CLINICAL FEATURES OF FUNCTIONAL GASTROINTESTINAL DISORDERS IN PRETERM INFANTS: AN ANALYTICAL STUDY

Godovanets O.S., Babintseva A.H.

Bukovinian State Medical University, Chernivtsi, Ukraine

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ABSTRACT

Background. Pathology associated with digestive system insufficiency in newborns occurs in 33.8% to 53.45% of cases.

Aim. To conduct a comparative analysis of the clinical manifestations of nutritional deficiency in preterm infants, considering the gestational age and severity of perinatal pathology.

Materials and Methods. Clinical signs of nutritional deficiency in 355 preterm infants with perinatal pathology of varying severity were analysed. Group I included 54 infants born at 26–31/6 weeks of gestation and with a serious condition at birth; Group II – 149 infants at 32–33/6 weeks of gestation (Subgroup IIA – 67 infants with severe forms of perinatal pathology, Subgroup IIB – 82 infants with moderate pathology); Group III – 102 infants at the gestational age of 34–36/6 weeks (Subgroup IIIA – 41 infants with severe forms of perinatal pathology, Subgroup IIIB – 61 infants with moderate pathology); Group IV – 50 conditionally healthy newborns at the gestational age of 34–36/6 weeks.

Results and Conclusions. Asphyxia, respiratory distress syndrome, primary pulmonary atelectasis, hyaline membrane disease, multiple organ failure syndrome with damage to the central nervous, respiratory, cardiovascular, urinary, and gastrointestinal systems, as well as haemorrhagic, convulsive and anaemic syndromes play a crucial role in the severity of the condition in preterm infants. The most frequent clinical markers of food intolerance in perinatal pathology in newborns were: residual volume of more than 50%, regurgitation and/or vomiting, enlarged liver or hepatolienal syndrome; intestinal meteorism, blood in coprofiltrate, acholic stools, jaundice and endotoxemia syndrome. The severity and frequency of food tolerance disorders correlate with the severity of perinatal pathology and the lower gestational age of newborns.

Keywords: *premature infants, digestive system, food tolerance disorders, laboratory diagnostics.*

Introduction

Every year, up to 16% of infants are born prematurely in the world. The consequences of preterm birth, especially at very low gestational age, are impaired postnatal adaptation, as well as the development of functional and chronic pathology in the later years of life. PreTerm Infants (PTI), compared to full-term infants, have a higher risk of physical and neuropsychological developmental disorders, which reduces the quality of life of patients [1–4].

Corresponding Author:
Oleksii Godovanets – MD, PhD, Associate professor, Department of Pediatrics, Neonatology and Perinatology Medicine, Bukovinian State Medical University (Chernivtsi, Ukraine).

✉ Ukraine, 58002, Chernivtsi, Teatralna sq., 2.
E-mail: godovanec.oleksij@bsmu.edu.ua

In the postnatal development of newborns, the full functioning of the GastroIntestinal System (GIS) plays an important role. Pathology associated with insufficiency of the digestive system occurs in 33.8% to 53.45% of cases and is one of the most frequently discussed in modern scientific sources [5]. Due to the Morphological and Functional Immaturity (MFI) of the body of infants at preterm birth, imperfections in the processes of digestion, absorption, and motility of the GastroIntestinal Tract (GIT) are noted, which causes problems in the formation of Enteral Nutrition (EN). Functional deficiency of the GIS is most common in infants of gestational age at birth less than 32 weeks and weighing less than 1500 g. At the same time, newborns have high nutritional needs that are difficult to meet through enteral feeding alone [6–9].

After birth, the PTI organism needs functional and structural maturation of the GIS to establish the processes of digestion and absorption of nutrients. It is important to develop intestinal motility, which includes the coordination of sucking and swallowing, gastroesophageal sphincter tone, as well as adequate gastric emptying, and intestinal peristalsis. In PTI, gastroesophageal reflux, significant gastric residues, and constipation are often observed due to insufficient gastric emptying, and insufficient intestinal motility, which is manifested by abdominal distention and delayed meconium passage [10–12].

Insufficient development of the basic functions of the gastrointestinal tract causes impaired food tolerance in PTI, especially in clinical forms of perinatal pathology, which is an important aspect of medical care in the neonatal intensive care unit – full provision of the newborn's body with basic food ingredients to ensure full functioning. Timely diagnosis and correction of Food Intolerance (FI) in the PTI is an important way to improve survival rates and the health and quality of life of this category of newborns.

The **aim** of the study was to conduct a comparative analysis of the clinical manifestations of nutritional deficiency in preterm infants, taking into account the gestational age and severity of perinatal pathology.

Materials and Methods

The total number of PTIs included in the research programme was 355 infants with gestational age at birth of 26–36/6 weeks: Group I consisted of 54 newborns with a gestational age of 26–31/6 weeks who had a serious condition at birth; Group II – 149 newborns with a gestational age of 32–33/6 weeks, of whom: Subgroup IIA – 67 infants with severe forms of perinatal pathology, Subgroup IIB – 82 infants with moderate perinatal pathology; Group III consisted of 102 infants with the gestational age of 34-36/6 weeks, including: Subgroup IIIA – 41 infants with clinical forms of severe perinatal pathology, Subgroup IIIB – 61 infants with moderate perinatal pathology; Group IV included 50 conditionally healthy newborns at a gestational age of 34–36/6 weeks.

The inclusion criteria for the study were: gestational age 26–37 weeks, birth weight <2500 g; the presence of adaptation disorders at birth and clinical signs of perinatal pathology during the neonatal period, manifestations of nutritional deficiencies, and informed consent of the child's parents to participate in the study. The exclusion criteria were: gestational age at birth <29 weeks and ≥37 weeks; weight ≥2500 g; congenital malformations, no food tolerance disorders, and parental consent to the newborn's participation in the clinical trial.

The clinical study was an open-label, single-center, stratified, cohort study. The duration of the newborn observation included the period of stay in the maternity facility. In order to form risk Groups for the predicted development of FI, a comparative analysis of the list of antenatal, perinatal, and postnatal risk factors, as well as pathological conditions of the neonatal period, taking into account the severity of the newborn condition, was carried out in the course of the research. The following were subject to analysis: exchange cards for pregnant women (Form (F)of medical documentation No.113/0), birth histories (F No. 096/0), and newborn development charts (F No.097/0).

The list of diseases of the early neonatal period included clinical diagnoses according to the ICD X revision. The diagnoses were made taking into account the current recommendations of the National Classifier of Ukraine "Classifier of Diseases and Related Health Problems NK 025:2021": Class 16. Certain conditions occurring in the perinatal period (P00–P96).

The diagnoses were verified in accordance with the current clinical guidelines and unified clinical protocols for neonatal care in the areas of neonatology and paediatrics approved by the Ministry of Health of Ukraine in 2015–2024. The correspondence of the degree of maturity of the child to the gestational age at birth was determined by taking into account anthropometric parameters (weight, body length, head circumference, trunk circumference), assessment of morphological and functional characteristics according to the Ballard scale, and using percentile tables [13]. The nature of adaptation was determined taking into account the Apgar score at 1 and 5 minutes of the newborn's life and the results of further dynamic clinical and laboratory observation. The severity of the condition in infants was determined according to a set of clinical signs, as well as using the Score for Neonatal Acute Physiology Perinatal Extension (SNAPPE II) [14; 15]. The diagnosis of multiple organ failure syndrome (MOFS) was made based on the Neonatal Multiple Organ Dysfunction Score (NEOMOD, 2001) [16; 17].

The studies were conducted in compliance with the GCP (1996), the Council of Europe Convention on Human Rights and Biomedicine (1997), the World Medical Association Declara-

tion of Helsinki on the Ethical Principles for Research Involving Human Subjects (1964–2008), and Order of the Ministry of Health of Ukraine No.690 of September 23, 2009 (as amended by Order of the Ministry of Health of Ukraine No.523 of July 12, 2012). Approval of the Commission on Bioethics of Bukovinian State Medical University (Protocol No.2 of February 09, 2015).

Statistical processing of the obtained results was performed on a Pentium MMX CPU personal computer using the Statistica 13 (StatSoft Inc., USA), Excel 2010 (Microsoft, USA), and MedCalc 16.1 (MedCalc Software Ltd., Belgium). After dividing into Groups and comparison Subgroups, descriptive and comparative analysis methods were applied to each of them. Randomisation was carried out by centralised computerised Group assignment, taking into account the results of a comprehensive clinical and paraclinical examination of newborns according to the severity of the general condition and gestational age at birth.

The type of distribution was assessed by determining the degree of central tendency between the arithmetic mean, mode, and median, as well as the slope (symmetry) and steepness (kurtosis). In the course of the statistical analysis, the arithmetic Mean of the sample (M), Standard deviation (S), and standard error (m) were determined using the Shapiro-Wilk test (normal distribution of values with a sample size of more than 30, $p>0.05$). The comparison of quantitative indicators in samples with a normal distribution was carried out using the Student's t-test. The significance of differences between relative values was determined using Fisher's angular transformation method «φ». To confirm the significance of differences, the generally accepted probability value (p) was taken into account – $p<0.05$. Statistical differences between the treatment and control Groups are presented with the Bonferroni correction.

Results and Discussion

Comparative characteristics of newborns in the observation Groups by gender ratio were as follows: in Group I – 24 (44.44%) boys and 30 (55.56%) girls; in Group II – 70 (46.98%) boys and 79 (53.02%) girls, respectively; in IIA Subgroup – 39 (58. 21%) and 28 (41.79%); in IIB Subgroup – 31 (37.80%) and 51 (62.20%); in Group III – 36 (35.29%) boys and 66 (64.71%) girls, respectively; in IIIA Subgroup – 22 (53.66%) and 19 (46.34%); in IIIB Subgroup – 14 (22.95%) and 47 (77.05%); in Group IV – 27 (54.00%) boys and 23 (46.00%) girls. There was a tendency for a higher percentage of boys with severe condition at birth, namely: 58.21% in Subgroup IIA and 53.66% in Subgroup IIIA compared to newborns with moderate severity of condition – 37.80% in Subgroup IIB and 22.95% in Subgroup IIIB, respectively, but without significant differences.

Comparative characteristics of anthropometric parameters in newborns of the study groups are presented in *Table*.

Taking into account the Apgar score of newborns, certain features of the respective observation Groups were noted. Thus, the average score in newborns of Group I was [4.20±1.11] points at the 1st minute, [5.52±1.12] points at the 5th minute; in infants of Subgroup IIA – [5.34±1.07] points and [6.56±0.78] points, respectively, Subgroup IIB – [6.17±0.74] and [6.85±0.32] points; in infants of Subgroup IIIA – respectively [5.44± ±1.29] and [6.54±0.71] points, Subgroup IIIB – [6.53±0.70] and [6.68±0.72] points with control indicators in newborns of Group IV, respectively [6.85±0.24] points and [8.32±0.35] points ($p_{I,IIA,IIB,IIIA,IIIB:IV}<0.0001$ at 1 and 5 min; $p_{IIA:IIIA}<0.0001$ at 1 min; $p_{I:IIA,IIIA}<0.0001$ at 5 min). Among all infants, 39 (72.22%) infants of Group I, 46 (68.66%) infants of Subgroup IIA, and 21 (51.22%) infants of Subgroup IIIA required the greatest volume of resuscitation measures to stabilise their condition after birth ($p_{I:IIIA}<0.05$).

Among the 355 newborns included in the study programme: 54 (100.00%) infants of Group I; 67 (44.97%) infants of Group II; and 41 (40.20%) infants of Group III (40.20%) had severe forms of perinatal pathology, according to gestational age, $p_{I:II}<0.0001$, OR 55.03%; 95% CI 44.62–62.79; $p_{I:III}<0.0001$, OR 59.8%; 95% CI 48.04–68.79).

It should be noted that most infants in Group I, who had significant severity of the condition at birth, were diagnosed with asphyxia – 32 (59.26%) cases, which was accompanied by Respiratory Distress Syndrome (RDS). A significant number of newborns in Group I had primary pulmonary atelectasis – 50 (92.59%) cases and hyaline membrane disease – 38 (70.37%) cases. In addition, a significant number of newborns in this Group had Multiple Organ Dysfunction Syndrome (MODS), which manifested itself in all 54 (100.00%) cases with Central Nervous System (CNS) and Respiratory System (RS) lesions, in 16 (29.63%) cases – CardioVascular System (CVS); haemorrhagic and convulsive syndrome was noted in 17 (31.48%) cases, 14 (25.93%) infants had Disseminated Intravascular Coagulation (DIC) syndrome, 15 (27.78%) infants had the anaemic

Table. Anthropometric parameters in newborns of the observation Groups (n, %)

Indicator	Group I, 26–31/6 weeks (n=54)	Group II, 32–33/6 weeks Subgroup IIA (n=67)	Group II, 32–33/6 weeks Subgroup IIB (n=82)	Group III, 34–36/6 weeks Subgroup IIIA (n=41)	Group III, 34–36/6 weeks Subgroup IIIB (n=61)	Group IV, 34–36/6 weeks (n=50)
Body weight (g)	1314.66± ±176.15*##	1776.49± ±241.13*+	1837.91± ±162.91*	2132.99± ±341.03	2145.82± ±334.17	2347.60± ±173.55
Body length (cm)	39.80±2.81*	42.85±1.97*	43.66±1.59*	44.30±2.14*	46.19±7.14	45.88±0.44
Head circumference (cm)	27.66±1.67*	29.80±1.85*	30.22±1.39*	31.79±3.10	31.34±1.48	32.00±1.11
Chest circumference (cm)	25.73±1.98*	27.44±1.91*	27.61±1.62*	28.71±1.65	29.14±1.95	29.85±1.44

Notes: p-values were adjusted using the Bonferroni correction;
* – statistically significant difference compared to the control Group, $p<0.01$;
# – statistically significant differences between Group I and Subgroup IIA, Group I and Subgroup IIIA, $p<0.017$;
+ – statistically significant differences between Subgroup IIA and Subgroup IIIA, $p<0.017$.

syndrome. Signs of food tolerance disorders, taking into account the main objective of the study, were observed in the PTIs of all observation Groups, respectively. Among newborns in Group I, compared with Subgroups IIA and IIIA, there was significantly more infants born prematurely – 19 (35.19%). In newborns of Subgroup IIA, compared with Subgroup IIIA, subependymal haemorrhage of grade I was diagnosed more often – 24 (35.82%) cases; a significantly higher number of infants had CNS lesions in the complex of MODS – 29 (43.36%) cases.

The development of severe forms of perinatal pathology in PTI, the clinical signs of which, among other things, were disorders of the functional state of the GIS, was statistically significantly associated with the following factors: gestational age at birth ($p_{I:IV}<0.0001$, OR 55.03%; 95% CI 41.44–66.34; $p_{IIA:IV}<0.0001$, OR 59.80%; 95% CI 43.20–73.34); low birth weight ($p_{I:IIA}<0.0001$, 461.83±39.25; 95% CI 384.11–539.55; $p_{I:IIIA}<0.0001$, 818.3±53.90; 95% CI 711.30–925.36; $p_{IIA:IIIA}<0.0001$, 356.50±56.114, 95% CI 245.25–467.75).

Taking into account the gestational age at birth, the severe condition of the PTI was determined: RDS against the background of severe asphyxia ($p_{I:IIA}<0.0001$, OR 56.72%; 95% CI 43.09–67.90; $p_{I:IIIA}<0.0001$, OR 48.78%; 95% CI 32.81–63.52); primary pulmonary atelectasis ($p_{I:IIA}<0.0001$, OR 58.21%; 95% CI 39.85–71.61); hyaline membrane disease ($p_{I:IIA}<0.0001$, OR 34.55%; 95% CI 16.74–49.34); MODS in the presence of CNS lesions ($p_{I:IIA}<0.0001$, OR 56.64%; 95% CI 43.01–67.83; $p_{I:IIIA}<0.0001$, OR 85.37%; 95% CI 70.05–93.12; $p_{IIA:IIIA}=0.0021$, OR 28.73%; 95% CI 10.96–42.94); RS ($p_{I:IIA}<0.0001$, OR 71.88%; 58.41–81.23; $p_{I:IIIA}<0.0001$, OR 73.17%; 95% CI 56.67–84.30); CVS ($p_{I:IIA}=0.0044$, OR 20.26%; 95% CI 6.21–34.35); US ($p_{I:IIA}=0.0178$, OR 20.20%; 95% CI 3.51–35.84; $p_{I:IIIA}=0.0084$, OR 25.52%; 95% CI 6.77–41.28); haemorrhagic syndrome ($p_{I:IIA}<0.0001$, OR 28.36%; 95% CI 15.31–41.81; $p_{I:IIIA}=0.0044$, OR 24.16 %; 95% CI 7.93–38.26); anaemic syndrome ($p_{I:IIA}=0.0001$, OR 24.66 %; 95% CI 12.14–37.96; $p_{I:IIIA}=0.0122$, OR 20.46 %; 95% CI 4.65–34.42); seizure syndrome ($p_{I:IIA}=0.0518$, OR 15.06 %; 95% CI 0.10–30.05); DIC syndrome ($p_{I:IIIA}=0.0069$, OR 21.05%; 95% CI 6.12–34.53).

A comparison of clinical pathology in newborns with moderate condition severity showed that significantly more infants in Subgroup IIB, compared to Group IIIB, had signs of asphyxia accompanied by moderate and mild respiratory disorders – 11 (13.41%) and 47 (57.31%) cases, respectively, as well as grade I extracardiac heart failure – 20 (24.39%) cases. Adaptation disorders in newborns of the IIIB Subgroup were mainly due to mild respiratory disorders – 16 (26.22%) cases. The diagnoses of MFI and low birth weight were also noteworthy – 4 (6.56%) and 10 (16.39%)

cases, respectively. The risk of developing a ventilator-associated tracheobronchitis at birth in infants of Subgroups IIB and IIIB was 20 (24.39%) and 13 (21.31%) cases.

Among the total number of newborns in Groups I–III, 46 (15.08%) had deterioration during the first week of life, accompanied by persistent metabolic disorders due to hypoxic damage against the background of morphological and functional immaturity. In our opinion, this confirms the fact that a purely clinical assessment of the adaptation of infants at birth using the Apgar score may not be sufficient to predict the risk of deterioration in the postnatal period.

The list of possible clinical and laboratory criteria for disorders of the functional state of the GIS in newborns is actively discussed in modern scientific sources. It is noted that there is currently no generalised list of criteria for FI in newborns, including those with PTI. The recommended list of clinical signs of digestive dysfunction in newborns includes an increase in residual stomach volume, vomiting, abdominal meteorism, and blood in the stool [18]. In our opinion, the formation of disorders of the functional state of the GIS at preterm birth has certain features, taking into account the degree of the body's MFI, given the severity of the course of perinatal pathology and the body's reserve capacity during the formation of short-term and long-term adaptation in the postnatal period of development.

The results of the analysis of published scientific sources indicate some discrepancies in the recommendations for the assessment of signs of FI in newborns, in particular in PTI. For example, the results of a multicentre randomised trial published in 2002 show that the colour of gastric residues in preterm infants is not always a confirmation of FI [19]. The guidelines for feeding very low birth weight infants state that the yellow or green colour of residual gastric volume alone is not appropriate as a guide for diagnosing FI and that abdominal circumference measurement is not appropriate for diagnosing FI. According to the latest published sources, signs of food intolerance in PTI are manifested by an increase in Total Gastric Volume of more than 50% of the previous feeding volume, accompanied by vomiting and/or meteorism, as well as the detection of blood in the stool [20].

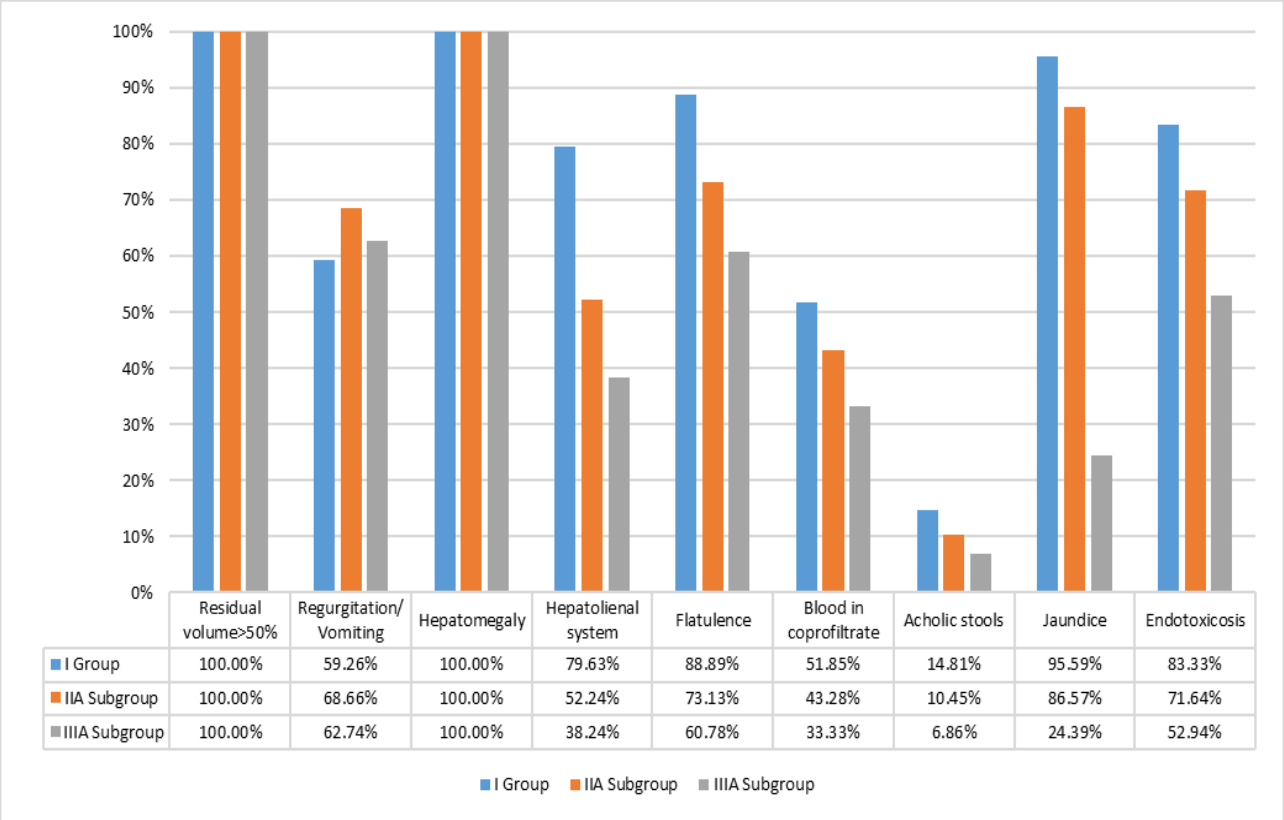
The research paper set the task of clarifying the list of clinical signs of FI in PTI, taking into account the severity of perinatal pathology and gestational age at birth.

Comparative characteristics of the frequency of clinical manifestations of FI in the PTI observation Groups with severe perinatal pathology are shown in *Fig. 1*.

The analysis of the clinical manifestations of FI, which was confirmed by a residual volume of more than 50%, showed the presence of disorders in newborns of all observation Groups, with the percentage of signs having some differences taking into account the gestational age of infants, in particular: regurgitation/vomiting – in Group I 32 (59.26%) cases, in Subgroup IIA – 46 (68.66%) cases, in Subgroup IIIA – 25 (60.98%) cases ($p>0.05$); an increase in liver size more than the physiological norm was noted in infants of all observation Groups – up to 100.00% ($p>0.05$); hepatolienal syndrome – 43 (79.63%) cases in Group I, 35 (52.24%) cases in Subgroup IIA, and 39 (38.24%) cases in Subgroup IIIA ($p_{I:IIA}=0.0018$; OR 27.39%; 95% CI 10.37–41.95; $p_{I:IIIA}<0.0001$; OR 41.39%; 95% CI 21.64–57.19); intestinal meteorism was significantly more common in infants of younger gestational age – 48 (88.89%) cases in Group I, 49 (73.13%) cases in Subgroup IIA and 62 (60.78%) cases in Subgroup IIIA ($p_{I:IIA}=0.0314$; OR 15.76%; 95% CI 1.39–28.83; $p_{I:IIIA}=0.0014$; OR 28.11%; 95% CI 10.72–44.46); blood impurities in coprofiltrate – 28 (51.85%) cases in Group I, 29 (43.28%) cases in Subgroup IIA and 34 (33.33%) cases in Subgroup IIIA ($p>0.05$); acholic stools – 8 (14.81%) cases in Group I, 7 (10.45%) cases in Subgroup IIA and 7 (6.86%) cases in IIIA Subgroup ($p>0.05$); jaundice – 50 (95.59%) cases in Group I, 58 (86.57%) cases in IIA Subgroup, 10 (24.39%) cases in IIIA Subgroup ($p_{I:IIIA}<0.0001$; OR 71.20%; 95% CI 53.68–82.20); endotoxaemia syndrome – respectively 45 (83.33%) cases in Group I, 48 (71.64%) cases in Subgroup IIA and 54 (52.94%) cases in Subgroup IIIA ($p_{I:IIIA}=0.0014$; OR 30.39%; 95% CI 11.63–47.10; $\chi^2=10.183$).

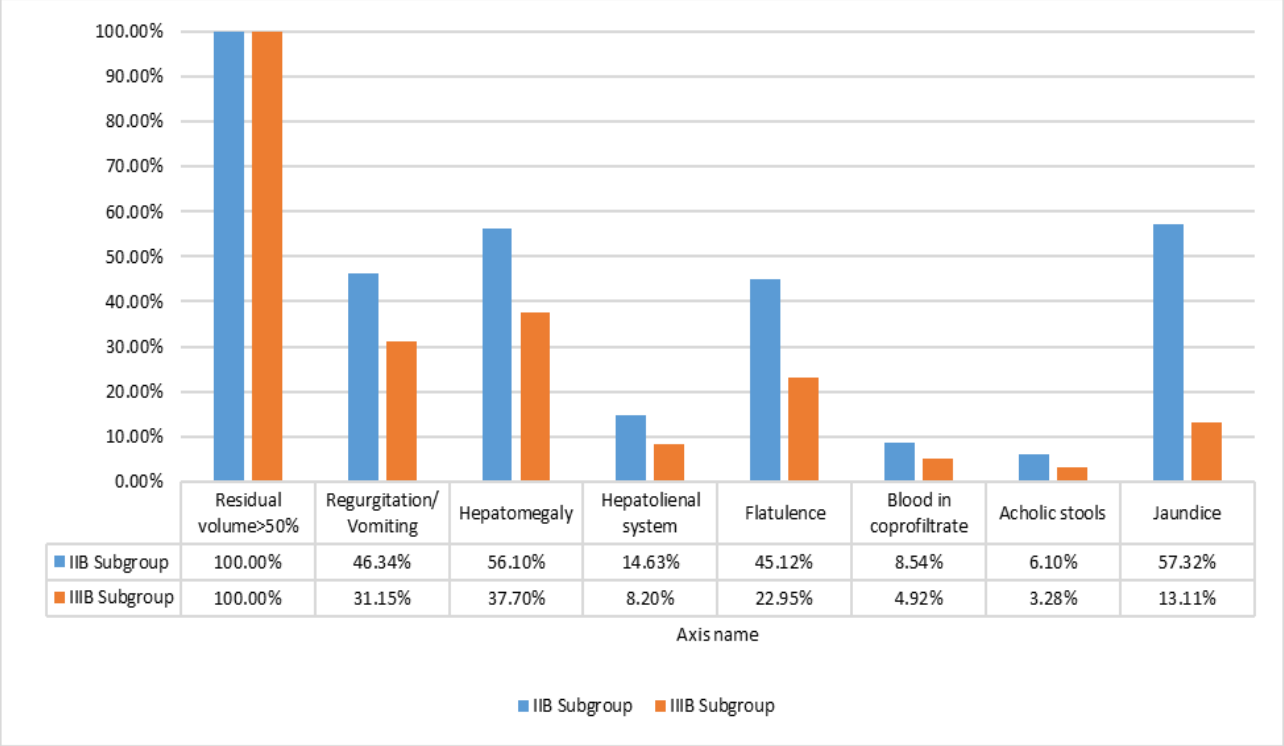
The results of the analysis showed that the incidence of clinical manifestations of FI tended to increase in correlation with a decrease in the gestational age of the PTI according to the entire list of these criteria.

Compared with PTI who had a severe condition due to perinatal pathology, a quantitatively lower percentage of clinical manifestations of FI was observed in newborns with moderate severity of the condition, but there was a tendency for their higher frequency at a lower gestational age of newborns (*Fig. 2*).



	Residual volume>50%	Regurgitation/ Vomiting	Hepatomegaly	Hepatolienal system	Flatulence	Blood in coprofiltrate	Acholic stools	Jaundice	Endotoxicosis
I Group	100.00%	59.26%	100.00%	79.63%	88.89%	51.85%	14.81%	95.59%	83.33%
IIA Subgroup	100.00%	68.66%	100.00%	52.24%	73.13%	43.28%	10.45%	86.57%	71.64%
IIIA Subgroup	100.00%	62.74%	100.00%	38.24%	60.78%	33.33%	6.86%	24.39%	52.94%

Fig.1. Comparative characteristics of clinical manifestations of FI in the PTI observation Groups with severe perinatal pathology.



	Residual volume>50%	Regurgitation/ Vomiting	Hepatomegaly	Hepatolienal system	Flatulence	Blood in coprofiltrate	Acholic stools	Jaundice
IIB Subgroup	100.00%	46.34%	56.10%	14.63%	45.12%	8.54%	6.10%	57.32%
IIIB Subgroup	100.00%	31.15%	37.70%	8.20%	22.95%	4.92%	3.28%	13.11%

Fig. 2. Comparative characteristics of the frequency of clinical manifestations of FI in the PTI observation Groups with moderate perinatal pathology.

Comparison of the results of the analysis of clinical manifestations of FI in newborns of IIB and IIIB Subgroups showed that all infants had a residual volume of more than 50%, but the percentage of other signs still prevailed at a lower gestational age – respectively, in Subgroup IIB compared to Subgroup IIIB. The following was noteworthy: regurgitation/vomiting was observed in infants of Subgroup IIB in 38 (46.34%) cases, in Subgroup IIIB – in 19 (31.15% of cases ($p>0.05$); increase in liver size compared to the physiological norm – 46 (56.10%) and 23 (37.70%) in infants of Subgroup IIB and Subgroup IIIB ($p_{IIB:IIIB}=0.0300$; OR 18.4%; 95% CI 1.86–33.49); hepatolienal syndrome was diagnosed in 12 (14.46%) and 5 (8.20%) cases, respectively, in Subgroup IIB and Subgroup IIIB ($p>0.05$); intestinal meteorism – in 37 (45.12%) and 14 (22.95%) cases in IIB and IIIB Subgroups, respectively ($p_{IIB:IIIB}=0.0064$; OR 22.17%; 95% CI 6.38–36.03); blood impurities in coprofiltrate were detected in 7 (8.54%) and 3 (4.92%) infants of Subgroup IIB and Subgroup IIIB ($p>0.05$); acholic stools were observed in 5 (6.10%) and 2 (3.28%) cases in newborns of Subgroup IIB and Subgroup IIIB, respectively ($p>0.05$); jaundice was detected in 47 (57.32%) and 8 (13.11%) cases in infants of Subgroup IIB and Subgroup IIIB, respectively ($p_{IIB:IIIB}<0.0001$; OR 44.21%; 95% CI 29.09–56.14).

The analysis of statistical data on the frequency of detection of clinical signs of digestive dysfunction in PTI of the corresponding gestational age at birth showed a significantly higher percentage of them in severe perinatal pathology compared to the average severity of the condition. Quantitative characterization of regurgitation/vomiting cases confirmed a significantly higher frequency in infants of Subgroup IIA compared to Subgroup IIB ($p_{IIA:IIB}=0.0065$; OR 22.32%; 95% CI 6.33–36.63), and also, Subgroup IIIA compared to the Subgroup IIIB (pIIIA:IIIB=0.0017; OR 31.59%; 95% CI 11.88–48.20); an increase in liver size compared to the physiological norm was more often detected in severe neonatal condition – respectively, 100.00% of cases in newborns of Subgroup IIA and Subgroup IIIA compared to the detected frequency in Subgroup IIB and Subgroup IIIB ($p_{IIA:IIB}<0.0001$; OR 43.90%; 95% CI 32.32–54.70; $p_{IIIA:IIIB}<0.0001$; OR 62.3%; 95% CI 47.11–73.38); hepatolienal syndrome was also detected in a significantly higher percentage of cases in newborns with severe condition compared to those whose condition was considered as moderate ($p_{IIA:IIB}<0.0001$; OR 37.61%; 95% CI 22.67–50.62; $p_{IIIA:IIIB}=0.0002$; OR 30.04%; 95% CI 13.68–45.99); clinical manifestations of intestinal flatulence were significantly more frequent in infants of Subgroup IIA and Subgroup IIIA compared to Subgroup IIB and Subgroup IIIB ($p_{IIA:IIB}=0.0015$; OR 26.01%; 95% CI 0.08–40.01; $p_{IIIA:IIIB}=0.0001$; OR 37.87%; 95% CI 18.50–53.87); in severe condition, blood impurities in the coprofiltrate were detected relatively more often in newborns ($p_{IIA:IIB}<0.0001$; OR 34.74%; 95% CI 20.96–47.41; $p_{IIIA:IIIB}= 0.0002$; OR 28.41%; 95% CI 13.30–44.05); the frequency of jaundice was higher in PTI with severe forms of perinatal pathology ($p_{IIA:IIB}=0.0001$; OR 29.25%; 95% CI 14.89–41.70).

Conclusion

Analysis of the data from clinical examination of newborns confirms the possibility of using an expanded list of criteria for the diagnosis of food intolerance in newborns in the presence of perinatal pathology, which includes: residual food volume of more than 50%, regurgitation and/or vomiting, increased liver size above the physiological norm or hepatolienal syndrome, intestinal flatulence, blood impurities in coprofiltrate, acholic stools, jaundice and endotoxemia syndrome.

DECLARATIONS:

Prospects for further research.

For a more precise diagnosis of gastrointestinal system dysfunction in preterm infants, an integrated approach is advisable, which allows the use of additional laboratory methods in addition to clinical ones.

Statement of ethics.

The authors have no ethical conflicts to disclose.

Data transparency.

Data can be requested from the authors.

Sources of funding.

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Consent to publication.

All authors consent to publication.

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