.
5. Odd, D. Hypoxic-ischemic brain injury: Planned delivery before intrapartum events / Odd D, Heep A, Luyt K, Draycott T. J Neonatal Perinatal Med, -2017. 10(4), -p.347-353.

It has been observed that survivors suffer from long-term disabilities, including cerebral palsy, intellectual or psychomotor developmental delays, seizures, blindness, and severe hearing impairment. In the long run, monitoring such infants is considered a complex and extremely costly process[6,7]. These conditions require continuous medical and social support, increasing the burden on the healthcare and social welfare systems.

When a newborn suffers from asphyxia, various clinical and biochemical changes occur, which can negatively impact the final outcome. Furthermore, the degree of electrolyte and metabolite imbalance may vary depending on the severity of asphyxia during birth[8,9].

The effectiveness of asphyxia treatment directly depends on the timeliness of medical care. The continuous development of treatment methods and technologies in neonatology requires ongoing training of medical staff and the implementation of new medical care protocols. This helps to reduce the number of asphyxia cases and improve treatment outcomes.

Effective neonatal resuscitation and rapid correction of electrolyte balance will help reduce neonatal mortality and long-term neurological complications[10].

---

6. Riley, C. Improving Neonatal Outcomes Through Global Professional Development / C.Riley, LA.Spies, L.Prater [et al] // Adv Neonatal Care, -2019. 19(1), -p.56-64.
7. Frajewicki, A. Perinatal Hypoxic-Ischemic Damage: Review of the Current Treatment Possibilities / A.Frajewicki, Z.Laštůvka, V. Borbélyová [et al] // Physiol. Res, -2020. Des;31. 69(3), -p.379-401,
8. Thakur, J. Prevalence of electrolyte disturbances in perinatal asphyxia: a prospective study / J.Thakur, NK.Bhatta, RR.Singh, [et al] // Ital J Pediatr, -2018. May;21. 44(1), -p.56.
9. Mota-Rojas, D. Pathophysiology of Perinatal Asphyxia in Humans and Animal Models / D.Mota-Rojas, D.Villanueva-García, A.Solimano [et al] // Biomedicines, -2022. Feb;01. 10(2), -p.347.
10. Acharya, A. Clinico-Biochemical Correlation in Birth Asphyxia and Its Effects on Outcome / A.Acharya, B.Swain, S.Pradhan [et al] // Cureus, -2020. Nov; 9. 12(11), -e.11407.

Overall, these factors highlight the relevance of perinatal asphyxia problems and strongly emphasize the necessity of further research, prevention, and the development of effective diagnostic and treatment methods in the future.

Research Objective.

To investigate the clinical and diagnostic significance of metabolic status and ion homeostasis parameters in neonates of different gestational ages during perinatal asphyxia.

Research tasks:

1. To analyze the relationship between antenatal risk factors influencing the development of perinatal asphyxia and the degree of central nervous system damage.
2. To study the clinical characteristics and metabolic adaptation status of newborns with perinatal asphyxia at different gestational ages.
3. To investigate metabolic homeostasis disorders in newborns with perinatal asphyxia and their impact on clinical outcomes.
4. To study the impact of neuro-specific enolase levels on neurological outcomes in newborns with perinatal asphyxia.
5. To determine the relationship between microelement levels and clinical manifestations in perinatal asphyxia.

Key provisions submitted for dissertation defense

- Analysis of antenatal risk factors has shown that the severity of perinatal asphyxia is closely associated with various pregnancy complications. The severity levels of hypoxic-ischemic encephalopathy lead to significant differences in clinical manifestations, especially between full-term and preterm newborns.
- Metabolic and respiratory disorders were observed in newborns with perinatal asphyxia, and these changes persisted throughout the neonatal period. The state of metabolic adaptation varied according to gestational age, highlighting the necessity of individualized treatment strategies.

- The dynamic changes in NSE levels can be used as an indicator of neonatal neurological injury. A prolonged increase in NSE levels was particularly observed in preterm newborns, indicating their exposure to higher neurological risks.
- Changes in the levels of Fe, Ca, Mg, Zn, Cu, and Mn microelements were observed during the neonatal period in children who experienced perinatal asphyxia. These changes were found to have a significant correlation with the Apgar score, lethargy syndrome, and muscle tone.
- The use of the NSE biomarker to monitor neuronal damage and the monitoring of metabolic indicators play an important role in neonatal rehabilitation. Regular monitoring of microelement levels and the application of targeted treatment approaches may help improve clinical outcomes.

The scientific novelty of the research:

It has been determined that the clinical manifestations and risk factors of children who have experienced perinatal asphyxia change depending on gestational age and antenatal factors, and this can play a significant role in the personalization of treatment and rehabilitation strategies. A systematic study of the metabolic adaptation status after perinatal asphyxia in newborns with different gestational ages, as well as the identification of differences in metabolic status and clinical significance in term and Pİ, has highlighted the importance of considering gestational age in the clinical management of these children.

An increase in the levels of neuron-specific enolase (NSE) during perinatal asphyxia, which indicates the degree of neuronal damage in the brain, has diagnostic significance in neurological outcomes. Changes in NSE levels were found to be longer-lasting and stronger in preterm infants. The role of changes in pH, pO_2, pCO_2, and HCO_3^- levels in assessing long-term metabolic and physiological disturbances associated with perinatal asphyxia has been studied. The correlation between changes in microelement levels and clinical signs during perinatal asphyxia, as well as the

significance of microelement status for clinical monitoring in the neonatal period, has revealed the clinical-diagnostic potential of these relationships.

The practical significance of the research:

- Considering antenatal risk factors and gestational age in the clinical management of newborns who have experienced perinatal asphyxia allows for the personalization of their clinical manifestations and treatment strategies. Studying the metabolic adaptation status in children with different gestational ages ensures better evaluation of these children's clinical status and the application of appropriate treatment approaches.
- The clinical-diagnostic significance of monitoring and assessing metabolic and ion homeostasis parameters during perinatal asphyxia in newborns according to their gestational age has been studied.
- The dynamic monitoring of neuron-specific enolase levels can be used as an important biomarker to assess the severity of brain injury and clinical outcomes. Changes in this biomarker help identify longer-term damage and rehabilitation needs in preterm infants.
- Monitoring the levels of microelements, particularly Fe, Ca, Mg, Cu, and Zn, supports the improvement of clinical status and the assessment of recovery processes during the neonatal period. When linked to clinical signs, these approaches become more effective in applying targeted treatment strategies and tracking the development of the children..

The methods of examination of the research:

A total of 97 newborns were examined within the scope of the study: 68 with a diagnosis of perinatal asphyxia, forming the main group, and 29 healthy newborns, forming the control group. The main group was divided according to gestational age into term (27 children) and preterm (41 children) newborns. Based on the severity of hypoxic-ischemic encephalopathy, three subgroups were created: Grade I (22 children), Grade II (30 children), and

Grade III (16 children).

The examination methods included: anamnestic (antenatal risk factors and birth characteristics), clinical examination (clinical signs of encephalopathy and metabolic disorders were evaluated), laboratory analyses (blood gases (pH, pO_2, pCO_2, HCO_3^-), microelements (Fe, Ca, Mg, Zn, Cu, Mn), and neuron-specific enolase (NSE) levels), and statistical analysis. The results of the study provided an opportunity to assess the clinical-diagnostic significance of perinatal asphyxia..

The approval of the work. The results of the research were discussed at the International Scientific-Practical Congress *International Scientific Review of the Problems and Prospects of Modern Science and Education* (Boston, USA, April 24-25, 2018), at the *Матеріали V Всеукраїнської наукової конференції студентів та молодих вчених з фізіології з міжнародною участю* (May 16, Kharkiv, 2018), and at the *Сборник статей XXXIV Международной научно-практической конференции “Современные научные исследования”* (Penza, August 15, 2023).

Application of the research results. The results of the research have been implemented in the work of the Teaching Surgery Clinic of the Azerbaijan Medical University, in the departments of the Scientific-Research Institute of Pediatrics after named K.Y. Farajova, and in the teaching process of the Department of Pediatric Diseases.

Publication. The results of the conducted research have been reflected in 11 published scientific works, eight of which are articles published in journals recommended by the Higher Attestation Commission (AAC) for dissertation work.

Volume and structure of the dissertation. The dissertation consists of 142 pages (196469 characters), including an introduction (7,848 characters), literature review (37,778 characters), materials and methods of examination (24,490 characters), three chapters reflecting personal research (40,026 characters), Chapter IV (43,093

characters), Chapter V (17,341 characters), conclusion (22352 characters), results (2,498 characters), practical recommendations (1,042 characters), and a list of references. The dissertation is illustrated with 12 tables, 4 graphs. The list of references includes 5 domestic and 149 foreign sources.

MATERIALS AND METHODS OF THE RESEARCH

The research was conducted between 2014 and 2016 at the Teaching Surgery Clinic of the Azerbaijan Medical University and the K.Y. Ferejov Scientific Research Institute of Pediatrics. During this period, 97 newborns were examined. To address the objectives of the research, studies on the physiology of newborns were carried out in the Department of Resuscitation and Intensive Care, as well as in the departments of Pathology of Newborns and Premature Infants at the K.Y. Ferejov Scientific Research Institute of Pediatrics, and in the Neonatology Department of the Teaching Surgery Clinic of Azerbaijan Medical University. The research was approved by the Ethics Committee of Azerbaijan Medical University. Informed consent for participation in the study was obtained from the parents.

A total of 68 newborns were included in the main group and were divided into two subgroups based on GA: Group 1 consisted of 41 preterm infants (born before 37 weeks of gestation), and Group 2 included 27 term infants (born between 37-42 weeks of gestation). Additionally, a control group was created, consisting of 29 healthy newborns matched by gestational age, 18 of whom were term infants and 11 were preterm infants. Among the preterm infants in this group, no illness or adaptation disorders were identified during the neonatal period. These preterm infants were considered as conditionally healthy due to their preterm birth.

Among the newborns included in the study, special attention was given to those who had experienced perinatal asphyxia. The condition of these children was categorized into three groups based on the severity of hypoxic-ischemic encephalopathy: Group 1 included 16 children with Grade III hypoxic-ischemic encephalopathy (severe form), Group 2 included 30 children with

Grade II hypoxic-ischemic encephalopathy (moderate form), and Group 3 included 22 children with Grade I hypoxic-ischemic encephalopathy (mild form). The evaluation of the neurological functions of these children and the severity of hypoxic-ischemic encephalopathy were determined based on the modified Sarnat H., Sarnat M., and Stoll B., Kliegman R. (2004) modification.

The inclusion criteria for the main group were as follows: newborns diagnosed with birth asphyxia; an Apgar score of 5 or less at the 5th minute of life; term newborns (37-42 weeks gestation); preterm newborns (<37 weeks gestation); newborns matching their gestational age. The exclusion criteria included: newborns with a smaller than expected gestational age; newborns with a larger than expected gestational age; newborns born after 42 weeks gestation; those with severe congenital developmental defects, requiring surgical intervention or incompatible with life; presence of neuroinfections, sepsis, or other infectious pathologies.

The inclusion criteria for the control group consisted of healthy newborns, without asphyxia; Apgar scores of 8-10 at the 1st and 5th minutes; and healthy newborns who did not experience any pathology during the neonatal period.

A retrospective analysis of the mothers' documents was also conducted. This included examining the mother's somatic and obstetric-gynecological history, as well as the pregnancy period and its analysis. The results of this retrospective analysis provided significant information to assess the impact of the mothers' health status on the health of the newborns and to identify risk factors. The average age of the mothers of the newborns in the main group was 28.3±1.9 years (ranging from 21 to 37 years).

The condition of all newborns was assessed using the Apgar scale (skin color, heart rate, facial and reflex excitability, muscle tone, and respiratory rate) at the 1st and 5th minutes after birth. The degree of asphyxia in the infants who experienced perinatal asphyxia was also determined based on this scale. Additionally, the level of consciousness, the functional status of the cardiovascular, respiratory, and urinary excretion systems, the duration of comatose state, the length of stay in the resuscitation department and hospital,

and the time of initiating enteral feeding were recorded. The anthropometric measurements of the newborns (body weight, body length, and head circumference) were assessed according to their gestational age.

Various instrumental examination methods were used for diagnostic and therapeutic purposes in hospitalized newborns with perinatal asphyxia, including neurosonography, Doppler ultrasound examination, electroencephalography, electrocardiography, pulse oximetry, and ultrasound of internal organs. Laboratory tests included a general blood analysis, acid-base balance, and blood gas analysis; for evaluating the metabolic status, blood samples were analyzed for electrolytes (Mg, Cu, Zn, Mn, ionized Ca, P), trace elements (Fe, Cu, Zn), and neuron-specific enolase (NSE) levels. The concentration of trace elements in all children was determined using the emission spectral analysis method on the 3rd to 5th day and the 21st to 28th day of life. The level of neuron-specific enolase was determined using the enzyme-linked immunosorbent assay (ELISA) method.

The results of the study were statistically processed and analyzed using modern biometric recommendations. During statistical processing, qualitative analysis was performed, with Pearson's correlation coefficient used to measure the strength and direction of the linear relationship between variables, and Fisher's exact test used to determine the congruence of variances and whether statistical differences were random. The statistical correlation method was employed to analyze the relationship between markers and clinical outcomes. The correlation coefficient (r) and p-value were used to assess the statistical significance of the results. All calculations were performed using statistical software on the Windows 7 operating system, and the results were summarized in tables and diagrams.

THE RESULTS OF THE RESEARCH AND THEIR DISCUSSION

Risk factors and clinical course characteristics of perinatal asphyxia. The antenatal risk factors leading to the severity levels of hypoxic-ischemic encephalopathy in neonates with perinatal asphyxia were analyzed. Factors such as pregnancy complications, preeclampsia, anemia, acute respiratory viral infections during pregnancy, perinatal infections, diseases of the respiratory, urinary, and endocrine systems, maternal age (<30 or >30), rapid delivery, umbilical cord prolapse around the fetus's neck, and cesarean section were studied. The risk of pregnancy complications showed statistically significant differences between the severity levels of hypoxic-ischemic encephalopathy (III-II and II-I), as in the third-degree hypoxic-ischemic encephalopathy, it was observed in 68.8%, in second-degree in 30.0%, and in first-degree in 4.5%. The difference between the third and second degree was PчI = 0.012, P_F< 0.050.

The statistical relationship between pregnancy pathologies such as preeclampsia and anemia has also been analyzed. In cases of preeclampsia, third-degree hypoxic-ischemic encephalopathy (HIE) was noted in 56.3%, second-degree HIE in 20.0%, and first-degree HIE in 13.6%. Based on statistical results, there was a significant difference between the third and second-degree groups (pчI = 0.013, pF< 0.05), whereas no significant difference was observed between the second and first-degree groups (pчI = 0.549, pF> 0.05). Anemia during pregnancy was observed in 37.5% of children with third-degree HIE, in 30.0% with second-degree HIE, and in 63.6% with first-degree HIE. In statistical results, there was no significant difference between the third and second-degree groups (pчI=0.606, pF>0.05), while a significant difference was found between the second and first-degree groups (pчI=0.016, pF<0.05). No significant statistical difference was observed between respiratory system diseases and the severity of HIE (p > 0.05), with third-degree HIE found in 18.8%, second-degree in 10.0%, and first-degree in 18.2%. The statistical analysis of urinary tract infections and endocrine system pathologies showed similar results. Urinary tract infections were observed in 12.5% of children with third-degree HIE, in 10.0% with second-degree HIE, and in 9.1% with first-degree HIE.

Endocrine pathologies were observed in 6.3% of children with third-degree HIE, in 13.0% with second-degree HIE, and in 9.1% with first-degree HIE. Chi-square tests (p>0.05) indicated that these relationships were not statistically significant. ARVЭ were present in 12.5% of children with third-degree HIE, in 33.3% with second-degree, and in 86.4% with first-degree HIE. Acute respiratory viral infections were more frequently observed in the first-degree HIE group (рчI=0.005, pF<0.05). In our study, intrauterine (TORCH) infections were noted in 6.3% of children with third-degree HIE, in 36.7% with second-degree, and in 81.8% with first-degree HIE (рчI=0.002, pF<0.05), showing a stronger association with first-degree HIE. Rapid delivery occurred in 6.3% of children with third-degree HIE, in 36.7% with second-degree, and in 68.2% with first-degree HIE. Rapid delivery was more strongly associated with first-degree HIE (рчI=0.025, pF<0.05). Umbilical cord prolapse around the fetus's neck was present in 62.5% of children with third-degree HIE, in 16.7% with second-degree, and in 9.1% with first-degree HIE. Umbilical cord prolapse was more frequently associated with severe third-degree HIE. In the third-degree HIE group, cesarean section occurred in 37.5%, in the second-degree group in 30.0%, and in the first-degree group in 27.3%. Among the mothers of children in our study, 68.8% of those over 30 years old had children with third-degree HIE, 60.0% had second-degree HIE (рчI=0.695, pF>0.05), and 54.5% had first-degree HIE (рчI=0.559, pF>0.05). Mothers under 30 years old had 31.3% of children with third-degree HIE, 40.0% with second-degree (рчI=0.695, pF>0.05), and 45.5% with first-degree HIE (рчI=0.559, pF>0.05).

Thus, this analysis reveals how various risk factors during pregnancy influence the development of hypoxic-ischemic encephalopathy and how these factors may contribute to asphyxia during birth. The results of the study indicate that factors such as the risk of pregnancy complications, preeclampsia, anemia, acute respiratory viral infections, intrauterine (TORCH) infections, rapid delivery, and umbilical cord prolapse around the fetus's neck all affect the severity of hypoxic-ischemic encephalopathy.

The evaluation using the Apgar scale based on the severity of hypoxic-ischemic encephalopathy revealed that children who scored 1-3 points on the Apgar scale were mainly associated with the third-degree hypoxic-ischemic encephalopathy group, those scoring 4-5 points were associated with the second-degree group, and those scoring 6-7 points were more related to the first-degree group. Statistical analyses showed significant differences between the degrees of hypoxic-ischemic encephalopathy based on the Apgar scale, particularly between the third and second-degree groups as well as between the second and first-degree groups.

For children with third-degree hypoxic-ischemic encephalopathy, their Apgar scores at the 5th minute mainly ranged between 2-4, and their condition remained severe, with 18.8% showing partial improvement. In the group with second-degree hypoxic-ischemic encephalopathy, Apgar scores of 5-7 (36.7% and 30.0%) were more common, suggesting relatively positive outcomes following the alleviation of oxygen deficiency. In the first-degree hypoxic-ischemic encephalopathy group, most children (81.8%) scored 7 or higher, emphasizing a good prognosis.

The frequencies of symptoms observed in premature infants with perinatal asphyxia at various clinical degrees of hypoxic-ischemic encephalopathy (HIE) were analyzed. For example, the occurrence of skin marbling was found to be 33.3% in the first degree of HIE, 41.7% in the second degree, and 100% in the third degree. According to the statistical results, no significant difference was found between the first and second degrees (p1чI=0.698 and p1F>0.050), but a statistically significant difference was confirmed between the second and third degrees (p2чI=0.017 and p2F<0.050).

Perioral cyanosis was observed in 44.4% of the first degree, 91.7% of the second degree, and 16.7% of the third degree cases. Statistically significant differences were noted between the degrees (p1чI=0.018 and p2чI=0.002; p2чI=0.002 and p2F<0.050 between the second and third degrees).

The occurrence of acrocyanosis was 66.7% in the first degree, 75.0% in the second degree, and 83.3% in the third degree, with no significant difference between the degrees (p1чI=0.676 and

p1F>0.050; p1чI=0.689 and p1F>0.050 between the second and third degrees).

Tachypnea was observed in 22.2% of the first degree, 75.0% of the second degree, and 100% of the third degree cases. A statistically significant difference was found between the first and second degrees (рчI=0.017 and p1F<0.050), but no significant difference was noted between the second and third degrees (p2чI=0.180 and p2F>0.050).

Bradypnea occurred mostly in the third degree (33.4%) and 8.3% in the second degree. No significant difference was found between the first and second degrees (p1чI=0.446 and p1F>0.050), but a statistically significant difference was observed between the second and third degrees (p2чI=0.034 and p2F>0.050). The disappearance of heart tones occurred in 33.3% of the first degree, 50.0% of the second degree, and 100% of the third degree. A significant difference was found between the second and third degrees (p2чI=0.034).

Tachycardia was observed in 66.7% of the first degree, 50.0% of the second degree, and 66.7% of the third degree, with no significant differences found between the degrees (p1чI=0.446 and p1F>0.050; p2чI=0.172 and p2F>0.050). Bradycardia was seen in 22.2% of the first degree, 33.3% of the second degree, and 50.0% of the third degree, with no significant difference observed between the degrees (p1чI=0.577 and p1F>0.050; p2чI=0.495 and p2F>0.050).

These results are clinically significant in predicting the damage to the peripheral and respiratory systems based on the degree of encephalopathy.

At the first degree of hypoxic-ischemic encephalopathy (HIE), edema was recorded in 33.3% of cases, in the second degree 41.7%, and in the third degree 83.3%. Statistical analysis showed no significant difference between the degrees (p1чI=0.698, p1F>0.050; p2чI=0.094, p2F>0.050). Hypothermia was observed in premature infants with HIE at 22.2% in the first degree, 25.0% in the second degree, and 33.3% in the third degree. No significant difference was found between the degrees (p1чI=0.883, p1F>0.050; p2чI=0.710, p2F>0.050).

Neonatal hyperbilirubinemia was observed in 44.4% of the first degree, 41.7% of the second degree, and 66.7% of the third degree cases of HIE. Statistical analysis did not show any significant differences between the degrees (p1чI=0.899, p1F>0.050; p2чI=0.318, p2F>0.050). Delayed separation of the umbilical cord indicates delayed regeneration processes in the body. In the first degree of HIE, delayed separation of the umbilical cord was observed in 33.3% of cases, in the second degree 25.0%, and in the third degree 33.3%. Statistical analysis showed no significant difference between the degrees (p1чI=0.676, p1F>0.050; p2чI=0.289, p2F>0.050). Delayed separation of the umbilical cord was observed in all three degrees of encephalopathy during HIE.

The analysis of clinical signs in term infants who experienced perinatal asphyxia and developed hypoxic-ischemic encephalopathy (HIE) shows that clinical manifestations such as skin mottling, perioral cyanosis, and acrocyanosis are directly related to the severity of the disease.

Specifically, skin mottling was observed in 15.4% of the first-degree cases, 61.1% of the second-degree cases ($p1\chi^2$=0.011, p1F<0.050), and 80.0% of the third-degree cases. Perioral cyanosis was seen in 53.8%, 88.9%, and 10.0% of cases in the first, second, and third degrees, respectively. Significant differences were observed between both the first and second degrees ($p1\chi^2$=0.028, p1F<0.050) and the second and third degrees ($p2\chi^2$=0.001, p2F<0.050).

Acrocyanosis was recorded in 30.8% of the first-degree, 72.2% of the second-degree ($p_1\chi^2$=0.023, p1F<0.050), and 90.0% of the third-degree cases. Statistical analysis indicates significant differences between some of the degrees.

Changes in respiratory and cardiac activity, such as tachypnea, were observed in 23.1% of first-degree, 33.3% of second-degree, and 80.0% of third-degree cases ($p_2\chi^2$=0.018, p_2F<0.050). Bradypnea was primarily recorded in the third degree (20.0%) but did not show a statistically significant difference. The loss of heart sounds was observed in 70.0% of third-degree cases, and tachycardia was seen in 90.0% of third-degree cases ($p_2\chi^2$=0.031, p_2F<0.050). Although

bradycardia differed between degrees, no statistically significant difference was found.

Edema was found in 30.8% of first-degree, 38.9% of second-degree, and 90.0% of third-degree cases ($p_2\chi^2$=0.009, p_2F<0.050), while hypothermia was only recorded in 10.0% of third-degree cases. No statistically significant difference was found for neonatal hyperbilirubinemia or delayed umbilical cord separation.

Therefore, most clinical signs do not show a significant difference based on the severity of hypoxic-ischemic encephalopathy. However, significant differences were noted primarily in clinical signs like skin mottling, perioral cyanosis, acrocyanosis, tachypnea, loss of heart sounds, tachycardia, and bradycardia, all of which are closely related to the increasing severity of the disease.

The characteristics of metabolic adaptation in newborns who have experienced perinatal asphyxia. An analysis of the acid-base balance and gas composition indicators of blood in newborns with different gestational ages who have experienced perinatal asphyxia was conducted. The acid-base balance (ABB) and gas composition indicators of blood in term newborns with perinatal asphyxia were compared between the main and control groups. In the main group, a decrease in pH levels was observed (Day 1: 7.18±0.01 (t=2.67, p<0.050) → Day 3: 7.35±0.02 → Days 5-7: 7.32±0.03), indicating metabolic and respiratory acidosis, while in the control group, pH levels were normal and showed a tendency to increase. The partial pressure of arterial oxygen (pO_2) in the main group decreased (Day 1: 37.6±2.4 (t=3.58, p<0.050) → Day 3: 38.8±2.0 mmHg → Days 5-7: 44.8±2.5 mmHg), while in the control group, it remained normal. The partial pressure of carbon dioxide (pCO_2) in the main group increased (Day 1: 34.9±1.1 mmHg, Day 3: 34.0±1.0 mmHg; Days 5-7: 31.8±2.0 mmHg), with a trend toward decrease over time. In the control group, pCO_2 levels were consistently lower (32.0±0.9 → 30.8±1.6 mmHg). Statistical differences between the two groups were significant (t1=2.04, p1<0.050; t2=2.23, p2<0.050; t3=2.34, p3<0.050). The bicarbonate (HCO_3^-) levels were lower in

the main group (Day 1: 18.4±1.4 → Day 3: 32.8±2.2 mmol/l → Days 5-7: 20.4±1.5 mmol/l), but no statistical differences were found between the main and control groups (Day 1: t1=2.08, p1<0.050, Day 3: t2=2.03, p2<0.050, Days 5-7: t3=2.06, p3<0.050). The results reflect the impact of perinatal asphyxia on acid-base balance and gas exchange, as well as the trends in recovery during treatment.

An analysis of the acid-base balance and gas composition indicators in the blood of preterm newborns with perinatal asphyxia was conducted. In the main group, the pH indicator was lower on Day 1 at 7.24±0.01 (t1=2.67, p1<0,050); however, a trend towards normalization was observed in subsequent days: Day 3: 7.35±0.02 (t2=0.45, p2>0,050), and Days 5-7: 7.38±0.04 (t3=0.71, p3>0,050). The pO_2 level was significantly lower in all periods in the main group compared to the control group, indicating persistent hypoxia. Specifically, the pO_2 values were: in the main group: Day 1: 36.8±2.4 mmHg, Day 3: 38.8±2.0 mmHg, Days 5-7: 36.0±1.8 mmHg; in the control group: Day 1: 46.4±1.2 mmHg, Day 3: 48.0±1.4 mmHg, Days 5-7: 48.6±1.6 mmHg. Statistical analysis showed significant differences on Day 1: t1=3.58, p1<0,050, Day 3: t2=3.77, p2<0,050, and Days 5-7: t3=5.23, p3<0,050. The pCO_2 levels in the main group were: Day 1: 31.8±2.2 mmHg, Day 3: 32.8±2.2 mmHg, Days 5-7: 38.0±1.8 mmHg; in the control group: Day 1: 35.9±1.1 mmHg, Day 3: 37.6±1.4 mmHg, Days 5-7: 40.5±1.6 mmHg. Statistical comparison showed no significant difference (Day 1: t=1.67, p>0,050; Day 3: t=1.84, p>0,050; Days 5-7: t=1.04, p>0,050). The bicarbonate (HCO_3^-) values in the main group were: Day 1: 20.4±1.2 mmol/l, Day 3: 21.6±1.4 mmol/l, Days 5-7: 22.8±1.8 mmol/l; in the control group: Day 1: 22.2±1.4 mmol/l, Day 3: 23.4±1.4 mmol/l, Days 5-7: 25.0±1.2 mmol/l. Statistical comparison revealed no significant difference (Day 1: t=0.98, p>0,050; Day 3: t=0.91, p>0,050; Days 5-7: t=1.02, p>0,050). No significant difference was found between the main and control groups for pCO_2 and HCO_3^- values (p>0,050). These results suggest the involvement of metabolic and respiratory compensation mechanisms.

An analysis of the acid-base balance and gas composition indicators in the blood of preterm newborns with perinatal asphyxia

was conducted. In the main group, the pH indicator was lower on Day 1 at 7.24±0.01 (t1=2.67, p1<0,050); however, a trend towards normalization was observed in subsequent days: Day 3: 7.35±0.02 (t2=0.45, p2>0,050), and Days 5-7: 7.38±0.04 (t3=0.71, p3>0,050). The pO_2 level was significantly lower in all periods in the main group compared to the control group, indicating persistent hypoxia. Specifically, the pO_2 values were: in the main group: Day 1: 36.8±2.4 mmHg, Day 3: 38.8±2.0 mmHg, Days 5-7: 36.0±1.8 mmHg; in the control group: Day 1: 46.4±1.2 mmHg, Day 3: 48.0±1.4 mmHg, Days 5-7: 48.6±1.6 mmHg. Statistical analysis showed significant differences on Day 1: t1=3.58, p1<0,050, Day 3: t2=3.77, p2<0,050, and Days 5-7: t3=5.23, p3<0,050. The pCO_2 levels in the main group were: Day 1: 31.8±2.2 mmHg, Day 3: 32.8±2.2 mmHg, Days 5-7: 38.0±1.8 mmHg; in the control group: Day 1: 35.9±1.1 mmHg, Day 3: 37.6±1.4 mmHg, Days 5-7: 40.5±1.6 mmHg. Statistical comparison showed no significant difference (Day 1: t=1.67, p>0,050; Day 3: t=1.84, p>0,050; Days 5-7: t=1.04, p>0,050). The bicarbonate (HCO_3^-) values in the main group were: Day 1: 20.4±1.2 mmol/l, Day 3: 21.6±1.4 mmol/l, Days 5-7: 22.8±1.8 mmol/l; in the control group: Day 1: 22.2±1.4 mmol/l, Day 3: 23.4±1.4 mmol/l, Days 5-7: 25.0±1.2 mmol/l. Statistical comparison revealed no significant difference (Day 1: t=0.98, p>0,050; Day 3: t=0.91, p>0,050; Days 5-7: t=1.02, p>0,050). No significant difference was found between the main and control groups for pCO_2 and HCO_3^- values (p>0,050). These results suggest the involvement of metabolic and respiratory compensation mechanisms.

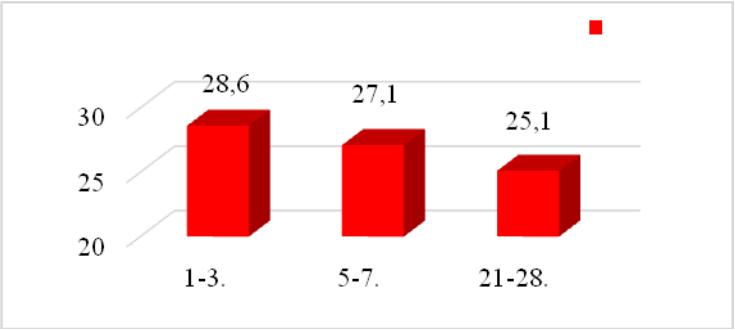


Figure 1. The dynamics of NSE (ng/ml) concentration in the blood of term infants who have undergone perinatal asphyxia

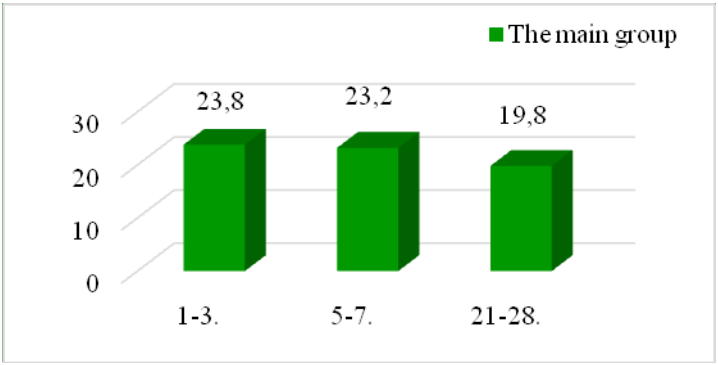


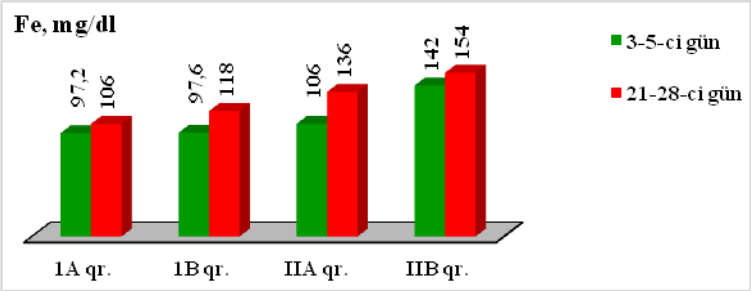
Figure 2. The dynamics of NSE (mcg/l) concentration in the blood of term infants who have experienced perinatal asphyxia

The concentration of neuron-specific enolase (NSE) in the blood of preterm infants was analyzed. In the 1-3 day age group, the NSE level in the main group was 23.8 ± 3.2 mcg/l, and in the control group, it was 15.9 ± 0.05 mcg/l, with a statistically significant difference between the groups ($t1=6.63$, $p1<0.050$). The level of neuron-specific enolase was significantly higher in the main group. In the 5-7 day old infants, the NSE level was 23.2 ± 2.4 mcg/l in the main group and 17.6 ± 0.06 mcg/l in the control group, with a statistically significant difference ($t2=7.68$, $p3<0.050$). In both groups, the level of neuron-specific enolase

decreased, but in the main group, it remained significantly higher than in the control group. In the 21-28 day old infants, the NSE level in the main group was 19.8 ± 2.1 mcg/l, and in the control group, it was 18.2 ± 0.05 mcg/l, with a statistically significant difference ($t3=8.08$, $p3<0.050$). The higher NSE level in infants with hypoxic-ischemic encephalopathy during the neonatal period indicates the impact of hypoxia on nerve cells and the weakness of reparative processes.

Correlation analysis revealed a connection between the severity of hypoxic-ischemic encephalopathy and the concentration of neuron-specific enolase. There was an inverse (negative) relationship between the concentration of neuron-specific enolase in the blood serum and the Apgar score (1st minute); in the 1st group, it was $r=-0.68$; -0.72; in the 2nd group, $r=-0.76$ ($p<0.01$). In other words, the more severe the asphyxia at birth, the higher the level of neuron-specific enolase in the blood serum, which is an indicator of central nervous system damage, and the higher the Sarnat score. Additionally, the likelihood of post-hypoxic encephalopathy forming with structural changes during severe asphyxia and preterm birth is higher.

The dynamics of trace elements in the blood of newborns who have experienced perinatal asphyxia. The levels of micro- and macroelements in newborns of different gestational ages were studied. The results of the study indicate that in preterm infants, there is a significant decrease in the concentration of trace elements, particularly Zn and Mg ($p<0.01$). This decrease can be explained by the insufficient supply of trace elements to the mother during pregnancy, as these elements mainly accumulate during the third trimester of pregnancy. When comparing the levels of trace elements in the early neonatal period (days 3-5) with those on days 21-28 of the child's life, various directional changes were observed. Specifically, an increase in Fe, Ca, and P concentrations was noted, while Mg, Cu, and Mn concentrations decreased. These changes are associated with the low activity of the ceruloplasmin enzyme. In preterm infants, the synthesis of this enzyme only becomes active in the 6-12 weeks of postnatal life.



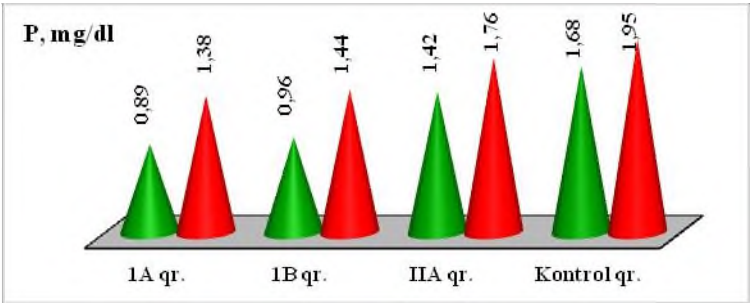


Figure 3. The dynamic changes in the levels of micro- and macro-elements in the blood of newborns who experienced perinatal asphyxia

Correlation relationships between the levels of microelements and clinical indicators have been identified. In this phase of the study, correlation relationships between the amount of microelements in the blood serum and the clinical signs of adaptation in newborns have been studied. In preterm infants during the acute adaptation period (days 3-5), positive correlations were found between the levels of microelements and gestational age as well as Apgar scores at the 5th minute.

Specifically, for magnesium (Mg) and iron (Fe), there were positive correlations with gestational age ($r=+0.59$, $r=+0.52$, $p<0.01$) and with the Apgar score ($r=+0.55$, $r=+0.56$, $p<0.01$). Similarly, copper (Cu) correlated positively with gestational age ($r=+0.41$, $p<0.05$), Apgar score ($r=+0.39$, $p<0.05$), and length

(r=+0.48, p<0.01), while zinc (Zn) showed positive correlations with both gestational age and Apgar score (r=+0.43, p<0.05, r=+0.51, p<0.01).

Additionally, there were inverse correlations with clinical signs of posthypoxic damage to the central nervous system: lethargy syndrome and decreased muscle tone with Fe (r=-0.32, p<0.05), Zn (r=-0.29, p<0.05), and Mg (r=-0.30, p<0.05). These relationships indicate that the more severe the perinatal asphyxia, the higher the levels of neuro-specific enolase and the Apgar scores, which correlate with more severe damage to the central nervous system in preterm infants. The study found significant relationships between the levels of various microelements in the blood serum and clinical indicators of adaptation, such as gestational age and Apgar score, as well as clinical manifestations like lethargy syndrome and muscle tone.

The analysis of the results showed that in preterm infants, a deficiency of microelements leads to more severe outcomes of hypoxic-ischemic brain damage. Thus, during pregnancy with complications and in infants born with perinatal asphyxia, there are prominent changes in neuro-metabolic status and ion homeostasis during the neonatal period, which depend on the gestational age and severity of hypoxic-ischemic encephalopathies.

CONCLUSİON

1. Analysis of antenatal risk factors has shown that in newborns who experienced perinatal asphyxia, Grade I hypoxic-ischemic encephalopathy is associated with anemia, perinatal infections, and rapid delivery, Grade II encephalopathy is primarily linked with anemia and preeclampsia, and Grade III encephalopathy is strongly associated with pregnancy complications, preeclampsia, and umbilical cord entanglement ($p<0.05$) [2,4].
2. Clinical manifestations of hypoxic-ischemic encephalopathy vary according to the severity of the condition in children who experienced perinatal asphyxia. In full-term infants, Grade I shows 53.8% perioral cyanosis ($p<0.050$), Grade II shows 61.1% marble-like skin, 88.9% perioral cyanosis, 72.2% acrocyanosis, and 50.0% tachycardia/bradycardia ($p<0.050$), and Grade III shows 90.0% acrocyanosis, 80.0% tachypnea, and 90.0% edema ($p<0.050$). In preterm infants, although no statistically significant differences were found, Grade II and III showed 61.1% and 100.0% marble-like skin, respectively, 91.7% perioral cyanosis and 75.0% tachypnea in Grade II ($p<0.050$) [2,3,9,10].
3. In term infants who experienced perinatal asphyxia, although a dynamic decrease in the levels of neuron-specific enolase (NSE) in the blood was observed during the neonatal period, these levels remained significantly higher compared to the control group ($p<0.050$). This indicates that neuronal injury is ongoing, though relatively decreasing. In full-term infants, the decrease in NSE levels suggests a more effective recovery potential, whereas in preterm infants, neuronal injury is stronger and more prolonged [10].
4. In children who experienced perinatal asphyxia, a disruption of metabolic homeostasis is observed, characterized by a decrease in pH and pO_2 levels, and an increase in pCO_2 and HCO_3^- levels. Despite treatment and rehabilitation measures, these

changes persist throughout the neonatal period and significant differences remain when compared to healthy children ($p<0.01$) [10].

5. In newborns who experienced perinatal asphyxia, the concentration of microelements (Fe, Ca, P, Mg, Cu, and Mn) undergoes directional changes when comparing the early neonatal period (days 3-5) to days 21-28 of the child's life. Specifically, there is an increase in the concentration of Fe, Ca, and P, and a decrease in the levels of Mg, Cu, and Mn ($p<0.01$). More pronounced changes are observed in preterm-born children [3,8].
6. In preterm infants who experienced perinatal asphyxia, during the early neonatal period, there are positive and direct correlation relationships between Mg, Fe, Cu, and Zn levels and Apgar scores ($r=+0.55$; $r=+0.56$; $r=+0.39$; $r=+0.51$, $p<0.01$, respectively). Additionally, negative inverse correlations are identified between Fe, Mg, and Zn levels and symptoms of lethargy syndrome ($r=-0.36$; $r=-0.46$; $r=-0.41$, $p<0.01$), as well as between Fe, Zn, and Mg levels and decreased muscle tone ($r=-0.32$; $r=-0.29$; $r=-0.30$; $p<0.05$) [1,4,5,11].

PRACTICAL RECOMMENDATIONS

1. It is recommended that newborns born to pregnant women who experienced complications during the antenatal period, such as anemia, preeclampsia, rapid labor, and umbilical cord entanglement, be included in the risk group for perinatal asphyxia and hypoxic-ischemic encephalopathy. These children should be carefully monitored and followed up with appropriate post-birth monitoring and early intervention.
2. In children who have experienced perinatal asphyxia, it is recommended to dynamically monitor the level of neuron-specific enolase (NSE) as a biomarker of neuronal tissue damage to assess the effectiveness of treatment, along with

evaluating the metabolic and respiratory status (pH, pO_2, pCO_2, and HCO_3^- levels) and the functional status of the nervous system.

3. Regular monitoring of the levels of microelements (Fe, Ca, P, Mg, Cu, Mn) in newborns who have experienced perinatal asphyxia is crucial for evaluating recovery processes and improving clinical conditions. Monitoring the levels of Mg, Fe, and Zn, especially in preterm infants, in correlation with clinical indicators (Apgar, lethargy syndrome, muscle tone), and applying targeted treatment approaches is recommended.

The list of published scientific works on the dissertation topic

1. Sadıqova Ş.A. Yenidoğulanlarda ion homeostazının perinatal aspektləri // Sağlamlıq jurnalı. 2017, №3, səh.13-18
2. Sadıqova Ş.A., Həsənov S.Ş. Yenidoğulanlarda perinatal asfiksiya zamanı mərkəzi sinir sisteminin zədələnmələrinin risk faktorları // Sağlamlıq jurnalı. 2017, №5, səh.113-117.
3. Sadıqova Ş.A., Həsənov S.Ş. Perinatal asfiksiya keçirmiş yenidoğulanlarda adaptasiyanın klinik əlamətləri ilə mirkoelementlərin miqdarı arasında korrelyasiya əlaqələri // Azərbaycan Perinatalogiya və Pediatriya jurnalı. 2017, Cild 3, №1, s.31-34.
4. Sadıqova Ş.A., Həsənov S.Ş. Perinatal asfiksiya keçirmiş yenidoğulanlarda qanda mikroelementlərin dinamikası // Azərbaycan təbabətinin müasir nailiyyətləri jurnalı. 2017, №3, səh.52-55.
5. Sadıqova Ş.A. The dynamics of blood microelements newborn with perinatal asphyxia. // «Вістник проблем біології і медицини» Випуск 2 (144), Україна 2018 рік, стр.224-228.
6. Sadıqova Ş.A. Нарушение клеточного метаболизма у новорождённых, перенесших перинатальную асфиксию / Матеріали V всеукраїнської наукової конференції студентів та молодих вчених 3 фізіології 3 міжнародною участю, 16 травня, Україна, Харків, 2018. стр.75.
7. Sadıqova Ş.A. Neuropsychological development and cognitive functions of the child / International scientific review of the problems and prospects of modern science and education, Boston, USA, April 24-25, 2018, -p.132.
8. Həsənov S.Ş. Sadıqova Ş.A., Babayeva B.A. Клиническое значение содержания микроэлементов у новорожденных, перенесших перинатальную асфиксию // Российский Вестник Перинаталогии и Педитарии. Россия, Москва, 2019, том 64, №6, стр.53-57.

9. Sadıqova Ş.A. Динамика уровней микроэлементов крови у новорождённых, перенесших перинатальную асфиксию //Медицинские новости. 2023, №10, стр.73-75. ISSN 2076-4812
10. Sadıqova Ş.A. Neonatal dynamics of of neuron-specific enolase in newborn with posthypoxic encephalopathy // World of medicine and biology, Ucraine, 2023. №4(86), -p.133-137.
11. Sadıqova Ş.A. Корреляционные взаимосвязи между уровнями микроэлементов в крови и клиническими проявлениями адаптации у новорожденных, перенесших перинатальную асфиксию / Сборник статей XXXIV международной научно-практической конференции “Современные научные исследования”, г. Пенза, 15 августа, 2023г, с.164.

Abbreviations

ABB	*acid-base balance*
ARVİ	*acute respiratory virus infection*
CNS	*central nervous system*
GA	*gestational age*
HİE	*hypoxic -ishemic ensefalophaty*
NSE	*neyron specific enolase*
PA	*perinatal asphyxia*
Pİ	*preterm infants*

Defense will be held on "04" April 2025 at "14⁰⁰" at the meeting of the Dissertation Council ED 2.27, operating at the Azerbaijan Medical University.

Address: AZ 1022, Baku, 14a Gasimzade, (conference hall).

dissertation is assesible at the library of the Azerbaijan Medical University.

Electronic versions of the dissertation and its abstract are available on the official website of Azerbaijan Medical University (www.amu.edu.az).

The abstract was sent to the requeried addresses on
"03" March 2025.

Signed for print: 26.02.2025
Paper format: 60x84 $^{1}/_{16}$
Volume: 36286 symbols
Number of hard copies: 30

“TABIB” publishing house