

RESEARCH ARTICLE

Analysis of the development of Hirschsprung-associated enterocolitis in children

Galymzhan Bauyrzhanovich Burayev¹, Vassiliy Mikhaylovich Lozovoy¹, Arturos Bronislavovich Kilda², Roza Agabekovna Karabekova¹, Elena Anatoliyevna Lozovaya¹, Medet Kurshirbayevich Khamitov¹, Kamshat Bauyrzhanovna Burayeva³

¹Department of Pediatric Surgery, Astana Medical University, Astana, Kazakhstan, ²Department of Pediatric surgery, Lithuanian University of Health Sciences, Kaunas, Lithuania, ³Department of Therapy, Akhmet Yassawi International Kazakh-Turkish University, Turkistan, Kazakhstan

Correspondence to: Galymzhan Bauyrzhanovich Burayev, E-mail: buraev.galymzhan@mail.ru

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ABSTRACT

Background: Hirschsprung disease (HD) - severe congenital anomaly of the colon, characterized by the violation of the innervation of the fragment, and even the entire department of the large intestine, is one of the leading places in the structure of the digestive tract pathology in children. **Aims and Objectives:** The research purpose is to carry out the retrospective analysis of the development of Hirschsprung-associated enterocolitis in children (HAEC). **Materials and Methods:** Despite the many different methods of surgical treatment and a significant improvement of results of surgical interventions, the rate of complications based on as large specialized hospitals and clinics with experience treating children with the HD, ranging from 22.7% to 38.5%. **Results:** Routinely in hospital hospitalized 140 patients, urgently - 22 children. HAEC symptoms occurred in 35 patients. The prevailing symptoms which were available for all 100% of patients were the unstable chair and meteorism; abdominal pains are slightly less often noted. **Conclusion:** The abdominal distention and unstable stool with a sequence of liquid stool with astrictions are the main symptoms of development of HAEC which are noted at all patients with this nosology.


KEY WORDS: Hirschsprung Disease; Hirschsprung-associated Enterocolitis; Retrospective Analysis; Pediatric Surgery

INTRODUCTION

For the first time, this disease was described in 1888 by the Danish pediatrician Harald Hirschsprung at 2 boys who died of chronic constipation. He included it in his hallmark description of congenital megacolon. Hirschsprung-associated enterocolitis in children (HAEC) is a condition of intestinal inflammation

characterized clinically by fever, abdominal distention, diarrhea, and sepsis. Hirschsprung also noted key pathologic findings of HAEC at autopsy; including crypt abscesses, mucosal ulceration, and transmural necrosis. Today HAEC is the leading cause of morbidity and is responsible for half of the deaths associated with Hirschsprung disease (HD). Despite many proposed etiologies, the biological mechanisms underlying HAEC are poorly understood. The number of patients with this pathology continues to increase also the frequency of diseases, according to most of the authors, makes 1 on 5000 newborns.^[1-3]

The main way of the treatment of HD is surgery, consisting at the resection of aganglionosis zone and partial removal of the changed site of the colon in a zone of prestenotic distensibility.^[4-6] Despite the many different methods of

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surgical treatment and a significant improvement of results of surgical interventions, the rate of complications based on as large specialized hospitals and clinics with experience treating children with the HD, ranging from 22.7% to 38.5%.^[7]

One of the most terrible complications after surgical treatment, is HAEC proceeding against the background of the expressed violation of local immune system in a gut wall, violations of the microbiocenosis with activation of the pathogenic microflora leading to disorder of microcirculation with the subsequent perforation of the gut wall and development of peritonitis.^[8-11] The sequela can develop both to, and after surgical treatment and is the most dangerous and life-threatening. Frequency of occurrence of the coloenteritis before operation fluctuates from 6% to 50% of cases while after the operation the frequency of occurrence of the coloenteritis varies from 2% to 35% of observations.^[12] Lack of correction of these violations brings into 10-15% of cases to sequelae in an anastomosis zone.^[13] The lethality remains high - 2.6-12.0%, especially in children of early age - 31-35% of patients.^[14-16]

The purpose of this study is to carry out the retrospective analysis of studying of Hirschprung-associated enterocolitis development in children.

MATERIALS AND METHODS

The age of children varied from 1 month to 15 years. There were 113 boys (69.7% of cases), girls - 49 children (30.2% of cases). The age and sexual structure of patients is presented in Table 1.

Primary diagnosis of HD is set in 139 patients (85.8% of cases). 23 child (14.2% of cases) has been reported with an established diagnosis.

Hospitalization in the clinic of earlier not examined patients was caused by the existence of the following main symptoms of the disease of girshprunga: Chronic constipation, vomiting, drum belly, and ileus clinic.

Statistical processing of results of the research it was carried out with use of the criterion of Pearson and Student's *t*-test by means of the software of biostatistics.

Table 1: Distribution of children by age and sex

Age/sex	n (%)		
	Boys	Girls	Total
1-6 months	24 (14.8)	12 (7.4)	36 (22.2)
6-12 months	20 (12.3)	11 (6.8)	31 (19.1)
1-3 years	33 (20.4)	10 (6.2)	43 (26.6)
3-6 years	26 (16)	11 (6.8)	37 (22.8)
6-11 years	7 (4.3)	4 (2.5)	11 (6.8)
Older than 11 years	3 (1.9)	1 (0.6)	4 (2.5)
Total	113 (69.7)	49 (30.2)	162 (100)

RESULTS

Routinely in hospital hospitalized 140 patients (86.4% of cases), urgently - 22 children (13.6% of cases). HAEC symptoms occurred in 35 patients (21.6% of cases). Due to these operations - in 11 children (6.8% of cases) in the period after the operation - in 24 cases (14.8% of patients). The frequency of occurrence of symptoms HAEC noted in Figure 1.

The prevailing symptoms which were available for all 100% of patients were the unstable chair and meteorism; abdominal pains are slightly less often noted.

The analysis indicated the prevalence of not ostomy patients - 110 people (67.9% of cases). At 52 children (32% of observations) in Municipal Children's Hospital No. 2, National scientific center of the maternity and the childhood and on to hospital stage (in other clinics) are imposed intestinal ostomies at the different levels of the intestinal tube (Figure 2). All children are operated with the use of various modifications of ways of surgical treatment.

Thus, in clinical work surgeons use imposing unloading sigmoidostomy and ileostomy more often.

Clinical signs of HAEC were observed at 19 children from total number 52 ostomy patients (36.5% of cases). Frequency of occurrence of HAEC depending on the level of imposing of intestinal ostomy is presented in Figure 3.

Follows from the provided drawing that in the postoperative period decrease in frequency of development of HAEC in all patients with an intestinal ostomy is observed. However, the results of statistical analysis showed that the dynamics of these indicators HAEC reduce the development of post-operative significant differences do not matter ($P > 0.05$).

In this group of patients had signs of HAEC in 12 patients (63.1% of cases) and after the imposition of the intestinal stoma.

The similar analysis is carried out at 110 patients of the patients treated without the use of imposing of unloading colostomy. Signs of HAEC were observed in 16 children (14.5% of observations). In the post-operative period, clinical signs of HAEC remained at 11 children - 68.7% of cases. Dynamics of patients' number decrease with HAEC before an operative measure is presented in Figure 4.

The influences of existence or lack of an ostomy on dynamics of the existence of HAEC given the comparative analysis are presented in Table 2.

Follows from the analysis of the drawing and the table that after expeditious treatment between groups there were distinctions in number of patients with HAEC, more

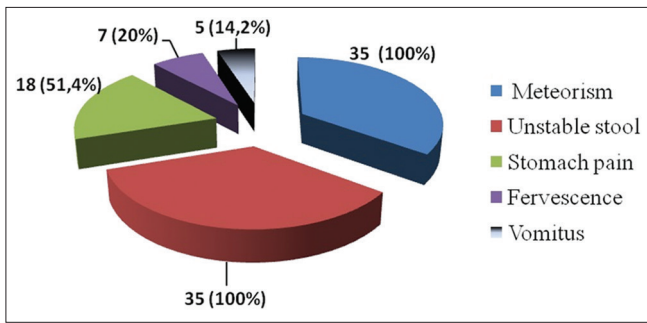


Figure 1: The frequency of clinical symptoms in Hirschsprung-associated enterocolitis in children

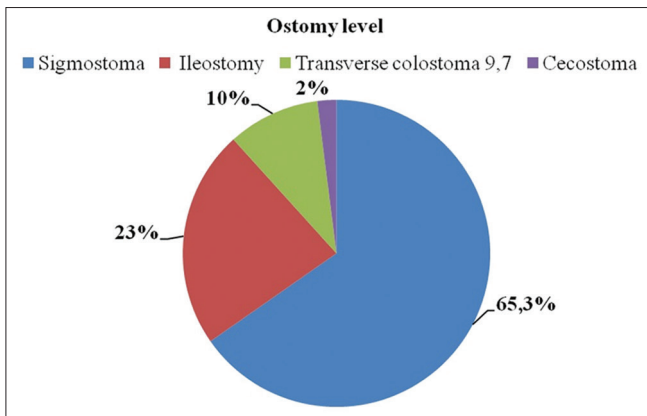


Figure 2: The distribution of ostomy patients the level of imposition of intestinal stoma

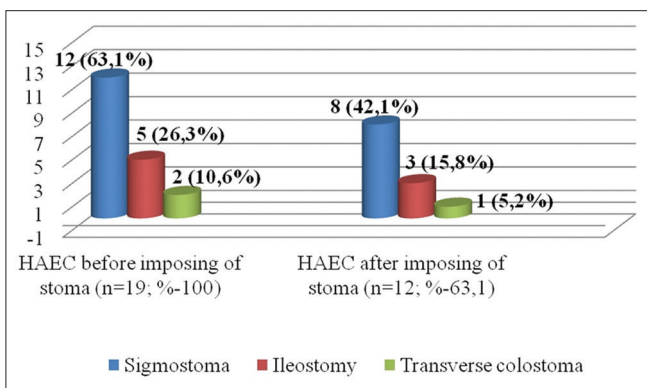


Figure 3: Frequency of occurrence of Hirschsprung-associated enterocolitis in children depending on the level of imposing of the intestinal ostomy

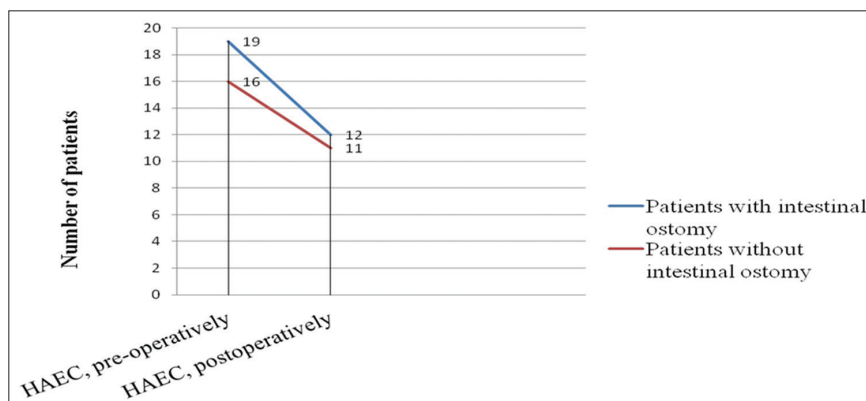


Figure 4: Dynamics of reducing the quantity of Hirschsprung-associated enterocolitis in children pre-operative and post-operative period

expressed decrease in number of patients with HAEC after operation in the ostomy group of patients in comparison with group of children without preliminary imposing of unloading ostomies was noted, however in the static analysis reliable distinctions of these indexes are not revealed ($P > 0.05$).

In the post-operative period at 52 (32% of cases) patients complications, the bound to the place an operative measure was observed. Such complications as a stenosis of the colorectal anastomosis zone, intestinal obstruction, peritonitis, intestinal fistula and others were more often noted. Moreover, complications associated with the place intestinal anastomosis (stenosis, insolvency) were more common in patients with HAEC, compared with patients without enterocolitis, in some cases, noted the repetition of the same complications (Table 3).

Follows from the analysis of data from the table that the most frequent complication in the post-operative period was the stenosis of colorectal anastomosis, and given complications more often developed at patients with HAEC in comparison with patients without coloenteritis ($P < 0.05$). By other types of complications in spite of the fact that, distinctions in absolute numbers on the frequency of development of complications were noted, at statistical analysis of reliable difference of these indexes is not revealed ($P > 0.05$).

The feces research on dysbacteriosis is conducted at 42 (25.9% of observations) patients. Decrease in a number of representatives intestines normoflor (bifidobacteria, lactobacilli, colibacillus with normal enzymatic activity, etc.) is more expressed at patients with HAEC in comparison with patients without coloenteritis. It is also revealed that patients with HAEC phenomena in comparison with patients without coloenteritis had increased body height of representatives of opportunistic intestinal microflora (*Proteus mirabilis*, *Providencia rettgeri*, etc.).

Data on specific and quantitative indices of intestinal microflora at patients with HAEC and without it is presented in Table 4.

Table 2: Distribution of patients with HAEC with intestinal ostomy and without ostomy

Developmental quotient of HAEC	Pre-operative HAEC	Post-operative HAEC	Confidence coefficient of result, <i>P</i>
	Quantity, ABS (%)		
Patients with HAEC with intestinal ostomy	19 (100)	12 (63.1)	<i>P</i> >0.05
Patients with HAEC with without ostomy	16 (100)	11 (68.7)	<i>P</i> >0.05

HAEC: Hirschsprung-associated enterocolitis in children, ABS: Absolute

Table 3: Types and the frequency of complications in the post-operative period

Type of complications	Total of complications, ABS	HD, without coloenteritis, ABS (%)	Exacerbation ABS (%)	HAEC, ABS (%)	Exacerbation ABS (%)
Stenosis of colorectal anastomosis zone	26 (16)	7 (4.3)	1 (14.3)	19 (11.7)*	6 (31.6)*
Anus stricture	10 (6.2)	4 (2.5)	1 (25)	6 (3.7)	2 (33.3)
Hypodermic eventration of intestines	4 (2.5)	4 (2.5)	-	-	-
Early adherent intestinal obstruction	3 (1.9)	2 (1.2)	-	1	-
Strangulated intestinal obstruction	1 (0.6)	1 (0.6)	-	-	-
Ostomy evagination	1 (0.6)	1 (0.6)	-	-	-
Stenosis thickly-colic anastomosis	2 (1.2)	-	-	2	1 (50)
Insolvency thickly - colic anastomosis, peritonitis	1 (0.6)	-	-	1	-
Colon fistula, peritonitis	2 (1.2)	1 (0.6)	-	1	1 (100)
Rectovestibular fistula	1 (0.6)	1 (0.6)	-	-	-
Perianal fistula	1 (0.6)	1 (0.6)	-	-	-
Total	52 (32)	26 (16)	2	25 (15.4)	10

*Reliability of difference at *P*<0.05. HD: Hirschsprung disease, ABS: Absolute

Apparently, from Table 4, decrease in the quantity of microorganisms intestines normoflor in relation to indexes of norm is noted in a group of patients with coloenteritis and without it, but in a group of patients with coloenteritis decrease is observed with the reliable difference which was more expressed statistically (*P* < 0.001). In the comparative analysis of indexes normoflor between groups of patients reliable distinction of decrease in the useful microorganisms of intestines at patients with HAEC is also noted (*P* < 0.001). In addition to this, there is a growing increase of opportunistic microorganisms due to lower amounts of the normal flora of microorganisms in the larger group of patients with enterocolitis with a reliable statistical difference (*P* < 0.01). Moreover, in patients with HAEC observed some species of pathogenic microorganisms (*P. rettgeri*, *Citrobacter diversus*, and others) with the indicators above the norm in the absence of these microorganisms in the group of patients without enterocolitis.

DISCUSSION

During the carried-out retrospective analysis when studying clinical current, influence of the intestinal ostomy on the development of HAEC, post-operative complications and bacteriological research of feces at HAEC significant aspects of the development of this pathology are revealed.

When carrying out the analysis of clinical features of HD was revealed that the main manifestations of development of HAEC are abdominal distention and unstable chair, which was observed in 100% of treated children. Development of other symptoms (abdominal pains, effervescence, and vomiting) depended on the weight of disease clinical course. In the children's coloproctology, important stage of correction of defects colon development and perineum is adequate imposing preventive or discharge of intestinal stoma, since, according to some writers, The impossibility of adequate emptying intestine leads to dilation of the large and sometimes small intestine, congestion of gases and fecal masses. Severe decompensated bowel expansion is the development of HAEC factor. All this is an indication to the imposition of the so-called unloading stoma, the aim of which is extended decompression intestine situated above aganglionosis area. In addition to congenital anomalies of development, the formation of intestinal stoma may be necessary in severe inflammatory bowel disease.^[17]

It is the most of all created sigmoidostomas in our research (in 65.3% of observations), HAEC at this category of patients is noted at 19 (36.5% of cases) children. In the analysis of aspects of enterocolostomy at Hirschsprung disease as a possible way of prophylaxis of HAEC was revealed that the quantity of cases of development of HAEC has

Table 4: Specific and quantitative indices of intestinal microflora

Microorganisms	Norm at children (industry standard 91500.11.0004-2003)	HD (without coloenteritis) (n=22)	HAEC (n=20)	P
		M±m	M±m	
Bifidobacterium	10 ⁹ -10 ¹¹ CFU/g	766×10 ⁶ ±15×10 ⁶ CFU/g ^{###}	17×10 ⁶ ±2.2×10 ⁶ CFU/g ^{###}	P<0.001
Lactobacterium	10 ⁶ -10 ⁸ CFU/g	6×10 ⁶ ±4×10 ⁶ CFU/g	35×10 ³ ±10×10 ³ CFU/g ^{###}	P<0.05
Colibacillus with normal enzymatic activity	10 ⁷ -10 ⁸ CFU/g	2.5×10 ⁶ ±987×10 ³ CFU/g ^{##}	183×10 ³ ±247×10 ³ CFU/g ^{###}	P<0.001
Conventionally -pathogenic enterobacteria	<10 ⁴	The number of patients with higher than normal bacteria; ABS (%)	The number of patients with higher than normal bacteria; ABS (%)	P<0.05
<i>Proteus mirabilis</i>	<10 ⁴	3 (13.6)	6 (30)*	
<i>Providencia rettgeri</i>	<10 ⁴	-	7 (35)	P=0.000
<i>Citrobacter diversus</i>	<10 ⁴	-	5 (25)	P=0.000
<i>Pseudomonas aeruginosa</i>	<10 ⁴	2 (9)	7 (35)**	P<0.01
<i>Klebsiella pneumoniae</i>	<10 ⁴	-	6 (30)	P=0.000
<i>Staphylococcus gallinarum</i>	<10 ⁴	-	5 (25)	P=0.000
<i>Staphylococcus aureus</i>	<10 ⁴	2 (9)	5 (25)*	P<0.05
Hemolytic fissile colibacillosis	<10 ⁴	-	4 (20)	P=0.000
Sporogenous anaerobe bacteria (clostridiums)	<10 ⁵	-	2 (10)	P=0.000
<i>Enterococcus faecalis</i>	>10 ⁷	3 (13.6)	4 (20)	P>0.05

Degree of reliance in relation to norm: (1) ^{##}Degree of reliance at P<0.01; (2) ^{###}Degree of reliance at P<440.001; in the section opportunistic enterobacteriaceae ^{***}degree of reliance of difference index groups (%) expressed as a percentage. HD: Hirschsprung disease, HAEC: Hirschsprung-associated enterocolitis in children, ABS: Absolute

no reliable distinctions between ostomy and not ostomy groups of patients. The certificate to it is the preservation of signs of coloenteritis at 12 ostomy patients (63.1% of observations) in the post-operative period that also statistically authentically does not differ from an index in a group of children without ostomy (11 patients, P > 0.05). Although expressiveness of decrease in number of patients with HAEC in the post-operative period is more noted in a group of ostomy patients. In this connection, particular positive effect of preventive intestinal ostomy as measures of the fight against HAEC unambiguously cannot be denied. It should also be noted that the incidence of post-operative HAEC not depends on the overlay intestinal stoma. Irrespective of the type of unloading intestinal ostomy the frequency of development of HAEC in the post-operative period statistically authentically does not differ (P > 0.05).

Most surgeons agree that surgical proctology surgery is an area with a very high risk of complications. Their frequency can be, according to different authors, up to 60% or more.^[7] HAEC is a complication of HD. According to the analysis of our patients treatment results, complications after operation were observed at 52 children (32% of observations). Among them, stenoses of colorectal anastomosis (26 children - 16% of observations) and anus strictures prevailed (10 patients - 6.2% of cases). It was revealed that the frequency of occurrence of complications at HAEC is

reliable above (P < 0.05), then at children without HAEC, in the comparative analysis. These complications have property to recur more often at patients with HAEC in comparison with patients without coloenteritis (P < 0.05). We give an example of case history of the patient with HAEC with a complication in the form of colorectal zone stenosis with relapsing current.^[18] Child T, 9 years, diagnosis: Congenital anomaly of GIT HD, and rectal form. A state after Soave operation in Boley modification. HAEC anastomosis stenosis complaints at revenues to abdominal distention, abdominal pains, periodic effervescence, liquid stool to 3-4 times a day, and loss of appetite. From the anamnesis: The child since the birth suffered from locks up to 7-10 days. 01.03.10 operation - the Laparotomy is made, endorectal bringing down of sigmoid gut on Soave on Boley modification. In the post-operative period, the picture of coloenteritis and stenosis of anastomosis developed. He was hospitalized quickly with the above-stated complaints.

Audit of anastomosis zone under the general anesthesia is carried out.

From the protocol of manipulation: At survey on rectal speculums - there is an anastomosis in distance of 2.5 cm from the gear line, the phenomenon anastomosis, fabrics edematous, and friable. Due to the inflammatory changes, the gleam of anastomosis is not visible, in attempt to pass through anastomosis of fabric bleed. Due to the

inflammatory phenomena, it was decided not to eliminate a stenosis. The intestines intubation through a colonoscope was made.

After subsiding of inflammatory process 14.09.10 operation on the elimination of stenosis - the Laparotomy, reconstructive colorectal anastomosis on Duhamel is executed. In the subsequent, the patient's anastomosis stenosis recurrence with HAEC phenomena is mentioned. Executed:

- 18.03.11. Section of colorectal anastomosis on Mikulich.
- 14.06.11. Rectal survey under the common anesthesia, a digital bougienage.

The recurrence of stenosis is eliminated.

In our opinion, the above-stated complications are bound, first of all, to the inflammatory process in intestines which induce development of pro-inflammatory processes and lead to stricture formation, possible insolvency of anastomosis and formation of colon fistulas with the subsequent development of peritonitis. One of the major factors of development of the inflammatory process in intestines is a violation of normal biocenosis. The healthy microflora suppresses body height of pathogenic microflora. The useful microorganisms occupying intestines are part of the protective mechanism of the mucosa of intestines, and constantly renewed part of an organism, regulate exchange and adaptation processes.^[19] In our observations results of bacteriological researches of feces showed that development of HAEC is intimately bound to violation of microbiocenosis of intestines. Decrease in the quantity of bifido-lactobacilli and colibacillus with normal enzymatic activity with body height of pathogenic microflora is more expressed were shown in a group of patients with HAEC in comparison with patients without coloenteritis ($P < 0.05$). In our opinion, from the point of view of HAEC development prophylaxis, this aspect is fundamental and demands further more in-depth studies.

CONCLUSIONS

The abdominal distention and unstable stool with a sequence of liquid stool with astrictions are the main symptoms of development of HAEC which are noted at all patients with this nosology. Imposing of a "unloading" colostomy, enterostoma was absolutely justified for the achievement of decompression of the intestinal path. Use of colostomy for the purpose of prophylaxis of post-operative HAEC is auxiliary, but not a principal component for achievement of goals. The data of changes of intestinal microflora in different groups of observations obtained at bacteriological researchers can confirm the key role of the broken biocenosis of the large intestine in development of HAEC. Decrease in a number of representatives of obligate flora in intestines leads to activation of the opportunistic microflora

with an increase in the risk of development of HAEC that threatens with strengthening of the inflammatory phenomena in a colon, increases the risk of gut stricture formation with recurrence, insolvency of anastomosis and formation of colon fistulas with the development of peritonitis.

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