

REPUBLIC OF AZERBAIJAN

On the rights of the manuscript

ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

**CATAMNESIS OF INFANTS WITH NECROTIZING
ENTEROCOLITIS AND THE WAYS OF THEIR
REHABILITATION**

Specialty: 3220.01 – Pediatrics

Field of science: Medicine

Applicant: **Sevinj Jamal Ismayilova**

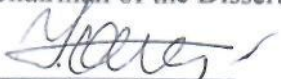
Baku – 2022


The work was performed at the Department of Childhood Diseases-1
of Azerbaijan Medical University


Scientific supervisor: honored scientist,
doctor of medical sciences, professor
Nasib Jafar Guliyev

Official opponents: honored scientist,
doctor of medical sciences, professor
Ibrahim Isa Isayev
doctor of medical sciences, professor
Aslan Ismayil Hasanov
doctor of philosophy in medicine
Saadat Arif Huseynova

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

Chairman of the Dissertation council:

doctor of medical sciences, professor
Yagub Ziyaddin Gurbanov

Scientific secretary of the Dissertation council:

doctor of philosophy in medicine,
associate professor
Tora Akif Sadigova

Chairman of the scientific seminar:

honored scientist,
doctor of medical sciences, professor
Amaliya Abdulla Eyyubova



İMZANI TƏSDİQ EDİRƏM
Azərbaycan Tibb Universitetinin
ELMİ KATİBİ
Tibb elmləri doktoru, professor
Nazim Adil oğlu Pənahov

12.09.2011

GENERAL DESCRIPTION OF WORK

The relevance of the subject. Necrotizing enterocolitis (NEC) in newborns is considered as a serious disease that causes death in 30-50% of infants¹. The course of the disease depends on the severity and the degree of maturity of the newborn. In recent years, perforation of the gastrointestinal tract, which is considered one of the most dangerous complications during NEC, continues to increase. In this case, the lethality rises to 40-80%. Sometimes the mortality rate is equal to 100% in patients with more severe side pathologies. Higher lethality occurs in premature infants weighing less than 1000 grams and fluctuates between 45-100%^{2,3}. According to the references, the high lethality is noted up to 18-40% among newborns who have undergone surgery but this figure reaches 95-100% in extensive intestinal necrosis. According to a number of authors, NEC occurs in only 16% of newborns with damage of gastrointestinal tract. In 84% of cases, NEC is accompanied by involvement of 2-3 and more organs and systems in the pathological process, multiple organ deficiency^{4,5}.

NEC held in the neonatal period has a direct impact on the further development and health of infants. Complications develop such as short bowel syndrome, malabsorption in infants, retardation of

¹*Bellodas Sanchez J., Kadrofske, M.* Necrotizing enterocolitis// *Neurogastroenterol Motil.*, – 2019. Mar. 31 (3), – e13569.

²*Kinstlinger, N.* Is necrotizing enterocolitis the same disease in term and preterm infants? / N.Kinstlinger, A.Fink, S.Gordon [et al.] // *J. Pediatr. Surg.*, – 2021. Aug. 56 (8), – p. 1370-1374.

³*Brown, J.V.* Multi-nutrient fortification of human milk for preterm infants / J.V.Brown, N.D. Embleton, J.E.Harding [et al.] // *Cochrane Database Syst Rev.*, – 2016. 8 (5), – p.343.

⁴ Wang, F.S. Intestinal tract and parenteral multi-organ sequential pathological injury caused by necrotizing enterocolitis / F.S.Wang, M.L.Yu, W.Z.Li [et al.] // *BMC Pediatr.*, – 2020. 20, – Article No.: 418.

⁵*Sampah, M.E.S., Hackam, D.J.* Prenatal immunity and influences on necrotizing enterocolitis and associated neonatal disorders // *Front. Immunol.*, – 2021. 12, – p. 650709.

physical development in 36%, functional disorders in the CNS, they do not have social adaptation⁶.

One of the most dangerous complications is short bowel syndrome (SBS), which leads to impaired absorption and consequently, reduction of nutrient absorption mainly leading to loss of proteins, electrolytes and fluid among children who underwent surgery during NEC. Absorption of fat-soluble vitamins is also directly impaired in SBS. In this regard, the doctor must solve a number of problems in the later stages of observation: II malabsorption, adaptive hypersecretion of the stomach, dysbiocenosis, stimulation of intestinal adaptation. Accordingly, complex specific measures - monitoring of fecal volume, excretion of carbohydrates in the feces and determination of lipid fractions (coprological examination of feces and lipidogram) should be carried out to determine the effectiveness of the processes of assimilation.

This examination allows the appointment of enzyme preparations. In addition, fat-soluble vitamins (A, E, D, K) and vitamin B12 should be prescribed parenterally^{7,8}. The issues of nutrition in the rehabilitation period and dispensary observation of children undergoing NEC are also relevant. Undoubtedly, breastfeeding is the basis of nutrition during this period. The child's condition and degree of immaturity should also be taken into account when prescribing complementary foods to infants undergoing NEC.

Thus, the rehabilitation of infants undergoing NEC is a very complex and laborious process, not limited to the perinatal period and poses new challenges in front of the state pediatric service. The implementation of treatment of these children requires a pediatrician

⁶*Brown, J.V.* Multi-nutrient fortification of human milk for preterm infants / J.V.Brown, L.Lin, N.D. Embleton [et al.] // *Cochrane Database Syst Rev.*, – 2020. 6, – Article No.: CD000343.

⁷*Cao, M.* Physical activity and gastric residuals as biomarkers for region-specific NEC lesions in preterm neonates / M.Cao, A.D.Andersen, Y.Li [et al.] // *Neonatology*, – 2016. Suppl. 7, – 110 (4), – p. 241-247.

⁸*Parker, L.A.* Effect of gastric residual evaluation on enteral intake in extremely preterm infants: A randomized clinical trial / L.A.Parker, M.Weaver, R.J.Murgas Torrazza [et al.] // *JAMA Pediatr.*, – 2019. 173 (6), – p. 534-543.

with in-depth knowledge and experience in this pathology. In this case, along with the elimination of damaged intestinal problems, measures and rehabilitation methods aimed at normalizing the functions of organs and systems of the whole organism should be implemented. For this reason, patients undergoing NEC should be supervised by a pediatrician, neurologist, ophthalmologist, gastroenterologist and other specialists^{9,10}. However, research performed in this area is unique, the health condition and developmental characteristics (features of neuropsychological, physical development, frequency and nature of diseases of internal organs and systems, CNS, the state of the immune system, etc.) of children undergoing NEC have not been sufficiently studied.

Object of the research: infants with necrotizing enterocolitis.

The purpose of the research was to study the catamnesis of infants undergoing NEC, to develop appropriate rehabilitation methods based on the information obtained.

Research objectives:

1. To conduct medical and statistical examinations among young children with necrotizing enterocolitis in Baku, to study the socio-epidemiological aspects of the incidence and development of this disease;
2. To clarify the relationship between the health status of the breastfeeding period of infants with necrotizing enterocolitis and the health of their mothers, the course of pregnancy and childbirth;
3. To assess the somatic and neurological status and indicators of physical development of children under one year of age who held necrotizing enterocolitis;
4. To develop a methodical approach to the implementation of

⁹Пасечник, И.Н. Современные подходы к ускоренному восстановлению пациентов после хирургических вмешательств / И.Н.Пасечник, А.Г.Назаренко, Р.Р.Губайдуллин [и др.] // Анестезиология и реаниматология, – 2015. 15 (116), – с. 10-17.

¹⁰Насирова, С.Р., Мехтиева, С.А., Гусейнова, Н.Г. Клинико-иммунологические особенности некротического энтероколита у новорожденных // Научный альманах, – 2016. № 3-3 (17), – с. 333-337.

complex treatment measures and appropriate rehabilitation measures for breastfed infants who held necrotizing enterocolitis.

Research methods: anamnestic, clinical, laboratory, biochemical, instrumental, epidemiological, bacteriological and statistical examination methods were used.

The main provisions of the dissertation submitted for defense:

- According to epidemiological data for 2011-2015, the specific gravity of morbidity with necrotizing enterocolitis in Baku is higher than other gastrointestinal tract (GIT) diseases found in newborns.
- The health of children with NEC has some characteristics: low physical development indicators and resistance to infections, high frequency of somatic and neurological pathology, low coefficients of psychomotor development.
- Development of algorithms for early diagnosis, maintenance, rehabilitation and medical examination of children who held NEC.
- In the first year of life, children undergoing NEC should undergo comprehensive rehabilitation measures by early, highly qualified medical and social workers in multidisciplinary clinics.

Scientific novelty of the research. For the first time in Azerbaijan, during carrying out a catamnestic examination, it was determined that the health of children with NEC is characterized by a high frequency of somatic and neurological pathology in the 1st year of corrected age, as well as lower rates of psychomotor development, physical retardation and low resistance to infections, and a high incidence of disability in the structure of the disease. Respiratory distress syndrome, retinopathy of premature infants and bronchopulmonary dysplasia predominate among the reasons for its emergence.

A straight correlation between the assessment of neurological status in the neonatal period (according to the A.B. Palchik scheme, 2008) and psychomotor development coefficients in the first year of life (on the CAT/CLAMS scale) was found. For the first time,

psychomotor development of children with NEC on the CAT/CLAMS scale was assessed according to the adjusted age, which revealed a delay in the mental and motor development of infants at an early age.

The dependence of level of morbidity of children with NEC related to socio-hygienic factors on the health status of the mother, the course of pregnancy and childbirth, hereditary predisposition, viral and bacterial infections has been identified.

For the first time in the Republic, the influence of medical and social factors on the prevalence, structure and clinical course of NEC in children was studied and a program of measures aimed at improving the methods of early detection, rehabilitation and dispensary of NEC in children.

Practical significance of the research. The need for carrying out early rehabilitation measures was substantiated and recommendations were made for carrying out differentiated medical observation in children with NEC. The proposed rehabilitation complex meets the quality algorithm and its suitability, effectiveness, lack of side effects give chance it to be recommended for wide application in medical practice. Assessment of the neurological status of children with NEC according to the A.B. Palchik scheme (2008) allows neonatologists to predict the risk of psychomotor developmental delay in the infant care phase corrected up to 1 year of age. In the practice of pediatricians, the use of the CAT/CLAMS scale in the first year of a infant's life encourages rapid assessment of the psychomotor development of a child with NEC and the timely initiation of rehabilitation measures.

Planned scientific research on the subject of "Early diagnosis, clinic and principles of treatment of necrotizing enterocolitis in newborns" has begun. In connection with this case, Ismayilova S.C together with the staff of the institute participated in the Grant Project conducted by the Science Development Foundation under the President of the Republic of Azerbaijan and won.

Approbation. Results of the research were discussed at the scientific-practical conference dedicated to the 90th anniversary of Agil Alirza oglu Aliyev (Baku, 2016), at the scientific-practical

conference dedicated to the 120th anniversary of A.Aliyev (Baku, 2017), at the XXV International scientific-practical conference (Moscow, 2019) on the topic of “Modern medicine: new approaches and current research”.

The initial discussion of the dissertation was held at the meeting of the Scientific Council of the Scientific-Research Institute of Pediatrics named after K. Farajova (25.12.2018, protocol No 05). The results of the research were also reported and discussed at the Scientific Seminar on the specialty 3220.01 - "Pediatrics" (29.11.2021, protocol No 09) operating under the ED 2.27 Dissertation Council of AMU.

Application of the results of the dissertation in practice. The results of the dissertation are applied in the clinical practice of the Scientific-Research Institute of Pediatrics named after K. Farajova, in the teaching process of the Department of Pediatrics I of the Azerbaijan Medical University.

The name of the organization where the dissertation has been accomplished: The research was carried out at the Scientific-Research Institute of Pediatrics named after K. Farajova and the Department of Pediatrics I of the Azerbaijan Medical University.

Publications. The main provisions of the dissertation on the main provisions and results of the work are reflected in 12 published scientific works (7 articles, 5 theses). 4 articles and 3 theses were published in local, 3 articles and 1 thesis in foreign press.

The structure and scope of research work. The dissertation was submitted on 182 computer pages (223097 characters) and consists of introduction (5 pages), literature review (25 pages), research materials and methods (11 pages), results of own research and chapters of their discussion (96 pages), conclusion (16 pages), conclusions (1,5 pages), practical recommendations (0.5 pages) and bibliography (22 pages). The work is illustrated with 46 tables, 27 graphics, 2 figures and 3 schemes. 9 references in the list of literature consisting of 209 sources are in Azerbaijani and 200 in foreign languages.

MATERIALS AND RESEARCH METHODS

The work has been performed the framework of the scientific program of the Department of Child Diseases of AMU in 2014-2016. As treatment of children with NEC in Azerbaijan was carried out at the Scientific-Research Institute of Pediatrics named after K.Farajova, the Perinatal Center and the Central Clinical Hospital, the databases and archives of these institutions have been used in the research work.

The data of clinical-laboratory examinations made it possible to form the following clinical groups: the main observation group - children with NEC (128 children), the control observation group - healthy children (64 children). Children in the main group were divided into 2 sub-groups: sub-group 1 (n=83) – children with NEC, treated conservatively and without complications; sub-group 2 (n=45) consisted of children with NEC, purulent-inflammatory complications and treated surgically (peritonitis with ileus, sepsis and pneumonia, non-treated anastomosis). The control group consisted of healthy newborns (n=64) after normal physiological deliveries. It was decided to include in the control group healthy children born on time, born at 38-41 weeks, children up to 12 months who have the opportunity to dynamically observe their growth and development.

The stage of the disease was determined according to the Walsh and Kliegman classification, according to clinical signs: group 1 – 83 (64.8±4.2%) newborns with NEC grades 1A, B and 2A (without complications) and group 2 – 2B and 45 (35.2±4.2%) newborns with grade 3A, B (with severe progress, general and local complications) NEC.

The gestational age of children in the 1st group was 31.2±1.23 weeks, in the 2nd group – 29.8±1.82 weeks ($p>0.05$), in the comparison group – 38.4±1.12 weeks, which is honestly higher than subgroups 1 and 2 ($p<0.05$). There were 85 (66.4±4.2%) boys and 43 (33.6±4.2%) girls. Among them, 53 (63.9±5.3%) boys in the first group, 32 (71.1±6.7%) in the second group, 33 (51.6±6.2%) in the comparison group; there were accordingly 30 (36.1±5.3%), 13

(28.9±6.7%) and 31 (48.4±6.2%) girls in the comparison group ($p>0.05$).

Immediately after setting the diagnosis of NEC, measures were taken within the protocol of conservative management of NEC in all children (total parenteral nutrition, decompression of the stomach and rectum, intravenous antibacterial therapy). If the symptoms of NEC developed against the background of antibacterial therapy, it was urgently corrected. Immediately after the diagnosis, enteral feeding and perosis intake of drugs were stopped in all newborns.

The child's condition was monitored for 1 day by a neonatologist (or RITU physician) and a neonatologist surgeon (peripheral blood examination, abdominal X-ray was performed every 12 hours).

Newborns who underwent surgical treatment constituted the 2nd group (45 children). In this group of patients, the main approach was the evaluation of clinical and additional examination methods.

In the study, a retrospective analysis of medical documents (consultative admission cards, individual exchange-warning cards of pregnant and lactating women, dates of birth, development and illness history of newborns) was carried out.

Descriptive-evaluation methods were applied during the analysis of morbidity according to the official registration data of morbidity and the results of the study of the registration-report documents of the Scientific-Research Institute of Pediatrics named after K.Farajova in Baku in 2011-2015. The method of retrospective epidemiological analysis of the prevalence of NEC in children in Baku was used. The prevalence of NEC in children was studied during the analysis of medical history over a 5-year period. The clinical characteristics of the disease, the characteristics of pregnancy, childbirth, the course of the postpartum period, the state of the fetus in 192 newborn children were analyzed.

For catamnestic observation, an observation card was developed on a 1 year old infant, which, in addition to the examination data of the children, included the anamnesis data of the examined children's mothers. At this time, the mothers of the examined children freely showed themselves by subjectively evaluating the social factors.

Clinical examination of newborns was carried out by generally accepted methods, assessment of the child's general condition and physical development, determination of morphofunctional maturity according to the Bollard scale, the severity of clinical symptoms of the disease, as well as pathological changes in GIT and CNS were determined.

In the diagnosis of NEC, laboratory examination, X-ray diagnosis, ultrasound and X-ray examination of the abdomen, laparocentesis (diagnostic, therapeutic) and laparoscopy methods were used.

In addition to general clinical examinations, transabdominal ultrasound and dopplerometry of the abdomen with GEProseriesLOGIQ 500 and SonoAcePICO devices with a 7.5 MHz transmitter were performed.

A complex of laboratory-instrumental examination methods was performed in all children in accordance with generally accepted standards: a general examination of blood and urine, examination of blood sugar, blood biochemical indicators (total protein and its fractions, total bilirubin and its fractions, transaminases, C-reactive protein, urea, creatinine, etc.); determining the acid-alkaline state of gases in the blood; coproscopy, stool examination according to dysbacteriosis and intestinal group.

The general clinical examination of blood was performed by the unified method on the automatic hematology analyzers "Cell-Dyn 3500R" of the company "Abbott diagnostics" (USA) and "Micros 60-OT18" of the company "ABX Diagnostics" (France).

Depending on the type of pathogen and the localization of the infectious-inflammatory process, materials were taken for examination. The first inoculation of samples of clinical material was carried out by standard methods on solid (5% sheep blood agar, Endo, Ploskiriyov, Saburo media, egg yolk-salt agar) and solid nutrient media (0.25% sugar broth). Identification of isolates was performed according to Bergy (1984). The frequency of occurrence of individual types of microorganisms in samples of clinical material was calculated based on the presence of growth in one sample and expressed as a percentage.

Assessment of children's psychomotor development was carried out on the CAT/CLAMS (Clinical adaptive test - CAT, clinical linguistic and auditory milestone scale - CLAMS and Gross motor - GM) scale. This scale allows for a quick and objective assessment of cognitive, speech, motor function and development. This scale was created as a result of combining several similar scales. Endorsed by the American Academy of Pediatrics, it is widely used worldwide. The question of whether the child is developmentally appropriate for his age is compared to his actual (chronological) age. The growth factor is calculated using the following formula:

Growth factor = developmental age/chronological age \times 100%.

A growth coefficient higher than 75% confirms that the child's psychomotor development corresponds to the actual age.

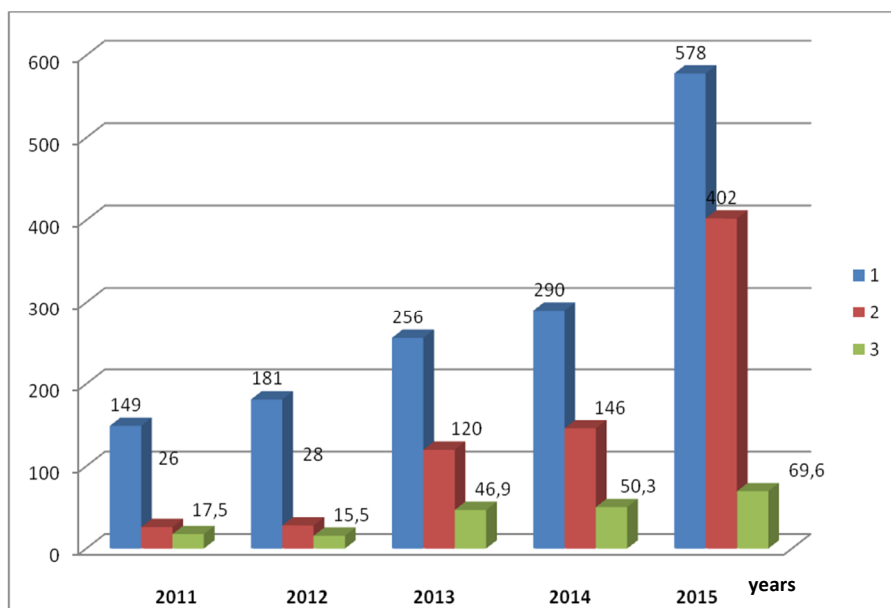
A.B. Palchik's (2002) screening scheme for evaluating the nervous system of newborns was used to assess the neurological status. At this time, all optimal indicators of neurological status were evaluated as 0, and suboptimal indicators were evaluated as different from 0.

Mathematical processing was performed directly from the general EXCEL 7.0 (Microsoft, USA) data matrix using the capabilities of the STATGRAPH 6 (Microsoft, USA) program. All numerical data were recorded in the form of MS Excel XR spreadsheets. Statistical analysis was carried out using the standard tools of the spreadsheet analysis package, in which the values of mean quantities, their errors, confidence intervals, Student's t test, Van der Waerden test, and χ^2 test were calculated. Only honest correlations were taken into account.

RESULTS OF THE RESEARCH AND THEIR DISCUSSION

In 2011-2015, the specific weight of spread of NEC in the structure of GIT morbidity in children was $49.7 \pm 1.3\%$ in Baku city. As a result of the analysis, it was determined that in 2011, $17.5 \pm 3.1\%$ of children with NEC, and in 2012, $15.5 \pm 2.7\%$ of children with NEC were recorded. Since 2013, the number of sick children registered with NEC started to increase and arranged $46.9 \pm 3.1\%$. In 2014, $50.3 \pm 2.9\%$ cases were recorded, and in 2015, $69.6 \pm 1.9\%$ cases.

Thus, the total number of cases of NEC in children in Baku during 2011-2015 was 722 cases, showing that NEC prevailed in children in 2015 (55.7±1.9%). The lowest incidence rates of NEC in children were recorded in 2011 and 2012 – 3.6% and 3.9%, respectively. The study of the pathologies of GIT recorded in children in Baku during 2011-2015 showed that NEC prevailed (49.7±1.3) compared to stoma carrier (23.9%) and bowel intussusception (10.5%). Torsion of the small intestine is not higher than 6.4%; Intestinal obstruction caused by adhesions was 3.5%, gastrointestinal bleeding was 2.1%, and strangulated intestinal obstruction was equal to only 1.23% (graphic 1).



Graphic 1. Indicators of NEC morbidity in children in Baku city (2011-2015): 1- Total number of patients with GIT; 2 - NEC in children, absolute number; with 3-%

The recorded pathologies of GIT in Baku city during 2011-2015 are presented in table 1.

Table 1

Pathology of GIT recorded in Baku city during 2011-2015

Diseases	2011	2012	2013	2014	2015	Total
	%	%	%	%	%	%
Pylorostenosis	0,7	-	-	-	0,2	0,14
Spontaneous perforation of the stomach	-	1,7	0,4		0,2	0,34
Necrotizing enterocolitis	17,5	15,5	46,9	50,3	69,6	49,7
Intestinal intussusception	12,8	13,3	12,5	12,4	7,3	10,5
Gastrointestinal bleeding	3,4	2,2	2,7	2,1	1,4	2,1
Intestinal obstruction	13,4	-	-	-	-	1,4
Intestinal obstruction (Bezoar)	0,7	0,6	-	-	0,2	0,21
Intestinal obstruction of adjacent origin	2,7	8,8	0,8	5,9	2,1	3,5
Suffocation of the intestine obstruction	-	1,7	0,9	0,9	0,9	1,23
Torsion of the small intestine	1,3	-	-	-	-	0,14
Acute appendicitis	4,7	8,2	11,0	6,6	3,9	6,4
Stoma carrier	39,4	48,0	23,0	21,0	14,2	23,9
Foreign body of the gastrointestinal tract	3,4	-	0,8	-	-	0,49
Total	100	100	100	100	100	100

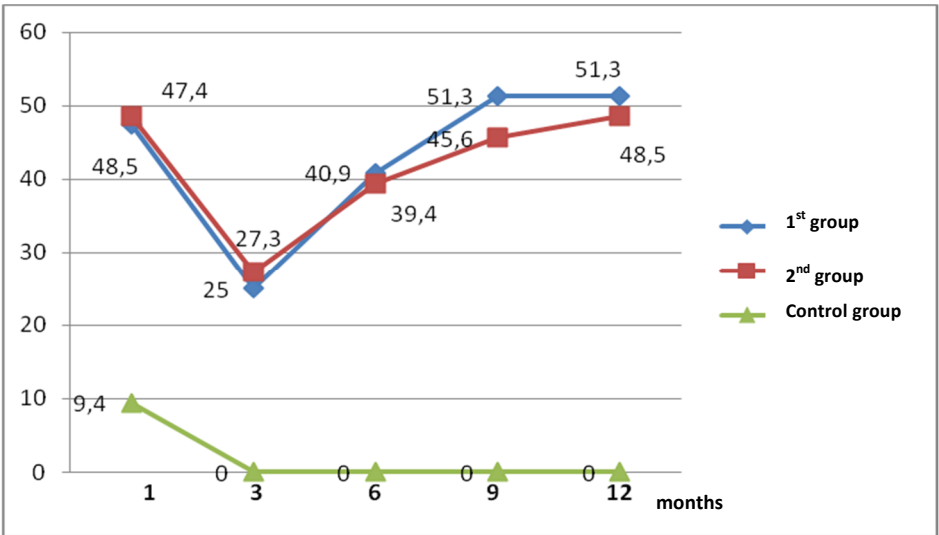
During the evaluation of the socio-epidemiological factors that are important in the spread of NEC among children, it was found that two factors have a complex negative impact on the components of health: the unfavorable financial situation of families, as a rule, is found together with their unsatisfactory housing conditions. It is no coincidence that children with NEC are found more often in children with unsatisfactory housing conditions than in children in the control group - 34.4 ± 4.2 and $26.6 \pm 4.7\%$, respectively ($t=3.02$; $p<0.01$).

In the next stage, during the clinical examination, anamnesis data were collected from the mothers and daily somatoneurological examination of the newborns was performed. Catamnetic examination of 109 children in 1, 3, 6, 9 and 12 months of corrected age after discharge from the hospital (76 children in group 1, 33 children in group 2) was performed. During the dynamic examination, the children's health condition, physical (according to the generally accepted methodology) and psychomotor development were evaluated using the CAT/CLAMS scale. The average coefficient of speech development was significantly lower in all children in the main group compared to the children in the comparison group during the entire observation period ($p<0.001$).

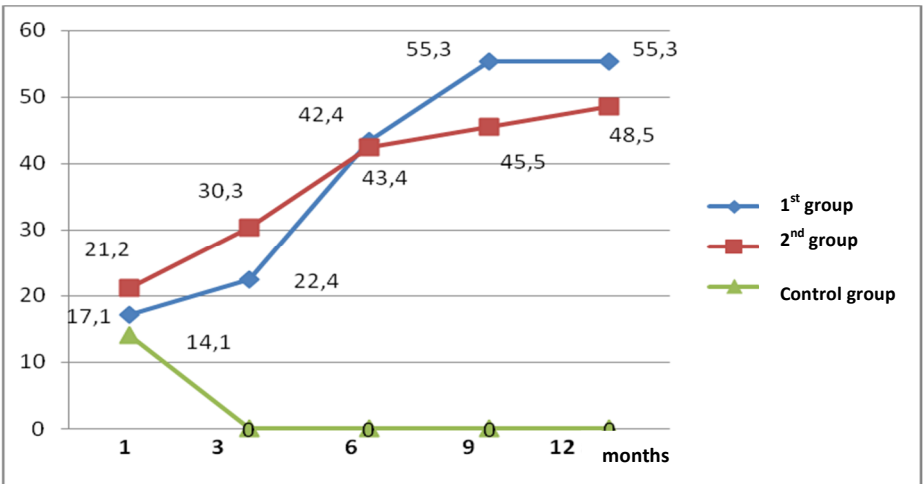
Children with a low coefficient of cognitive development were encountered in each observation group (Graphic 2).

Such children were significantly more among children who underwent NEC ($p<0.01$). Almost half of the children who underwent NEC before the age of 1 year were retarded on the indicator of cognitive development without statistically significant differences between the groups (51.3% in the 1st group, 45.6% in the 2nd group).

During the dynamic observation in the main group, the number of children lagging in terms of motor development increased in the first year of life (without statistically significant differences, $p>0.05$) and by the first year of corrected age, 53.9% of children in group 1, the coefficient of motor development of 45.7% of children in group 2 was below 75% (Graphic 3).



Graphic 2. Number of children who underwent NEC with a low (<75%) coefficient of cognitive development on the CAT/CLAMS scale in the first year of life



Graphic 3. Number of children who underwent NEC with a low (<75%) coefficient of motor development on the CAT/CLAMS scale in the first year of life

Among the children in the control group, no children were lagging in all indicators of psychomotor development on the CAT/CLAMS scale.

We also studied the perinatal history of 128 neonates with NEC. In the examined groups of newborns, the most common obstetrical and gynecological anamnesis complications in mothers include: cases of intrauterine growth retardation ($48.4\pm 4.4\%$), chronic fetoplacental insufficiency ($46.1\pm 4.4\%$), chronic intrauterine hypoxia ($12.5\pm 3.9\%$). During the birth of children with NEC, the risk of miscarriage and chronic FP was one of the frequent complications of pregnancy ($p<0.05$). Mothers in the main observation group had statistically significantly more cases of nephropathy, hypotrophy of the fetus compared to the comparison group ($p<0.05$). In vitro fertilization (IVF) was recorded only in the main observation group (3 cases, 2.4%).

Based on our research, the most important point affecting the state of the fetus during childbirth and future postnatal events is the method of delivery. It was determined that the births of the mothers in the main group ended with emergency cesarean section in most cases, $62.6\pm 5.3\%$ of cases in the 1st group of mothers of children with NEC, 44.4 ± 4 in the 2nd group of mothers of children with NEC, 1% ($p>0.05$) was a case. Planned cesarean section was prescribed in $13.3\pm 3.8\%$ of mothers of children with NEC in group 1, and in $15.6\pm 5.6\%$ of mothers of children with NEC in group 2.

From all the factors that characterize the presence of chronic somatic pathology of the mother and the pathology of the antenatal and intranatal period, the most significant ($p<0.1$) for the performance of the discriminant model are: the presence of a threat of pregnancy disruption, the presence of hysteria, the presence of spontaneous abortions in the anamnesis, delivery by cesarean section, presence of somatic pathology.

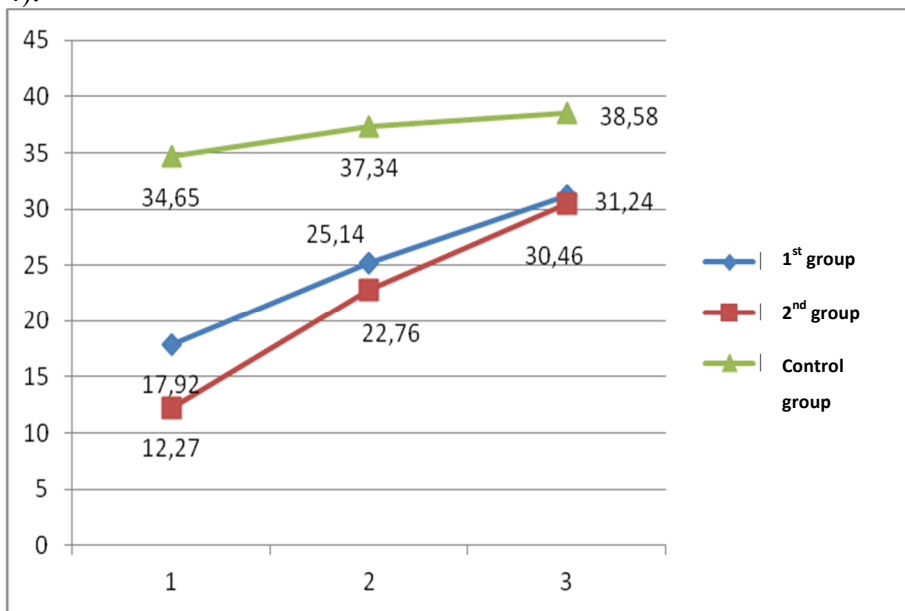
Physical development of children who underwent NEC differed significantly from children in the control group on all indicators ($p<0.001$). During the assessment of the physical development of newborns, it was detected that the age-relevant harmonious development ($44.6\pm 5.5\%$) was statistically less common in children

who underwent NEC than in the comparison group ($65.6 \pm 5.9\%$, $p < 0.001$). The assessment of the Apgar scale at the 1st and 5th minutes of the child's life was significantly lower in children who underwent NEC ($p < 0.001$). During the assessment of the condition of the children at birth, it was identified that all the children in the main group were born in a severe condition, and in the comparison group, they were born in a satisfactory condition.

All children with NEC had respiratory diseases, nervous system diseases, and small abnormalities of heart development (AOP, AAA) during the newborn period. Respiratory distress syndrome (RDS) of newborns prevailed among the diseases of the respiratory organs, which occurred with the same frequency in children of groups 1 and 2, despite the fact that the mothers of children with NEC received antenatal prophylaxis of RDS: accordingly $89.2 \pm 3.4 \pm \%$ and $86.7 \pm 5.0\%$ ($p = 0.425$). Cerebral ischemia was the most common pathology of the nervous system and was detected in the majority of infants who underwent NEC ($91.7 \pm 3.9\%$ infants in group 1 and $93.3 \pm 3.8\%$ infants in group 2). In the main group, an open oval window was recorded in 100% of children. Neonatal jaundice was found in $80.1 \pm 4.4\%$ of children in group 1 and $75.6 \pm 6.4\%$ in group 2 ($p = 0.779$). Severe anemia prevailed in group 2 infants ($80.0 \pm 5.9\%$, $p < 0.05$). In children with NEC, grade 1-2 retinopathy was more common in children in group 2 than in children in group 1 ($66.6 \pm 7.0\%$ vs. $44.6 \pm 5.5\%$, $p = 0.145$). The high frequency of diseases of the nervous system and respiratory system (RDS, small anomalies of heart development, cerebral ischemia) in children with low body weight is determined by the immaturity of these systems before birth.

In dynamics, an examination of the neurological status was carried out 3 times: the first examination of children with NEC in groups 1 and 2 was carried out on the first day of hospitalization, the second - during their transfer from the intensive care unit to the neonatal pathology department, and the third - when they were discharged home. Most of the children had below-normal scores on admission: 72.3% of children in group 1 and 93.4% of infants in group 2. The normal indicator was more common in children in the 1st group ($p < 0.01$). As seen from the results of the evaluation of the

neurological status that despite the positive dynamics of the evaluation in the third examination, during the entire observation period, the children who had NEC in the 2nd group showed lower scores compared to the 1st group. During the evaluation of the neurological status according to the A.B. Palchik scale (2008), children with NEC in group 2 had lower scores compared to children with NEC in group 1 during the entire observation period (Graphic 4).



Graphic4. The results of the neurological examination according to the average sum of points in all groups of examined newborn children: 1 – I examination; 2 – II examination; 3 – III examination.

In analyzing the acquired data, it was identified that the total lethality among 128 newborns who underwent NEC was $14.8 \pm 3.2\%$ (19 children). In the course of conservative treatment, among 83 newborns in group 1, 7 ($8.4 \pm 3.2\%$) children had a lethal outcome against the background of exacerbation of NEC and widespread intrauterine infection (IUI). 12 ($26.7 \pm 6.6\%$) out of 45 newborns in

the 2nd group were fatal. The causes of death of 19 children with NEC were as follows: generalized IUI with multiple organ failure – 42.1%, sepsis with the development of multiple organ failure – 26.3%; multiple developmental defects – 15.8%, severe organic pathology of the CNS – 15.8%.

It is important to note that isolated or co-incident infections were observed in all children with NEC. Most of the newborns had pneumonia 57.0±4.4%, intestinal infections – 24.2±3.8%, sepsis – 22.7±3.3%, and in rare cases, myocarditis – 1.6%, meningoencephalitis – 1.6 %, osteomyelitis – 2.3%. Bacteriological examination of the flora taken from different loci (intestine, oral cavity, intubation tube, umbilical wound, peritoneal exudate) showed that the representatives of conditionally pathogenic microflora were more common: Staphylococcus aureus – 21.1%, Staphylococcus epidermidis – 18.7%, Escherichia coli – 10.2%, Klebsiella pneumoniae – 6.3%, Enterobacter – 20.9%, Pseudomonas aeruginosa – 12.5%, Proteus mirabilis – 3.1%, Clostridium perfringens – 1.6%, genus Candida mushrooms – 5.5%. Dysbiosis was found in 100% of preterm children with NEC and in 29.7% of children in the control group (p=0.000). In newborns with NEC in groups 1 and 2, conditionally pathogenic microorganisms in various associations (enterococci, enterobacteria, proteus), as well as Staphylococcus aureus, Citrobacter and Candida fungi were detected with a very high frequency.

As catamnestic, we examined 109 children aged 1, 3, 6, 9, 12 months who underwent NEC in the catamnesis cabinet of the Scientific-Research Institute of Pediatrics named after K. Farajova. The children of the main group were divided into 2 groups: 1st group (n=76) – consisted of children with NEC who received conservative treatment and had no complications; The 2nd group (n=33) consisted of children with NEC and purulent-inflammatory complications, treated surgically (peritonitis with ileus, sepsis and pneumonia, failure of anastomosis healing). Statistically significant differences were found between the 1st and 2nd groups of children with NEC during the assessment of physical development in children who were examined at 3, 6, 9 and 12 months of corrected age in children who

had NEC. Body weight of children in group 2 increased significantly compared to children in group 1 and children in the control group. Body length significantly increased in the comparison group ($p<0.01$). During the entire observation period on children from 1 month to 1 year of corrected age, it was found that the increase in body weight was significantly lower in children who underwent NEC compared to children in the control group ($p<0.001$). Among children who underwent NEC, the increase in body weight of infants in group 2 was significantly higher ($p<0.01$). Height growth of children in all observation groups was not significantly different. Head and chest circumferences were significantly increased in infants in the main group than in children in the control group.

At 12 months of corrected age, harmonious development was found in children in all examination groups, and no statistically significant differences were found in the indicators ($p>0.05$). Disharmonic development was identified at the same frequency in children with NEC ($p<0.001$) and children in the control group ($p<0.001$). Acute disharmony development was found without honest differences in all groups of children with NEC examined.

When examining the frequency of respiratory diseases in the examined children, it was found that during the 1st year of life, on average, 7.9% of children with NEC in group 1 did not have diseases, while in the comparison group it was $32.8\pm 5.4\%$ of children. was recorded ($p<0.001$). There are no children without respiratory diseases in the 2nd examination group of children who have undergone NEC. $67.1\pm 5.4\%$ of children in group 1 and $72.4\pm 7.7\%$ of children in group 2 were included in the group of children with frequent illness (more than 4 morbidity or resistance index above 0.33), included 3.1% children in the comparison group. As it can be seen, there are honestly more children who get sick frequently in the main group than among the children in the control group ($p<0.001$).

Violations of the autonomic nervous system, pyramidal deficiency syndrome, PMDD, cerebral palsy (CP) were found only in children who underwent NEC. Pyramidal deficiency syndrome was the most common clinical syndrome in children with NEC, it was recorded in

40.8±5.6% to 90.9±4.9% of those children, but this syndrome was honest in group 2 children ($p<0.05$). A tendency to increase the number of infants with PMDD in the 1st year of corrected age was noted: in practically half of the children who underwent NEC: 50.0±5.7% of children in group 1 and 45.6±5.6% of children in group 2 PMDD was recorded, but no significant differences were observed between the two groups ($p>0.05$).

A minor anomaly of cardiac development (MAA) – open oval window (OOW) was found in the majority of children with NEC. In the 1st year of the corrected age, the OOW was closed in all the children in the 1st group, and it remained open in 5 (15.2±6.2%) children in the 2nd group. A patent arterial aneurysm (AAA) of no hemodynamic significance was found in all groups of children with NEC without significant differences. By 1 year of age, AAA was closed in all infants in the main group. Ventricular septal defect (VSD) with congenital heart defect (CHD) was observed in all groups of children with NEC without significant differences. Pulmonary artery valve stenosis (PAS) was the cause of disability and was found in 1 (1.9%) child in group 1 and 1 (1.0%) child in group 2 ($p<0.001$). In the comparison group, no cardiological pathology was detected in the children.

Pathological changes in NSG were found in infants in group 2 compared to children in group 1 and the control group in a significantly larger number. In the comparison group, changes in NSG were determined only in 1 month in 7 (10.9±3.9%) children. The frequency of pathological changes in NSG at 6, 9 and 12 months did not differ significantly between groups 1 and 2 at birth ($p>0.05$). Most of the pathological changes in the CNS found in preterm children with NEC are related to incomplete development of the brain at birth, which leads to structural changes in the CNS. This, in turn, is considered the cause of severe neurological pathology in this group of children and leads to the limitation of opportunities for infants who have undergone NEC.

It was identified that periventricular leukomalacia (PVL) was found only in group 1 children. At 1, 3, and 12 months of corrected age, cysts in the caudothalamic furrow were significantly more

frequent in group 2 infants than in group 1 children ($p < 0.05$). Ventriculomegaly (enlargement of cerebral ventricles), enlargement of the interhemispheric fissure and subarachnoid area were found in observation groups 1 and 2 without significant differences. Cysts in the caudothalamic furrow were detected at 1 month in only 7 ($10.9 \pm 3.9\%$) children in the comparison group without honest differences in children in groups 1 and 2 ($p > 0.05$). Symptoms of gastrointestinal syndrome were found in children who underwent NEC in catamnesis. These signs were more noticeable in children in the 2nd group. The following were found more often in children from this group: disturbances of motor-evacuation dysfunction of the stomach in the form of signs of stagnation - in 9 children born prematurely in the main group ($27.2 \pm 7.2\%$) ($\chi^2 = 19.16$, $p < 0.001$), vomiting and retching syndrome - in 8 children ($24.2 \pm 7.1\%$) ($\chi^2 = 6.42$, $p = 0.012$); delay in defecation was recorded in $51.5 \pm 8.7\%$ of children, which was significantly different from dynamic bowel obstruction syndrome in children of group 1 ($\chi^2 = 9.44$, $p < 0.001$). Flatulence was significantly more common among children in group 2 compared to children in group 1 - $63.6 \pm 8.5\%$ ($\chi^2 = 5.32$, $p < 0.01$; $\chi^2 = 6.48$, $p < 0.001$). Short bowel syndrome developed in $18.2 \pm 6.7\%$ of children who underwent surgical resection of the intestine. $21.2 \pm 7.1\%$ of children have symptoms of diarrhea, dehydration, critical loss of electrolytes, vomiting, flatulence, gastroesophageal reflux, weight loss, liver damage, infectious symptoms are possible.

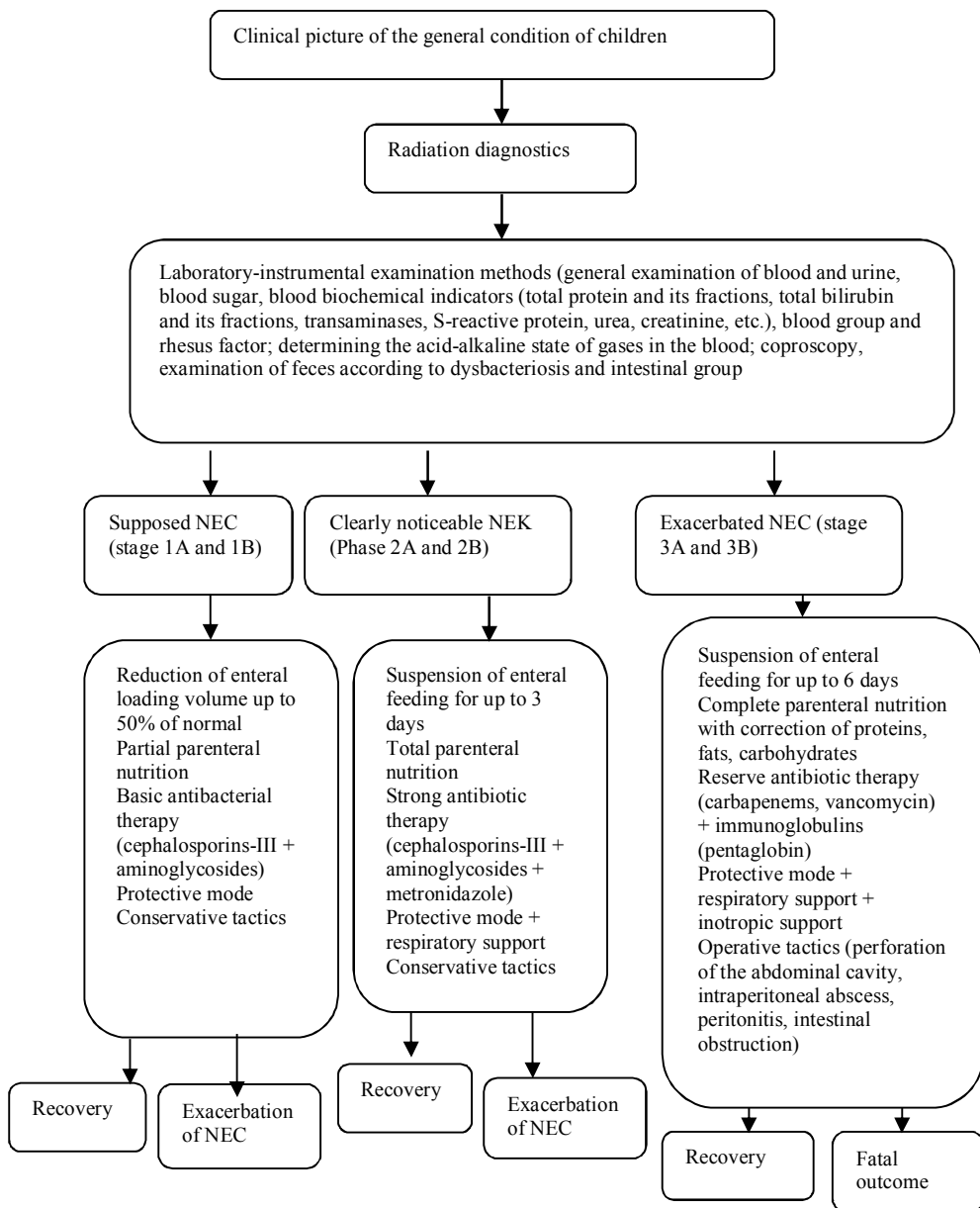
Cholestasis syndrome is considered one of the complications of NEC, and it was recorded in $10.5 \pm 3.4\%$ of children in group 1 and $12.2 \pm 5.7\%$ in group 2 during the study ($p < 0.001$). Intestinal resection (cholestasis was observed in 30-60% of children with short bowel syndrome), long-term parenteral nutrition, and the development of bacterial and fungal infection are risk factors for the development of cholestasis. During long-term cholestasis, it is necessary to take soluble vitamins A, D, E.

Pneumonia and BAD were the cause of hospitalization in the main group during the entire observation period without significant differences. Children in group 2 at 3, 6 and 9 months of corrected age have more need for hospitalization due to neurological disorders. In

the 1st month and 12th month of the corrected age, children in the main group received inpatient treatment for neurological pathologies without honest differences, but the number of children in the 2nd group was higher ($p>0.05$). No child in the comparison group required hospitalization in the first year of life.

Rehabilitation of children with NEC should be carried out early, highly qualified, differentiated depending on the predicted outcome, and should be complex in nature, at which time the activities of medical workers (neurologists, pulmonologists, ophthalmologists), educators, psychologists, social workers should be combined, and the whole family should necessarily join the rehabilitation process. The frequency of observation by a pediatrician is 1 time in 3 months during the first year after an exacerbation, and then 1 time in 12 months, by a gastroenterologist once a year, by an ENT doctor and a dentist - once a year, according to the instructions of other specialists. Examination methods: examination of blood, urine, examination of faeces for occult blood, coprogram is carried out once every 3 months during the first year after an exacerbation, and once every 6 months thereafter; examination of feces for worm eggs, giardia, dysbacteriosis is carried out once every 6 months. X-ray examination of the intestine is performed according to the instructions. In this regard, the tactics of treatment-diagnostic measures for children with NEC were carried out in accordance with the algorithm for monitoring newborns (Scheme 1).

Taking into account the 1.5 times higher rate of morbidity in children who have undergone NEC, the detection of pathologies of the endocrine system, nutritional disorders, diseases of the nervous system and sensory organs, diseases of the respiratory organs, diseases of the urinary system, as well as the increase in the specific weight of children who often get sick receiving, this group of infants requires high attention from the field pediatric service, the treatment is consistently applied using new organizational technologies, and targeted rehabilitation of children who have undergone NEC. One of the forms of organizing special assistance to children who have undergone NEC is considered to be catamnetic observations on children.



Scheme 1. Algorithm of observation of newborns depending on the stages of NEC

Thus, the purpose of conducting catamnetic observations is the full implementation of medical and social rehabilitation of children who have undergone NEC. Children who have had NEC in the first year of life require BPD, ultrasound, RP, timely prevention and diagnosis of retardation of psychomotor development, early detection of risk factors for the purpose of correction of health disorders in infancy, provision of medical and social assistance, differential medical observation by a neurologist, pulmonologist, and ophthalmologist in multi-profile clinics. The rehabilitation of children born with very low and extremely low body weight should be early, highly qualified, differentiated, depending on the predicted outcome, and should be complex by combining the activities of medical professionals (neurologists, pulmonologists, ophthalmologists), educators, psychologists, and social workers, and at this time, all members of the family should be involved in the rehabilitation process.

CONCLUSIONS

1. As a result of the epidemiological analysis, it was determined that in the structure of GIT morbidity in Baku in 2011-2015, the incidence of NEC in children was $49.7 \pm 1.3\%$ (722 people) and the highest rate of this pathology was recorded in 2015 - 402 ($55.7 \pm 1.9\%$) people. Other pathologies were detected with the following frequency: carrier of stoma - 23.9%, intestinal intussusception - 10.5%, small bowel torsion - 6.4%, intestinal obstruction of adhesion origin - 3.5%, gastrointestinal bleeding - 2.1%, strangulation intestinal obstruction - 1.23. During the assessment of socio-epidemiological factors important in the spread of NEC among children, it was found that the most negative impact on the health of infants is the unfavorable financial situation of families and unsatisfactory housing conditions [3, 4, 5].
2. It was found that the risk of miscarriage, hestosis, spontaneous abortion in the anamnesis, delivery by caesarean section, somatic pathologies found in the mothers of children

- who have had NEC have a significant impact on the health of infants during the breastfeeding period [6, 8, 11, 12].
3. Children who held NEC were characterized by low levels of physical development and resistance to infections, high frequency of somatic and neurological pathology, and low rates of psychomotor development. In 100% of them, diseases of the respiratory system, nervous system and small abnormalities in the development of the heart were found during the neonatal period. Respiratory distress syndrome (RDS) predominated among these pathologies - 88.3% [9].
 4. Pyramidal insufficiency syndrome is being the most common clinical syndrome in children with NEC ($40.8\pm 5.6\%$ to $90.9\pm 4.9\%$) and is more common than in group 2 children ($p < 0, 05$). PMDD was registered in almost half of the children who underwent NEC - $50.0\pm 5.7\%$ of children in group 1 and $45.6\pm 5.6\%$ of children in group 2. In children who have undergone NEC in catamnesis, the symptoms of gastrointestinal syndrome were more pronounced than in children in group 2 ($p < 0.01$). Cholestasis syndrome was one of the complications of NEC, occurring in $10.5\pm 3.4\%$ of children in group 1 and $12.2\pm 5.7\%$ of children in group 2 ($p < 0.001$). $18.2\pm 6.7\%$ of children who underwent surgical resection of the intestine developed “short bowel syndrome” [9, 10].
 5. In order to prevent timely delays in physical and psychomotor development, children who have undergone NEC need differentiated medical observation in the first year of life. Depending on the predicted outcome, rehabilitation of children born with very low and extremely low body weight should be complex, combining the activities of medicine (neurologist, pulmonologist, ophthalmologist) and social workers and in this case, all members of the family must be involved in the rehabilitation process [1, 2, 7].

PRACTICAL RECOMMENDATIONS

1. It is recommended that children who have undergone NEC be registered at a dispensary and the dispensary observation complex should include a pulmonologist, neurologist, ophthalmologist, gastroenterologist according to the instructions.
2. Taking into account the identified features, it is considered expedient to develop an individual treatment-and-prophylaxis complex for each infant.
3. As late detection of NEC significantly increases the likelihood of an infant's lethal outcome, it is recommended that NEC be diagnosed as early as possible.

LIST OF SCIENTIFIC WORKS, PUBLISHED ON THE TOPIC OF THE DISSERTATION

1. İsmayılova, S.C., Quliyev, N.C. Nekrotik enterokolit keçirmiş körpələrdə südəmər dövrün katamnezi // – Bakı: Sağlamlıq, – 2014. № 3, – s. 169-175.
2. İsmayılova, S.C., Nəsirova, S.R. Nekrotik enterokolit keçirən uşaqların katamnezi // Tibb elmləri doktoru Əzəm Təyyar oğlu Ağayevin anadan olmasının 70 illiyinə həsr edilmiş elmi konfransın materialları. İctimai sağlamlıq və səhiyyə, Bakı, III cild, – s.143.
3. Исмаилова, С.Дж. Оценка факторов повышенного риска заболеваемости детей некротизирующим энтероколитом // – Москва: Фундаментальные исследования, – 2015. № 1, – с. 1166-1169.
4. İsmayılova, S.C. Nekrotik enterokoliti olan uşaqların analarında hamiləliyin gedişinin xüsusiyyətləri // Aqil Əlirza oğlu Əliyevin 90 illik yubileyinə həsr olunmuş elmi-praktik konfransların materialları, – Bakı, – 2016. – s. 197-199.
5. İsmayılova, S.C. Nekrotik enterokolit keçirmiş uşaqların instrumental müayinə metodlarının məlumatları // Ə.Əliyevin

- 120 illik yubileyinə həsr olunmuş elmi-praktik konfransın materialları, – Bakı. – s. 212-213.
6. İsmayılova, S.C. Uşaqlarda nekrotik enterokolitin formalaşmasının risk amillərinin təhlili // – Bakı: Azərbaycan Təbabətinin Müasir Nailiyyətləri, – 2018. № 2, – s.152-157.
 7. İsmayılova, S.C. Bakı şəhərində uşaqların nekrotik enterokolit ilə xəstələnmə dinamikası və yayılma səviyyəsi // – Bakı: Sağlamlıq, – 2018. № 2, – s. 152-157.
 8. Исмаилова, С.Дж. Факторы риска и распространенности некротического энтероколита среди детей в г.Баку // – Баку: Биомедицина, – 2018. № 3, – с.10-13.
 9. Исмаилова, С.Дж. Особенности акушерстко-гинекологического и соматического статуса матерей детей с некротическим энтероколитом // – Минск: Медицинские новости, – 2019. № 10, – с. 66-69.
 10. Исмаилова, С.Дж. Состояние здоровья детей перенесших некротический энтероколит в анамнезе // XXV международная научно-практическая конференция «Современная медицина: новые подходы и актуальные исследования», – Москва. – с. 36-40.
 11. Ismayilova, S.J. Importance of combinations of risk factors in the development of necrotizing enterocolitis in newborn children // Український журнал медицини, біології та спорту, – 2022. 7, No 3 (37), – p. 139-142.
 12. Исмаилова, С.Дж. Катамнез и реабилитация новорожденных, перенесших некротический энтероколит // XXXV International Multidisciplinary Conference "Recent Scientific Investigation", – Москва, – 2022. – с. 53-56.

LIST OF CONDITIONAL ABBREVIATIONS

BPD	– bronchopulmonary dysplasia
CAT/CLAMS	– The Cognitive Adaptive Test/ Clinical Linguistic and Auditory Milestone Scale (scale for assessing children's psychomotor development)
CNS	– central nervous system
CNS CPD	– complications of CNS perinatal damage
CNS PD	– perinatal damage of the central nervous system
CP	– cerebral palsy
GIT	– gastrointestinal tract
IGH	– intragastric hemorrhage
IUI	– intrauterine infection
IUGR	– intrauterine growth retardation
IVF	– <i>in vitro</i> fertilization
NEC	– necrotizing enterocolitis
NSG	– neurosonography
PMDD	– psychomotor developmental delay
RP	– retinopathy of premature births
SBS	– short bowel syndrome
VSD	– ventricular septal defect

The defense will be held on 13 October 2022 at 14⁰⁰ at the meeting of the Dissertation council ED 2.27 of Supreme Attestation Commission under the President of the Republic of Azerbaijan operating at Azerbaijan Medical University

Address: AZ 1022, Baku, A.Gasimzade str., 14

Dissertation is accessible at the Library of Azerbaijan Medical University

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

Abstract was sent to the required addresses on 12 September 2022

Signed for print: 02.09.2022

Paper format: 60 x 84 1/16

Volume: 38753

Number of hard copies: 30