THE ETIOLOGICAL STRUCTURE OF INFECTIOUS GENESIS DIARRHEA IN HIV-INFECTED CHILDREN

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ABSTRACT

During the study, 261 HIV-infected children were examined. The diagnosis was made based on patient complaints, clinical, anthropometric, serological, bacteriological, immunological, virologic and instrumental examinations. It was observed that viruses infected 51,7% of children with human immunodeficiency viruses (HIV).Diarrhea, called by viruses and bacteria, occurred in children in the form of mono and mix. Under observation, viruses and bacteria rarely called diarrhea in the form of mono-infection in children. Infectious Genesis diarrhea in HIV infection is most often manifested in the form of mixed viral-viral, viral-bacterial and bacterial-bacterial diarrhea (34,1%; 31,0% and 24,9%, respectively). The main causative agents of viral diarrhea are noro and rotaviruses (34,1% and 27,4%, respectively), while Salmonella and Shigella provoked bacterial diarrhea (42,1% and 32,5%, respectively). In mono and mixed infection, adeno and astroviruses and echerixies, diarrhea caused by campylobacter are rarely encountered. Cytomegalovirus (CMV) and herpesviridae did not call diarrhea in children with HIV in the form of mono-infection. Only in mixed diarrhea, we can detect them.

Keywords: HIV-infection, sick children, diarrhea, virus sample, a bacterial disease.

I. INTRODUCTION

HIV infection remains one of the major problems of global public health. According to The Joint United Nations Programme on HIV/AIDS (UNAIDS), 78 million cases of HIV infection were recorded in epidemics of all periods. In 2018, 91,7 million patients infected with HIV was recorded in the whole world. Today, more than 300,000 people in Uzbekistan were infected with HIV. Diarrhea is one of the main clinical symptoms of HIV-infected children. This case occurs in 70% of children infected with HIV. Most of them contain viral diarrhea [5]. But although the epidemiology, pathogenesis, and clinical features of diarrhea have been adequately studied, not only in children with HIV but also in healthy children, aetiology is not detected in 50-60% of cases [2].

Viral diarrheaoccurs, especially among small children. Opportunistic viruses that cause viral diarrhea in children infected with HIV include rotaviruses, adenoviruses, astroviruses, caliciviridae, coronaviruses, cytomegalovirus, types I and II of the common herpes virus [4]. Norwalk viruses, which enter the family of caliciviridae, account for 30% of viral diarrhea in developed countries [3]. Rotavirus is one of the main causes of viral diarrhea. Rotavirus was the main agent that caused 27% of all worldwide recordeddiarrhea in 2011 [6]. The recording of viral diarrhea against antiretroviral therapy background is slightly occurred [1]. The features of clinical signs of viral diarrhea in children infected with HIV are one of the areas not studied in Uzbekistan. As a result of a violation of the B-cell ring function of the immunity in the body of a child infected with HIV, the body can not provide complete humoral protection against the new antigen. As a result, clinical signs of various opportunistic infections begin to manifest.

II. MATERIALS AND METHODS

HIV infectionin children was diagnosed based on a Decree "On the implementation of the national clinical protocol on HIV infection" adopted by the Ministry of Health of the Republic of Uzbekistan in 2018. The research was conducted at the specialized clinic of infectious diseases under the Republican Center for the fight against AIDS, the Center for the fight against Aids in Tashkent, the Department of Children's HIV infection of the scientific research institute of Virology of the Ministry of Health of the Republic of Uzbekistan, the children's infectious Diseases Hospital.During the research, 261 HIV-infected children were examined. It was divided into groups by age, sex, route of infection and stages of HIV infection of the sick children. The diagnosis was made based on patient complaints, clinical, anthropometric, serological, bacteriological, immunological, virologic and instrumental examinations.

A sample of faeces for viral and bacterial diarrhea diagnosis was examined using Polymerase chain reaction (PCR). This method was carried out on the first day of hospitalization of children. 1 gr is taken from the faeces' sample using a sterile swab and inserted intoa sterile probe which was the previously prepared 1 ml of physiologic solution. A drop of glycerin was injected onto it, and PCR analysis was performed. In the diagnostics for PCR, it was possible to identify rotavirus, noro-, astro-, adenoviruses, as well as Salmonella, Shigella, escherichia.

III. RESULTS

The study of the incidence of viral and bacterial agents in the general structure of diarrhea in HIV – infected children showed that in our observation, 261 children with acute diarrhea under the age of 18 years – 51.7% of (135) viruses, 48.3% of (126) bacteria were detected. The analysis included the occurrence of detected agents in diarrhea in HIV - infected children with mono-or in the form of a mixed infection.

Table 1

The general structure of mono and mixed diarrheain children infected with HIV

Etiology	Diarrhean=261	
	Abc.	%
Viral	14	5,4
Bacterial	12	4,6
Viral-viral	89	34,1
Viral-bacterial	81 (32+49)	31,0
Bacterial-bacterial	65	24,9

According to this, mono-infection of viral and bacterial agents in children infected with HIV was recorded in very rare cases (5,4% and 4,6% respectively, R>0,05). In most children under control, viral-viral and viral-bacterial diarrhea was manifested in the form of a mixed infection.Bacterial-bacterial mixed diarrhea (BBD) was found to be almost 1.4 times more common than viral-viral mixed diarrhea (VVD) and 1.3 times less common than virus-bacterial-mixed diarrhea (VBD) (34.1%; 31,0% and 24,9% respectively, R>0.05).

The incidence of infectious diarrhea pathogens in HIV-infected children was studied separately. In our observation, 261 children with acute diarrhea were diagnosed with 6 different viruses, namely rotavirus, norovirus, astrovirus, adenovirus, cytomegalovirus, and herpesviruses, as well as bacterias, namely Salmonella, shigella, escherichia and campylobacter.

Table 2

The degree of occurrence of viruses in diarrhea in children infected with HIV

	Mono-diarrhea		Mixeddiarrhea				Total	
	VD		VVD		VBD			
	Abc.	%	Abc.	%	Abc.	%	Abc.	%
Rotavirus	4	28,6	24	27,0	9	28,1	37	27,4
Norovirus	6	42,9	29	32,5	11	34,3	46	34,1
Astrovirus	1	7,1	8	9,0	3	9,4	12	8,9
Adenovirus	3	21,4	13	14,6	5	15,6	21	15,6
Cytomegalovirus	0	0,0	7	7,9	2	6,3	9	6,7
Herpesvirus	0	0,0	8	9,0	2	6,3	10	7,4
Total	14	10,4	89	65,9	32	23,7	135	100,0

Viral diarrhea observed in children with HIV was detected in 65,9% of cases in the form of viral-viral agent-mixed diarrhea; virus-bacterial agent-mixed diarrhea was detected in 2.8 times fewer cases than in them (23,7%). In only 10.4% of patients (14 people), viral diarrhea occurred in the form of mono-infection.

According to the etiological structure, noroviruses and rotaviruses were considered to be the main causators of viral diarrhea observed in children infected with HIV. In comparison with noroviruses, rotaviruses were detected 1,2 times (R>0,05) in controlled children, adenoviruses 2,2 times, and astroviruses 3,8 times less often (34,1%; 27,4%; 15,6% and 8,9% respectively, R<0,05). There was no clear difference between the occurrence of cytomegalovirus and herpes in HIV-infected children (6,7% and 7,4% respectively, R>0,05).

Viral diarrhea in 14 children occurred in the form of mono-infection, in which the occurrence of viral agent pathogens was studied. It was found that in 42,9% of cases, diarrhea was caused by noroviruses, rotaviruses in 28,6% of cases, and adenoviruses in 21.4% of cases. Only one patient (7,1%) allocated astroviruses.

In comparison with noroviruses rotaviruses, viral diarrhea in children is 1.5 times more likely to occur in the form of mono-infection (42,9%; 28,6% respectively P<0,05), whereas in the case of the appearance of mixed virus-viral diarrhea (VVD) and mixed virus-bacterial diarrhea (VBD), a clear difference between them is evident (32,5%; 27,0% and 34,1%); 27,4% respectively, R>0,05). Adenoviruses called diarrhea 3 times more in the form of mono-infection than astroviruses in children (21.4% and 7.1% respectively, P<0.05), 1.6 times more in VVD mixed infection (14.6% and 9.0% respectively, P<0.05), and nearly 1.7 times more in VBD mixed infection (15.6% and 9.4% respectively, P<0.05). Cytomegaloviruses and herpesviruses did not call for diarrhea in the form of mono-infection in children. Cytomegaloviruses were detected in 7,9% of cases in HIV-infected children, that is, in the mixed VVD. In the mixed VBD, 9,0% of cases, both viruses were recorded in the patient from 2 people (6,3% and 6,3% respectively, R>0,05).

Noroviruses are detected in most cases in viral diarrhea in the form of mono-infection in children (42,9%), while between VVD and VBD can occur in mixed infections, a clear difference is evident (32,5% and 34,4% respectively, R>0,05). Adenoviruses were detected in 21.4% of children under control in VD mono-infection, about 1.4 times less common in VVD and VBD mixed infections than it (14.6% and 15.6% respectively, R>0.05). Clear differences between mono and mixed in viral diarrhea in children under observation were not detected (28,6%; 27,0%; 28,1% and 7,1%; 9,0%; 9,4% respectively, R>0,05). In children with HIV infection, cytomegaloviruses VVD was detected almost 1.3 times less often than in children, and in herpesviruses 1.4 times less often (7,9%; 6,3% and 9,0% 6,3% respectively, R>0,05).

Table 3

The degree of occurrence of bacteria in diarrhea in children infected with HIV

	Mono diarrhea	Mixed diarrhea		
	BD	BBD	VBD	Total

	Abc.	%	Abc.	%	Abc.	%	Abc.	%
Salmonella	5	41,7	26	40,0	22	44,9	53	42,1
Shigella	4	33,3	22	33,8	15	30,6	41	32,5
Escherichia	2	16,7	14	21,5	8	16,3	24	19,0
Campylobacter	1	8,3	3	4,6	4	8,2	8	6,3
Total	12	9,5	65	51,6	49	38,9	126	100,0

In total, in 126 of 261 children infected with HIV were detected bacterial pathogens. Diarrhea with bacterial etiology was manifested in this group's children in mono and mixed infectious diarrhea. Accordingly, 9,5% (12) bacterial diarrhea in HIV-infected children occurred in the form of mono-infection, 51.6% (65) bacterial-bacterial mix diarrhea and 38.9% (49) viral-bacterial mix diarrhea. When analyzing the etiological structure of bacterial Genesis diarrhea in children, it was found that Salmonella was the main causative agent of bacterial diarrhea. Compared to them, it was found that shigellas were recorded 1.3 times, escherichia were nearly 3 times, campylobacter was recorded 3.5 times less (42,1%; 32,5%; 14,3% and 11,9% respectively, R<0,05). There was no clear difference between diarrhea in children with HIV infection by escherichia and campylobacter (R>0,05).

If analyzing the occurrence of pathogens in the mono-infection of bacterial diarrhea in children with HIV-infected, we can see that Salmonella dominated 41,7% (5) of children of 12 patients and 33,3% (4) by shigella. It was found that in children under observation, the mono-infection of escherichia was noted in 2 times more cases than in campylobacters mono-infection (16,7%; 8,3% respectively, R<0,05).

It was found that Salmonella was partially predominant compared to shigella,but there was not observed a clear difference between their occurrence (40,0%; 33,8%, respectively, P>0,05). While it was recorded that escherichia was detected in 4.7 times more cases than campylobacteria (21,5%; 4,6%, respectively, R<0,05).

A comparative analysis of the occurrence of bacterial diarrhea in HIV - infected children in the form of mono-and mixed infection showed that clear differences between UCH - occurrence of Salmonella and Shigella and mixeddiarrhea are evident (41,7%; 40,0%; 44,9% and 33,3%; 33,8%; 30,6% respectively, P>0,05). It was recorded that escherichia was detected in almost 1,3 times fewer BD mono-infection and mixed VBDs than when 21,5% of HIV-infected children were detected in mixed BBDs (16,7% and 16,3% respectively, P>0,05). In controlled children, the clear difference between campylobacteria mono BD and mixed VBD occurs in diarrhea. In comparison with them, it was found that nearly 1.8 times fewer cases were reliable (8,3 %; 8,2% and 4,6% respectively, R<0,05).

IV. DISCUSSION

The main causes of diarrhea in HIV-infected patients worldwide are intestinal bacteria, particularly *Shigella flexneri*, *Salmonella enteritidis* and *Campylobacter jejuni* [6]. Cytomegalovirus (CMV), cryptororidiosis, microdistria, and Mycobacterium avium complex (MAC) are important pathogens in the development of immunability in case of gastrointestinal lesions in HIV infection.Also, the cause of diarrhea can be pathogens belonging to the population of HIV in people infected with HIV or pathogens that the immunocompetent boss calls diarrhea. For example, Salmonella, Shigella, Campylobacter, Escherichia coli and neurotropic viruses are both immunocompetent and call for diarrhea in persons. These conditionalpathogen infectionsare divided into four main categories of microorganisms: simple animals, fungi, viruses and bacteria.CMV is the most damaging virus of the gastrointestinal tract in patients. It damages the entire gastrointestinal tract, but it usually leads to diarrhea, which leads to colitis and systemic symptoms such as rectal bleeding, abdominal pain, and fever and weight loss [5, 6].

HIV infection itself can call diarrhea syndrome, and many other viruses are manifested as pathogens of diarrhea, including adenovirus, coronavirus, simple herpes virus, rotavirus and noroviruses. Salmonella, Shigella, Campylobacter, and intestinal colic are bacterial infections of the gastrointestinal tract, manifested by diarrhea. One of the most common causes of bacterial diarrhea in HIV-infected patients was Clostridium difficile, which accounted for 53.6% of 1115 diarrhea episodes called bacterial pathogen [11].

According to the data of the Federal Center for hygiene and epidemiology of the infection indicator ofsalmonellosis (Tyumen, Russian Federation), from January to October of 2017 amounted to 19,24 for 100 thousand inhabitants. If the previously observed occurrence of salmonellosis in cooperation with abdominal typhus and dysentery, the association with rota-, noro-, adenoviruses is being determined in recent years. In 2017,

a retrospective analysis of the disease histories of patients aged 1 to 62 years who were treated in the Clinical Hospital of infectious diseases (Tyumen) was carried out, of which 17 were diagnosed with salmonellosis and 13 with mixed infection. The diagnosis was made based on clinical laboratory data (examining faeces on pathogen Enterobacteria and determination of rota-, adeno-, noro-antigens in human coprophiltratethe enzyme-linked immunosorbent assay (ELISA)). S.enteritidis was detected in all patients, the following antigens in the ELISA method: adenovirus F + A gr.rotavirus – in 31% (n=4), 1,2 type norovirus– in 23% (n=3), adenovirus F + 1,2 type norovirus + a gr.rotavirus – in 15,3% (n=2), adenovirus F – in 15,3% (n=2), adenovirus F + 1,2 type norovirus – in 7,7% (n=1), a gr.rotavirus – in 7,7% (n=1). Thus, the association between salmonellosis and its intestinal viral infections was 56,6% (n=17) and 43,3% (n=13), respectively. The association of Salmonella with intestinal viral infections was found in almost 50% of cases, mainly in patients in 2017. Adenoviruses, noroviruses were detected in every third of patients, while rotaviruses were detected in rare cases [1].

Prospective studies conducted in 3 hospitals in Lima found that an intestinal stick called diarrhea in children. The study examined 70 HIV-infected diarrhea and 70 HIV-infected diarrhea-free control samples. 19% of the control group had long-term watery diarrhea, 3% - dysentery diarrhea, and 33% - moderate or severe dehydration [8].

V. CONCLUSION

1. In the general structure of acute diarrhea in children infected with HIV, a clear difference between the level of occurrence of viral, bacterial agent diarrheawas not identified (51,7%; 48,3%, respectively). Viral and bacterial agents mono-infection was recorded in very rare cases (5,4% and 4,6% respectively, R>0,05).

2. Viral-viral and viral-bacterial diarrhea were manifested in the form of a mixed infection (34,1% and 31,0%, respectively). Bacterial-bacterial agent diarrhea was found to be almost 1.4 times more common than viral-viral diarrhea and 1.3 times less common than viral-bacterial diarrhea (24.9%).

3. Viral diarrhea observed in children infected with HIV occurred in virus-viral agents mixed diarrhea in 65.9% of cases. Noroviruses and rotaviruses were considered to be the main causative agents of viral diarrhea (34.1% and 27.4%, respectively).

4. Salmonella was considered the main causative agent in children infected with HIV in bacterial genesis diarrhea mono and mixed infection (41,7%; 40,0%; 44,9% respectively).

CONFLICT OF INTERESTS AND CONTRIBUTION OF AUTHORS

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