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V.P. Prytula[1,2], O.O. Kurtash[3], V.F. Rybalchenko[4], S.F. Hussaini[1,2]

Clinical features of the course of Hirschsprung's disease in newborns and infants with consideration of the extent of colonic aganglionosis

[1]Bogomolets National Medical University, Kyiv, Ukraine
[2]National Children's Specialized Hospital «OKHMATDYT», Kyiv, Ukraine
[3]Ivano-Frankivsk National Medical University, Ukraine
[4]Shupyk National Healthcare University of Ukraine, Kyiv, Ukraine

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The clinical course of Hirschsprung's disease (HD) in newborns and infants depends on the extent of colonic aganglionosis, the age of patient, the presence of associated malformations and complications.

The aim — to study the peculiarities of the clinical course of HD in newborns and infants.

Materials and methods. An analysis of the clinical course of HD in 483 in newborns and infants. There were 100 (20.71%) patients with the rectal, 192 (39.75%) with rectosigmoid, 150 (31.05%) with subtotal, and 41 (8.49%) with total form of HD. 98 (20.29%) patients were found to have associated malformations.

Results. 64 (13.25%) patients with a rectal form, 72 (14.91%) — with rectosigmoid, 150 (31.05%) — with subtotal, and 41 (8.49%) with total form had an acute clinical course and subacute clinical course was observed in 36 (7.45%) patients with rectal and 120 (24.85%) with rectosigmoid forms of HD. 327 (67.70%) infants with HD were diagnosed with varying degrees of hypotrophy, 315 (65.22%) had HD-associated enterocolitis, 16 (3.31%) had toxic megacolon, and 241 (49.89%) patients had varying degrees of anemia.

Conclusions. In the presence of associated malformations in newborns and infants, in 8.07% of cases, clinical symptoms may prevail over the classic signs of HD. The severity of the course and late diagnosis are the main reasons for the appearance of severe complications of HD in newborns and infants — hypotrophy (67.70%), HD-associated enterocolitis (65.22%), toxic megacolon (3.31%) and anemia (49.89%).

The research was carried out in accordance with the principles of the Declaration of Helsinki. The research protocol was approved by the Local Ethics Committee of all institutions mentioned in the work. Informed consent of the children's parents was obtained for the research.

No conflict of interests was declared by the authors.

Keywords: Hirschsprung's disease, children, enterocolitis, anemia, hypotrophy, associated malformations.

Особливості клінічної картини хвороби Гіршпрунга в новонароджених і дітей грудного віку з урахуванням протяжності аганглiонозу

В.П. Притула[1,2], О.О. Курташ[3], В.Ф. Рибальченко[4], С.Ф. Хуссейні[1,2]
[1]Національний медичний університет імені О.О. Богомольця, м. Київ, Україна
[2]Національна дитяча спеціалізована лікарня «ОХМАТДИТ», м. Київ, Україна
[3]Івано-Франківський національний медичний університет, Україна
[4]Національний університет охорони здоров'я України імені П.Л. Шупика, м. Київ

Клінічний перебіг хвороби Гіршпрунга (ХГ) у новонароджених і дітей грудного віку залежить від протяжності аганглiонозу, віку пацієнта, наявності супутніх вад розвитку та ускладнень.

Мета — дослідити особливості клінічного перебігу ХГ у новонароджених і дітей грудного віку.

Матеріали та методи. Проаналізовано клінічний перебіг ХГ у 483 дітей першого року життя. З ректальною формою ХГ було 100 (20,71%) пацієнтів, із ректосигмоподібною — 192 (39,75%), із субтотальною — 150 (31,05%), із тотальною — 41 (8,49%) дитина. У 98 (20,29%) пацієнтів виявлено супутні вади розвитку.

Результати. Гостру форму клінічного перебігу ХГ мали 64 (13,25%) пацієнти з ректальною формою аганглiонозу, 72 (14,91%) — із ректосигмоподібною, 150 (31,05%) — із субтотальною, 41 (8,49%) — із тотальною формою аганглiонозу. Підгостру форму клінічного перебігу ХГ мали 36 (7,45%) пацієнтів із ректальною та 120 (24,85%) дітей із ректосигмоподібною формами аганглiонозу. У 327 (67,70%) дітей першого року життя з ХГ діагностовано різного ступеня гіпотрофію, у 315 (65,22%) — ентероколіт, асоційований з ХГ (ЕКАХГ), у 16 (3,31%) — токсичний мегаколон, а у 241 (49,89%) пацієнта — різного ступеня анемію.

Висновки. За наявності супутніх вад розвитку в дітей першого року життя клінічна симптоматика у 8,07% випадків може превалювати над класичними ознаками ХГ. Гострота перебігу та запізніла діагностика є основними причинами появи тяжких ускладнень ХГ у дітей першого року життя — ентероколіт, асоційований з ХГ (65,22%), токсичний мегаколон (3,31%) та анемія (49,89%).

Дослідження виконано відповідно до принципів Гельсінської декларації. Протокол дослідження ухвалено Локальним етичним комітетом зазначених у роботі установ. На проведення досліджень отримано інформовану згоду батьків дітей.

Автори заявляють про відсутність конфлікту інтересів.

Ключові слова: хвороба Гіршпрунга, діти, ентероколіт, анемія, гіпотрофія, супутні вади розвитку.

Introduction

Hirschsprung's disease (HD) or colonic aganglionosis (CA) belongs to a group of complex malformations that is usually diagnosed shortly after birth due to the absence of meconium within 24 hours of life. In addition, the main clinical manifestations include abdominal distension, vomiting of stagnant gastric and intestinal contents, leading to the development of enteric insufficiency, anemia and hypotrophy [1,3]. The form of HD varies depending upon the extent of colon affected by the CA, which can be divided as short segment that effects the rectum and sigmoid colon in 75%–80%, the long segment that effects the sigmoid colon and part of proximal colon in 10% to 15%, and the total aganglionosis where entire colon is effected in 5–7% of cases [2,9].

The presence of different anatomical forms of HD and clinical course of their manifestation leads to the fact that in some patients with HD are not diagnosed in time in the neonatal period, until the development of complications [1–3,16].

In addition, according to the data of various researchers, in some patients (up to 15–20%), clinical course of HD is significantly affected if it is associated with other malformations [10].

The most serious complications of HD is HD-associated enterocolitis (HAEC) and toxic megacolon (TM), which are diagnosed in 57% to 68%, depending on the extent of CA and the patient's condition at the time of hospitalization [9,15]. According to various data these complications are the cause of further development of sepsis, organ and multi-organ failure with fatal consequences, which currently range from 5% to 50% [4,8,9,11,15].

Therefore, early detection of clinical symptoms of HD in newborns and infants, taking into account the extent of CA and the association with developmental malformations, determine the relevance of this study.

The aim of the research — to study the peculiarities of the clinical course of HD in newborns and infants and to determine the significance of clinical symptoms for the early detection and verification of this pathology.

Materials and methods of the study

From 1980 to 2021, at the pediatric surgery department of the Bogomolets National Medical University based at the National Children's Specialized Hospital «OKHMATDYT» and in the pediatric surgery department of the Ivano-Frankivsk National Medical University based at Ivano-Frankivsk Regional Children's Clinical Hospital, 483 infants with HD were examined and treated — 389 (80.54%) boys and 94 (19.46%) girls. Among them, 100 (20.71%) patients had rectal form, 192 (39.75%) had rectosigmoid form, 150 (31.05%) had subtotal form and 41 (8.49%) had total form of HD. Among the infants hospitalized 280 (57.97%) were under the age of 6 months, and 203 (42.03%) were between the ages of 7 months to 1 year.

We performed a retrospective analysis of the clinical course of HD in newborns and infants, taking into account the extent of CA and to determine the significance of clinical symptoms for early detection and verification of this pathology.

To study the clinical course, we considered the anamnesis, physical examination, data of general clinical laboratory indicators of blood and urine, and coprological, microbiological examination of feces, electrocardiography (ECG), neurosonography (NSG), echocardiography, ultrasound (US) of the abdominal cavity and retroperitoneal space, X-ray of the chest and abdominal cavity.

The research was carried out in accordance with the principles of the Declaration of Helsinki. The research protocol was approved by the Local Ethics Committee of all institutions mentioned in the work. Informed consent of parents and children was obtained for conducting research.

Results of the study

When studying the features of the clinical course of various forms of HD in infants, first of all, the family status was investigated. Careful study of the anamnesis established that 436 (90.27%) patients had full families, and 47 (9.73%) — incomplete families.Mothers age above 40 was noted in 87 (18.01%) cases. The first child in the family was in 196 (40.58%) cases, the second — in 162 (33.54%), the third — in 107 (22.15%), the fourth and more — in 18 (3.73%) cases. In 36 (7.45%) cases assisted reproductive technology was used to conceive a child. In 185 (38.30%) pregnant women were exposed to harmful working conditions (chemical industry and others) and 93 (19.25%) pregnant women lived in environmentally polluted areas, and we found 24 (4.97%) families. had hereditary succession of HD (parents and brothers and sisters).

The study of the course of pregnancy as per hydramnios showed in 94 (19.46%) cases had hypohydramnios, and in 76 (15.73%) — polyhydramnios. The course of pregnancy was accompanied by: various degrees of anemia — in 204 (42.24%), acute respiratory viral infection — in 182 (37.68%), various degrees of preeclampsia in — 97 (20.08%), urogenital infection in 72 (14.91%), bleeding in — 35 (7.25%). Mode of delivery was Natural in 429 (88.82%), Caesarean section — in 54 (11.18%). According to the gestation period, 471 (97.51%) patients were full-term, and 12 (2.49%) were premature.

The first clinical features and course of different forms of HD in newborns and infants at the time of hospitalization significantly depended on the extent of CA (Table 1) Research has established that 39 (8.07%) patients were hospitalized during the first and the second day after birth. The main reasons for hospitalization of these infants were associated malformations: like esophageal atresia —

Table 1

The age of hospitalization of newborns and infants with Hirschsprung's disease to surgical departments

Age of patients	Total	The extent of CA			
		Rectal HD	Recto-sigmoid HD	Subtotal HD	Total HD
1–2 days	39*	–	2*	27*	10*
1st month	58	5	20	22	11
2nd month	39	3	10	12	14
3rd month	43	1	17	19	6
4th month	35	1	11	23	–
5th month	34	1	15	18	–
6th month	32	3	17	12	–
7th month	43	8	31	4	–
8th month	41	11	26	4	–
9th month	28	13	12	3	–
10th month	21	7	12	2	–
11th month	31	18	10	3	–
12th month	39	29	9	1	–
All Together:	483 (100%)	100 (20.70%)	192 (39.75%)	150 (31.06%)	41 (8.49%)

Note: * — associated malformations that prevailed in the clinical course.

Table 2

Associated congenital malformations in patients with Hirschsprung's disease

Associated congenital malformations	Number	%
Meckel's diverticulum	5	1.03
Congenital heart defects	18	3.73
Cleft of the hard and soft palate	9	1.86
Pylorostenosis	12	2.48
Microcephaly	4	0.83
Hydronephrosis	5	1.03
Other kidney malformations	2	0.42
Atresia of the colon	15	3.10
Colonic atresia and gastroschisis	3	0.62
Atresia of the ileum	9	1.86
Esophageal atresia	3	0.62
Internal abdominal hernia	2	0.42
Incomplete bowel movement	10	2.07
Ovarian cyst	1	0.21
Total	98	20.29

in 3 (0.62%), gastroschisis and intestinal atresia — in 3 (0.62%), colon and ileal atresia — in 24 (4.96%), cleft of the hard and soft palate — in 9 (1.86%). The clinical symptoms of associated malformations in these patients prevailed over the symptoms of HD from the first days of life, which led to their early hospitalization to surgical clinics.

In addition, during the first and second week of life, 31 (6.42%) patients were hospitalized due to lack of bowel movements and defecation. At 3–4 weeks of life, 27 (5.59%) patients were hospitalized with complaints of lack of defecation and vomiting of curdled milk, of which 12 (2.48%) cases were diagnosed with pylorostenosis, and 15 (3.11%) — pylorospasm.

The clinical course of forms of HD largely depended on the presence of associated developmental defects. Table 2 presents the quantitative characteristics of newborns and infants with HD with associated developmental defects.

All newborns and infants with HD had a delay in the passage of meconium of 48 hours or more. However, in the presence of associated developmental defects, some specific clinical symptoms, which are characteristic of each of the associated developmental defects, prevailed over HD symptoms.

Thus, in 3 (0.62%) patients with esophageal atresia, the picture of aspiration syndrome appeared first, and in 27 (5.58%) children with

Table 3

Distribution on the form of Hirschsprung's disease and the development of clinical manifestations ailments and complications

Clinical manifestation of the disease	Age of patients								Total
	0-6 months				7–12 months				
	1	2	3	4	1	2	3	4	
Absence of the meconium more than 24 hours after birth	39	98	102	41	61	94	48	–	483
Abdominal distension	39	87	86	29	61	94	48	–	444
with contouring of intestinal loops on the abdominal wall	–	11*	16*	12*	–	–	–	–	39*
Delay in physiological weight gain due to alimentary insufficiency (hypotrophy).	34	45	85	41	20	41	61	–	327
Vomits at the beginning of the illness	39	87	86	29	61	94	48	–	417
with stagnant contents, over time green, and	1**	2**	5**	4**	–	–	–	–	12**
with prolonged brown vomiting	3***	3***	4***	5***	–	–	–	–	15***
There is no physiological bowel movements, and when the colonic catheter is inserted in anus, there is an explosive emptying up to diarrhea.	18	50	–	–	51	49	–		168
Enterocolitis	21	48	102	41	10	45	48	–	315
Toxic megacolon	–	–	–	–	–	7	9	–	16
Anemia of various degrees	8	29	102	41	4	9	48		241
Total by groups:	280 (57.97%)				203 (42.03%)				

Notes: **1** — rectal form of HD, **2** — rectosigmoid form of HD, **3** — subtotal form of HD, **4** — total form of HD; * — accompanying malformations, ** — pylorostenosis, *** — pylorospasm.

different levels of intestinal atresia, signs of acute intestinal obstruction first appeared.

However, 9 (1.86%) patients had feeding problems associated with various types of hard and soft palate clefts. Kidney malformations were diagnosed in 7 (1.45%) patients, of which hydronephrosis — in 5 (1.03%) and other defects: hypoplasia of the right kidney and polycystic left kidney — in 2 (0.42%).we found associated cardiac malformations (atrial septal defect, ventricular septal defect, open oval window, and others) in patients 18 (3.73%).

To some extent, the manifestation of clinical symptoms was caused by the presence of microcephaly in 4 (0.83%) patients, which was manifested by impaired swallowing and coughing during eating.

We found intraoperative associated malformations like: Meckel's diverticulum in 5 (1.03%) and congenital cyst of the right ovary in 1 (0.21%) patient. In addition, the clinical course of various forms of aganglionosis at the examination stages was influenced by other associated malformations, namely: incomplete bowel rotation — in 10 (2.07%) children, and internal abdominal hernia — in 2 (0.42%) patients.

Studying the clinical course of HD in newborns and infants the dependence of the development of clinical manifestations of this pathology on the extent of CA and the development of complications was established (Table 3).

Research has established that 39 (8.07%) of 280 (57.97%) patients in the first 6 months of life did not have abdominal distension before contouring of the intestinal loops on the anterior abdominal wall due to Associated malformations: colonic atresia — in 15 (3.10%), atresia of the colon with gastroschisis — in 3 (0.62%), atresia of the ileum — in 9 (1.86%), atresia of the esophagus — in 3 (0.62%), cleft of the hard and soft palate in 9 (1.86%), and therefore had an atypical clinical picture in relation with different forms of aganglionosis. On the other hand, the other 241 (49.89%) among 280 patients under 6 months and 203 (42.03%) over 6 months had the classic pattern of abdominal distention from the contouring of intestinal loops on the anterior abdominal wall, and with the presence of malnutrition, the contouring was even more distinct, among the 27 (5.59%) patients who had vomiting with curdled milk, among them we found pyloric stenosis in 12 (2.48%), and pyloric spasm in 15 (3.11%).

All patients had a delay in physiological weight gain due to the nutritional insufficiency, however 327 (67.70%) had varying degrees of hypotrophy. The development of enteric insufficiency and hypotrophy were significantly influenced by Associated malformations of the digestive tract in 63 (13.04%) patients, of which 46 (9.53%) patients required surgery in the first weeks of life due to vital needs.

We had cleft of the hard and soft palate in 9 (1.86%) patients who had swallowing disorders, and as a result, enteral insufficiency developed, which required nasogastric tube

feeding for correction. Further violations of the passage through the intestines with the presence of stagnant contents in the stomach and constipation were the basis for further evaluation with contrast enema.

It was established that 417 (86.34%) infants with HD had stasis in the stomach and pathological vomiting, and 27 (5.59%) first curdled milk, in whom on further investigations we established — pylorostenosis in 12 (2.48%) and pylorospasm in 15 (3.11%). Studies have established that the appearance of stasis in the stomach in the presence of vomiting was correlated with the extent of CA and the presence of Associated malformations of the gastro intestinal tract in 63 (13.04%) patients. However, the appearance of the symptom depended in a certain way on the speed of filling the intestine with food and air. At first, the vomit was with stagnant gastric contents, and later, with greater filling of the stomach and duodenum, with bile admixtures, the color of which changed to green over time with stagnation. With a long-term violation of the passage, the vomit acquired a brown color with admixtures of small-intestinal or large-intestinal contents.

Independent physiological bowel movements were absent in all 483 patients. In addition, 383 (79.30%) patients had a violation of passing gases, which depended on the extent of CA, of which 41 (8.49%) had a total form, 150 (30.23%) had a subtotal form, and 192 (17.80%) had rectosigmoid form of HD. On the other hand, in 100 (11.18%) patients with rectal form, in 37 (7.66%), emptying (leakage) of feces and intestinal gases occurred after complete bowel filling and 63 (13.04%) required placement of colonic catheter for emptying of feces and gases. However, over time (7–11 days) the involuntary leakage came down. Progression of abdominal distension and lack of emptying required placement of colon catheter, and when the catheter was inserted into the anus, explosive emptying occurred up to diarrhea in 168 (34.78%). On the other hand, the lack of emptying and stasis in the intestine served as the cause of enterocolitis in 315 (65.22%), of which 16 (3.31%) further developed TM.

Usually, the normal body temperature in infants can be extremely labile under the influence of such factors as mental or emotional excitement, physical exertion, sleep, the nature of clothing and feeding. It is known that in case of HD, due to the presence of different extent of CA lesions, the transit of the food bolus is disturbed. Over time, stagnation appears in the lumen of the intestine with the development of putrefactive processes and intraintestinal hypertension, which leads to the translocation of toxins and microorganisms into the lymphatic and circulatory system, and as a result, the body reacts in the form of hyperthermia. Our research established the following indicators of body temperature in children, depending on the degree of complication of the HAEC disease and associated developmental defects. So, normal temperature is set (up to 37.0°C) in 168 (34.78%), subfebrile (37.1°C–38.0°C) — in 142 (29.40%); moderate febrile (38.1°C–39.0°C) in 94 (19.46%); highly febrile (39.1°C–41.0°C) — in 63 (13.04%) and hyperpyretic (more than 41.0°C) — in 16 (3.31%) who had TM. In 310 (64.18%) patients normal and subfebrile temperature was achieved after effective intestinal irrigation with adequate wash out the intestinal contents. On the other hand, in 157 (32.50%) with moderate to high febrile temperature, first attempt of intestinal irrigation had no effect and required further attempts, while intestinal distension progressed. In 16 (3.31%) patients with HAEC, further lead to TM due to obturation created by of the narrowed aganglionic colon due to the presence of a long form of aganglionosis which didn't allow us to wash out colon contents or to pass colonic catheter, and required more effective tactics — as emergency indications we imposed a protective colostomy in these patients.

The clinical course of HD in 315 (65.22%) infants was complicated by HAEC, and further in 16 (3.32%) by TM. Table 4 presents quantitative characteristics of patients on HAEC depending on the extent of CA lesion. HAEC was confirmed clinically by: swelling of the abdominal cavity; lack of emptying, and when the colonic catheter was placed, explosive emptying, like diarrhea; hyperthermia, which indicated an inflammatory process, and the temperature leukocytosis and anemia were normalized after washout of foul smelling intestinal stagnated contents with colonic catheter. During the coprological examination, the main indicators were the presence of leukocytes (32.53±2.18 in sight), erythrocytes (12.18±2.18 in sight) and mucus (in a significant amount). It is appropriate to point out that all patients had digestive disorders, and therefore had hypotrophy of various degrees, which was established in 327 (67.70%) patients.

Table 4

Correlation of the extent of colonic aganglionosis and the development of Hirschsprung's disease associated enterocolitis

Extent of CA	Total patients in the group	Total patients who had HAEC	Age	
			0–6 months	7–12 months
Rectal	100	31	21	10
Rectosigmoid	192	93	48	45
Subtotal	150	150	102	48
Total	41	41	41	–
Sum	483 (100%)	315 (65.22%)	212 (43.89%)	103 (21.33%)

Table 5

Correlation of the degree of severity of anemia in newborns and infants with Hirschsprung's disease

Extent of CA	Total patients in the group	Total patients who had anemia	Degree of severity of anemia		
			mild	moderate	severe
Rectal	100	12	2	9	1
Rectosigmoid	192	38	3	31	4
Subtotal	150	150	13	121	16
Total	41	41	3	30	8
Sum	483 (100%)	241 (49.89%)	21 (4.35%)	191 (39.54%)	29 (6.00%)

Clinical examinations and monitoring of laboratory tests during treatment revealed anemia in 241 (49.90%) of 483 infants with HD. Table 5 presents the quantitative characteristics of patients with different degrees of anemia and extent of CA. When determining the degree of anemia, the following indicators were used: mild anemia — hemoglobin level 110–90 g/l, erythrocyte count — up to 3.5×10^{12}/l; moderate anemia — hemoglobin level 90–70 g/l, erythrocyte count — up to 2.5×10^{12}/l; severe anemia — the hemoglobin level is less than 70 g/l, the number of erythrocyte count is less than 2.5×10^{12}/l. Regarding leukocytosis, moderate leukocytosis ($9–15\times10^{9}$/l) and high level of leukocytosis ($15–50\times10^{9}$/l) were distinguished [18].

When interpreting the obtained results, we took into account the fact that in 39 (8.07%) there were associated malformations, and in 30 (6.21%) patients the primary operations were due to esophageal atresia in 3 (0.62%), gastroschisis with colonic atresia in 3 (0.62%) and ileal and colonic atresia in 24 (4.96%) patients.

The study with hemoglobin and erythrocyte count indicated the following degree of anemia: mild in 21 (4.35%), moderate in 191 (39.54%), severe in 29 (6.00%). On the other hand, 242 (50.11%) patients had hemoglobin and erythrocyte count values within the normal range as per age. The degree of anemia in the study was correlated with the severity of the course of CA, or rather — with its extent and the development of HAEC in 315 (65.22%) patients, as well as the evaluation of various degrees of hypotrophy in 327 (67.70%). The study of the number of leukocytes also indicated that it was within the normal range in 168 (34.78%), moderate leukocytosis in 209 (43.27%), and high leukocytosis — in 106 (21.95%) patients. It was established that leukocytosis was also directly correlated with the severity of complications of aganglionosis — with HAEC and TM.

Clinical examinations and monitoring of physical data in 327 (67.70%) infants with HD revealed hypotrophy of various degrees of severity. The first degree had a body weight deficit of 10–20%, the second had 20–30%, and the third had more than 30%. A lag in body weight gains up to 10% was considered insignificant [16]. The first degree of hypotrophy was found in 89 (18.42%), the second — in 207 (42.86%) and the third — in 31 (6.42%) patients. Table 6 presents the quantitative characteristics of infants with HD with varying degrees of hypotrophy and extent of CA.

All 238 (49.28%) patients who had the second and third degree of hypotrophy previously had HAEC and enteric insufficiency. In 36 (7.45%) postponed operations for HD as associated malformations were corrected first due to vital needs, Thus, in the first two weeks of life, patients who underwent surgery for esophageal atresia in 3 (0.62%), small and large intestine atresia in 24 (4.96%), gastroschisis and colonic atresia had nutritional deficiency in the first two weeks of life, as well as internal intestinal hernia in 1 (0.21%) and incomplete bowel rotation in 6 (1.24%). In 12 (2.48%) patients, the cause

Table 6

Correlation of the extent of colonic aganglionosis and degree of hypotrophy

Extent of CA	Total patients	Degrees of hypotrophy			
		1	2	3	sum
Rectal	100	**27**	**21**	**6**	54 (11.18%)
Rectosigmoid	192	**20**	**56**	**10**	86 (17.80%)
Subtotal	150	**19**	**112**	**15**	146 (30.23%)
Total	41	**23**	**18**	–	41 (8.49%)
Sum	483 (100%)	89 (18.42%)	207 (42.86%)	31 (6.42%)	327 (67.70%)

of enteric insufficiency was pylorostenosis. Meanwhile, in the second month of life, 5 (1.03%) patients had a clinical presentation of small bowel obstruction, and the cause was internal intestinal hernia in 1 (0.21%) and incomplete bowel rotation in 4 (0.83%).

Thus, the clinical features of the course of HD in infants depends on the presence of associated malformations, identified in 63 (13.04%) patients. In the clinical picture of the disease, the main symptoms prevailed: the absence of meconium discharge and physiological emptying in 483 (100%) patients, abdominal distension and vomiting of stagnant gastric and intestinal contents — in 444 (91.93%), and in case of complications — the development of HAEC in 315 (65.22%), TM — in 16 (3.31%) and hyperthermia (moderate and high febrile body temperature) — in 173 (35.82%) cases. Enteric insufficiency and hypotrophy of various degrees of severity were complications in 327 (67.70%) patients, and anemia — in 241 (49.89%) cases.

It was established that the clinical course of HD differed depending on the extent of CA. 64 (13.25%) patients with rectal form, 72 (14.91%) patients with rectosigmoid form, 150 (31.05%) patients with subtotal and 41 (8.49%) children with total in the form of HD. 36 (7.45%) patients with rectal and 120 (24.85%) patients with rectosigmoid forms of HD had a subacute clinical manifestation. There was no chronic clinical course of HD in newborns and infants.

Discussion

Our research correlates with the data of review publications by E.M. Gershon et al. [6] and P.K. Frykman & S.S. Short [4], that there is a predominance of male patients over female patients with HD in newborns and infants with the ratio of 4:1.

The extent of CA varies from the lesion of a short segment involving the rectum and sigmoid colon in 75–80% of cases, total aganglionosis of the colon in 5–7%. From 10 to 15% we had aganglionosis extending proximal to the sigmoid colon, or subtotal aganglionosis which is also called «long segment disease» [6]. In our study the extent of CA was as follows: rectal form — in 11.18%, rectosigmoid form — in 17.80%, subtotal form — in 30.23%, total form — in 8.49%.

HD as an isolated malformation is diagnosed in 70% of patients, in combination with associated congenital malformations — in 18–20%, and in combination with chromosomal abnormalities — in 10–12% of cases. In a review publication, J. Amiel & S. Lyonnet indicate associated malformations of other organs and systems in 18% of patients, and in our study, these indicators were 20.29% [1].

According to H. Lampus, the hereditary succession (parents and children — brothers and sisters) of HD is from 5% to 20% [4,11]. According to our data, hereditary succession of HD was noted in 24 families, which was 4.97%.

HAEC is a severe and potentially fatal complication of HD. According to E.M. Gershon et al the frequency of HAEC ranges from 5% to 50% of cases [11]. HAEC can have different clinical manifestations, but usually presents as hyperthermia, intoxication, lethargy, hypovolemia, abdominal distension, foul smelling defecation, and explosive diarrhea, sometimes with blood. The mortality associated with HAEC according to various researchers ranges from 5% to 50%, with a higher prevalence and frequency in the neonatal period [7,8,10,14,15]. A widely approved method of providing emergency care for HD complicated with HAEC is the imposition of a protective intestinal stoma, as the first stage of surgical correction of HD [1,6,12,16]. In our study, HAEC was established in 315 (65.22%) patients, with no cases of mortality.

TM is one of the most severe and unpredictable complications of HD. According to R. Khasanov et al. [9] and S.R. Garg et al. [5] TM is defined as acute dilatation of the colon accompanied by clinical signs of toxemia. The leading symptoms of this complication are abdominal distension, con-

stipation, decreased intestinal motility, and intoxication symptoms such as hyperthermia, tachycardia, or hypotension, as well as radiologically confirmed distended bowel loops [4,8,17]. Our own research and data from the literature indicate that the most effective method of treatment while providing emergency care is the imposition of a protective intestinal stoma as the first stage of surgical correction of HD [2,3,12,13,18]. In our study, TM was diagnosed in 16 (3.31%) of 483 infants with HD.

The result of timely diagnosis and treatment of HD, regardless of the extent of CA and the development of complications (HAEC and TM), is indicator of mortality rate. In our study, all infants with HD who were admitted to clinics remained alive.

Thus, 444 (91.93%) infants with HD had a typical classic clinical picture of various extent of CA. At the same time, 39 (8.07%) patients had an atypical clinical picture, which was caused by associated developmental malformations, which prevailed in terms of the severity of the course at the time of hospitalization. In our clinical study, the causes of an atypical clinical picture for HD were colonic atresia — in 15 (3.10%), colonic atresia with gastroschisis — in 3 (0.62%), ileal atresia — in 9 (1.86%), esophageal atresia — in 3 (0.62%), cleft of hard and soft palate in 9 (1.86%). During the follow-up examination, HAEC occurred in 313 (65.22%) patients, of which 212 (75.71%) of 280 children were patients under 6 months of age. The severity of the course of HD in the presence of alimentary and enteric insufficiency, as well as with HAEC contributed to the development of hypotrophy in 327 (67.70%) and anemia in 241 (49.89%) patients.

Conclusions

The course and severity of the clinical picture of HD in newborns and infants depends on the extent of CA and the presence of associated malformations.

In the presence of associated malformations in newborns and infants, in 8.07% of cases, clinical symptoms may prevail over the classic signs of HD.

The severity of the course and late diagnosis are the main reasons for the appearance of severe complications of HD in newborns and infants: hypotrophy (67.70%), HAEC (65.22%), TM (3.31%) and varying degrees of anemia (49.89%).

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Відомості про авторів:
Притула Василь Петрович — д.мед.н., проф. каф. дитячої хірургії НМУ імені О.О. Богомольця. Адреса: м. Київ, вул. В. Чорновола, 28/1. https://orcid.org/0000-0001-9023-5898.
Курташ Олег Олегович — к.мед.н., доц., доц. каф. дитячої хірургії Івано-Франківського НМУ. Адреса: м. Івано-Франківськ, вул. Галицька, 2. https://orcid.org/0000-0003-0675-6952.
Рибальченко Василь Федорович —- д.мед.н., проф., проф. каф. дитячої хірургії, анестезіології, ортопедії та травматології НУОЗ України імені П. Л. Шупика. МОЗ України. Адреса: м. Київ, вул. Дорогожицька, 9. https://orcid.org/0000–0001–1872–6948.
Хуссейні Саед Файзула — к.мед.н., асистент каф. дитячої хірургії НМУ імені О.О. Богомольця. Адреса: м. Київ, вул. В. Чорновола, 28/1. https://orcid.org/0000-0001-6801-3092.
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