

Etiological Varieties of Acute Infectious Diarrhea in Children under Three Years of Age

Kimyokhon Ahatovna Mulladjanova¹, Gulnara Karimovna Khudaykulova²

¹Department of Infectious Diseases, Andijan State Medical Institute, Andijan, Uzbekistan

²Department of Infectious Diseases, Tashkent Medical Academy, Tashkent, Uzbekistan

Abstract The review is devoted to the current features of the etiology of acute intestinal infections in young children. The point of view of a number of researchers on the varieties of infectious and non-infectious intestinal infections is presented. Questions of various etiological aspects are considered. Given the specific etiology of the disease, it is possible to prevent it and reduce child mortality.

Keywords Young children, Infectious diarrhea, Etiology, Bacteria, Viruses

1. Introduction

When preparing a review of the selected problem, we took into account a number of different etiological aspects. Among the reasons of leading importance were bacterial and viral agents. Diarrhea in young children is infectious and non-infectious etiology. Many publications have proved with an argument that has clearly characterized the etiological aspects.

Diarrhea is one of the main causes of child mortality and morbidity in the world. It develops mainly as a result of the consumption of contaminated food and water. Around the world, about 780 million people do not have access to improved water and 2.5 billion people do not have access to basic sanitation. Diarrhea caused by infection is widespread in developing countries. Currently, an increasing proportion of all diarrhea-related deaths are attributed to other causes, such as septic bacterial infections. Children suffering from malnutrition or people with weakened immune systems are at the highest risk of life-threatening diarrhea. The main pathogenic mechanisms of diarrhea are reduced to two main factors: accelerated passage of contents through the intestine due to nervous and humoral influences (irritation of intramural nerve plexuses or violations of central regulation of intestinal motility) and delayed absorption of fluid from the intestinal lumen due to a decrease in the permeability of the intestinal wall and sharp shifts in the regulation of osmotic processes in the intestine [1].

Acute intestinal infections (AII) — occupy one of the leading places in infectious pathology of children. According to who, more than 1 billion people suffer from acute gastrointestinal infectious diseases (diarrhea) every year, of

which 65-70% are children under the age of 5 years. The etiological structure of intestinal infections in children of different age groups varies. In young children, mainly rotavirus, enter pathogenic *Escherichia*, staphylococcus, *Salmonella* and especially often opportunistic enter bacteria (*Klebsiella*, *Proteus*, *Citrobacter*, etc.) are caused. Less common are shigellosis, clostridiosis, and cholera. Of children (school) age is dominated by shigellosis and salmonellosis with food route of infection, as well as arsines, typhoid, paratyphoid etc. [2].

Functional disorders of the gastrointestinal tract (GIT) are one of the most widespread problems among children of the first months of life [3,42]. A distinctive feature of these conditions is the appearance of clinical symptoms in the absence of any organic changes on the part of the gastrointestinal tract (structural abnormalities, inflammatory changes, infections or tumors) and metabolic abnormalities. With functional disorders of the gastrointestinal tract, motor function, digestion and absorption of food substances, as well as the composition of the intestinal microbiota and the activity of the immune system can change [4,26].

With congenital sodium diarrhea in the last trimester of pregnancy, there may be polyhydramnios; the child is born with a delay in intrauterine development. From birth, there is profuse diarrhea with the release of very liquid watery feces, which has a persistent course without any effect from dietary correction. In some cases, there are dysmorphism of the face, atresia of the Hoan. Developing is severe hyponatremia, metabolic acidosis. In the future, various levels of intellectual and physical development disorders are formed. Persistent profuse diarrhea from birth, increased excretion of sodium with feces, hyponatremia and metabolic acidosis are of diagnostic significance. The disease should be differentiated with a solterayuschey form of adrenogenital syndrome, VHD, malabsorption of monosaccharides,

disaccharides insufficiency. Timely (early) diagnosis of a number of hereditary diseases with the selection of adequate nutrition (in the presence of therapeutic mixtures) and parenteral support gives a chance for survival and normal development of the child [5].

2. Results and Discussion

Many risk factors of the gastrointestinal tract in young children are due to the immaturity of mechanisms for regulating propulsive activity of the gastrointestinal tract. With age, as these mechanisms mature, the risk factors of this Genesis disappear without a trace [6].

The proportion of children among all cases of shigellosis is 60-70%, mainly children aged 2-7 years, especially those who attend preschool institutions and schools. Children of the 1st year of life suffer from shigellosis much less often [2]. The genus *Shigella* comprises the most infectious and diarrhea genic bacteria causing severe diseases, mostly in children under five years of age. This study aimed to detect nine virulence genes (*ipaBCD*, *VirA*, *sen*, *set1A*, *set1B*, *ial*, *ipaH*, *stx*, and *sat*) in *Shigella* species (spp.) using multiplex polymerase chain reaction (MPCR) and to determine the relation of *Shigella* spp. from pediatric diarrheal samples with hospitalization and bloody diarrhea in Tehran, Iran. Methods research *Shigella* spp. were isolated and identified using standard microbiological and serological methods. The virulence genes were detected using MPCR. This study revealed a high prevalence of enterotoxin genes in *S. flexneri*, especially in serotype 2a, and has presented relations between a few clinical features of shigellosis and numerous virulence determinants of clinical isolates of *Shigella* spp. [7].

In this study, 676 patients with the mean age of 24.94 months were enrolled. Eighty-eight (42%) *Salmonella* spp., 85 (40%) *Shigella* spp., 33 (16%) *E. coli* and 5(2%) *Candida albicans* were isolated from 211 positive stool cultures. Among 85 *Shigella* spp. isolates, *S. sonnei*, *S. flexneri* and other *Shigella* spp. were isolated from 39 (46%) isolates, 36(42%) and 10 (12%), respectively. Among 88 isolated *Salmonella* spp., 36 (41%) isolates were *Salmonella* Serogroup D, 26 (30%) were *Salmonella* Serogroup B, 20 (23%) isolates were *Salmonella* Serogroup C and 6 (7%) were other *Salmonella* spp. isolates. In conclusion, *Shigella* and *Salmonella* serogroups can be considered as important etiological agents of acute diarrhea in children [8].

Diarrhea can be one of the manifestations of many acute and chronic diseases. Among the acute ones, a special place is occupied by gastrointestinal infections. In their diagnosis, an epidemiological history is of great importance. Group diarrhea is always suspicious of its infectious nature. Meanwhile, some cases of gastro-intestinal infections have no specific anamnesis [9].

Diarrhea is the leading infectious cause of childhood morbidity and mortality. Among bacterial agents, diarrhea genic *Escherichia coli* (DEC) is the major causal agent of

childhood diarrhea in developing countries, particularly in children under the age of 5 years. Here, we performed a hospital-based prospective study to explore the path type distribution, epidemiological characteristics and antibiotic resistance patterns of DEC from <5-year-old diarrheal children. DEC strains were identified in 7.9% of the 684 stool samples. Among them, the most commonly detected path type was EPEC (50.0% of DEC), of which 77.8% were classified as atypical EPEC (aEPEC). Age and seasonal distribution revealed that DEC tended to infect younger children and to occur in summer/autumn periods [10]. Intestinal infections caused by enter pathogenic escherichiosis (EPE) occur mainly in young children and newborns. The etiological role in the pathology of young children was established in 30 serovars, of which the most common are serovars 018 as: K77, 020:K84, 026:K60, Ozz:C, 044:C74, 055:C59, 075:C. 086: KB 1.0111 AV:C58, 0114:C90, 0119:C69, 0125:C70, 0126:C71, 0127:C63, 0128:C67, 0142:C86. Individual epidemic EPE serovars are capable of exotoxin formation (018, 020:KH, 025:K98, 0114:H21, 0119. 0128:H12, 0128:H21, etc.) and can cause "cholera-like" diseases. Enterotoxin genic escherichiosis (ETE) observed in children and adults of any age occasions. Currently, there is a predominantly allocated ETE to 48 surfers and 61 patients, of which the most significant value in human pathology is directly 06: K15: H16, 015: H 11, 027: H7 (H20), 078: H12. 0112av, 0114: H21, 0148: H28, 0159 H4, the mode will meet with the judge 07 L18. 08. K47. H (K) 40 L9), 09. K35. H (kyuz:H), 020: KH (K101:H), 025:C98:H, 063:I12, 079:H45, 0101:C28, 0115: H51, 0128: H21 (H12), 0138: H, 0139: C82: H, 0141: H4, 0149: 0153: HY, 0157: H19.

Enter invasive escherichioses are created mainly in children older than 3 let and in adults. The group of EIE pathogenic to humans includes 13 serovars, of which those contained in children's pathology are 0124 and 0151, mode - 025, 028, 032, 0112, 0115, 0129, 0135, 0136, 0143, 0144, 0152.

In enter hemorrhagic escherichiosis, EGE produces exotoxin-verocytotoxin, which has a pathological effect not only on the intestinal wall, but also on other organs and tissues (kidneys, liver, hematopoietic system, etc.). The ability to produce verocytotoxin during reproduction is established in *Escherichia* serovars 0157:H7, 026:H11, as well as in some *Escherichia* strains 0111, 0113, 0121, 0145 [2].

Enter aggregative *Escherichia coli* (EAEC) cause acute and persistent diarrhea, mostly in children worldwide. Outbreaks of diarrhea caused by EAEC have been described, including a large outbreak caused by a Shiga toxin expressing strain. This study investigated the association of EAEC virulence factors with diarrhea in children less than 5 years. We characterized 428 EAEC strains isolated from stool samples obtained from moderate-to-severe diarrhea cases (157) and healthy controls (217) children aged 0-59 months recruited over 3 years as part of the Global Enteric Multicenter Study (GEMS) in The Gambia [11].

Infectious diarrhea is endemic in most developing countries. We aimed to investigate the protozoan, viral, and bacterial causes of acute diarrhea in Taif, Saudi Arabia. A cross-sectional prospective 1-year study was conducted on 163 diarrheal patients of various ages. Stool samples were collected, 1 per patient, and tested for 3 protozoa, 3 viruses, and 9 bacteria with the Luminex Gastrointestinal Pathogen Panel. Overall, 53.4% (87/163) of samples were positives (20.8% protozoa, 19.6% viruses, 2.8% bacteria, and 9.8% mixed). Rotavirus (19.6%), *Giardia duodenalis* (16.5%), and *Cryptosporidium* spp. (8.5%) were the mostly detected pathogens. Adenovirus 40/41 (4.2%), *Salmonella* (3%), Shiga toxin-producing *Escherichia coli* (3%), and *Entamoeba histolytica* (2.4%) were also detected. Norovirus GI/II, *Vibrio cholera*, *Yersinia enterocolitis*, and *Clostridium difficile* toxin A/B were not detected in any patients. All pathogens were involved in coinfections except *E. histolytica*. *Giardia* (5.5%) and rotavirus (3%) were the most commonly detected in co-infections. Enterotoxigenic *E. coli* (2.4%), *Campylobacter* spp. (2.4%), *E. coli* 0157 (1.8%), and *Shigella* spp. (1.2%) were detected in patients only as co-infections. Infections were more in children 0-4 years, less in adults <40 years, and least >40 years, with statistically significant differences in risk across age groups observed with rotavirus ($P<0.001$), *Giardia* ($P=0.006$), and *Cryptosporidium* ($P=0.036$) infections [12].

In low-income countries, children under the age of three get diarrhea on average three times a year. Each time, children are deprived of the nutrition necessary for their development. As a result, diarrhea is one of the main causes of malnutrition, and children who suffer from malnutrition are more likely to get diarrhea [1].

In the group of viral diarrhea included rotavirus infection, a disease caused by viruses of the group of Norfolk, astroviruses, caliciviruses, the adenovirus, the enterovirus, coronavirus, etc. In children, the most common are rotavirus gastroenteritis and the diseases associated with viruses of Norfolk. [2] Noroviruses are the leading cause of food-borne gastroenteritis outbreaks and childhood diarrhea globally, estimated to be responsible for 200,000 deaths in children each year 1-4. Thus, reducing norovirus-associated disease is a critical priority. Development of vaccines and therapeutics has been hindered by the limited understanding of basic norovirus pathogenesis and cell tropism. While macrophages, dendritic cells, B cells and stem-cell-derived enteroids can all support infection of certain noroviruses in vitro 5-7, efforts to define in vivo norovirus cell tropism have generated conflicting results. Some studies detected infected intestinal immune cells 8-12, other studies detected epithelial cells 13, and still others detected immune and epithelial cells 14-16 [13].

Salmonella contains a thermally stable somatic O-antigen and a thermolabile flagellated H-antigen. According to the structure of the O-antigen, *Salmonella* is divided into groups A, B, C, D, E, etc.; and according to the flagellated H-antigen, it is divided into serovars. There are about 2000 serovars. More than 700 serovars were allocated from a person. There

are more than 500 registered in our country, among them *Salmonella* groups b, C, D), E — *Salmonella enteritidis*, *S. typhimurium*, *S. infantis*, *S. panama*, *S. virchow*, *S. anatum*, *S. choleraesuis* dominate. *Salmonella* can persist for a long time in the external environment. Most *Salmonella* strains not only survive for a long time in food products (in milk — 2-40 days, kefir — about 30 days, in smoked meat — from 4 to 6 months, etc.), but also multiply with the accumulation of toxic substances and primarily endotoxins in them. Infection of children usually occurs from adult carriers of *Salmonella* or from patients with erased forms of the disease, in preschool institutions—most often from service personnel. The source of infection for newborns is often the mother. Contact-household path of infection is noted mainly in young children, especially in newborns, premature babies and those weakened by other diseases. Infection often occurs in hospitals through care items, staff hands, towels, dust, changing tables, pots. Salmonellosis is registered throughout the year with a maximum rise in the incidence in summer and autumn. The incidence varies in different territories and varies by year [2].

Diarrhea is a symptom of infections caused by a wide range of bacteria, viruses and parasites, most of which are spread through fecal-contaminated water. Infections are most common where there is a lack of clean water for drinking, cooking, and personal hygiene. The two most common causative agents of diarrhea - both moderate and severe - in low-income countries are rotavirus and *Escherichia coli*. Other pathogens, such as *cryptosporidium* and *shigella*, may also have significance [1]. Differences in definitions of acute pediatric diarrhea result in variable estimates of morbidity and mortality, treatment coverage, and associations with risk factors and outcomes. We reviewed published literature and guidelines focused on acute pediatric diarrhea in low- and middle-income countries. Clinical guidelines most commonly defined diarrhea in terms of quantity of loose or watery stool with consideration of normal stool patterns, whereas research studies often relied exclusively on a quantitative definition. The most commonly used quantitative definition, ≥ 3 loose or watery stools in a 24-hour period, has been compared to gold standards of caregiver perception and visual inspection of stool, with variable agreement. Age, breast-feeding status, and setting (facility vs household-based) influence the performance of quantitative diarrhea definitions in children. Universal adoption of a set of valid gold standard definitions specifically aligned with various programmatic and research goals will lead to more accurate coverage estimates and better-informed resource prioritization [14].

The development of the disease in bacterial intestinal infections begins when microorganisms with water and food enter the lumen of the esophageal tract, where the multiplication of pathogens begins and the release of their toxins: Exo - or enterotoxins (true toxins) and endotoxins. It is the toxins that determine all the variety of clinical symptoms and pathogenesis of acute intestinal infections [15].

Nosocomial salmonellosis is most often caused by antibiotic-resistant strains of *Salmonella* (*S. typhimurium*, etc.). The disease usually begins gradually, with a slow increase in clinical manifestations and later damage to organs and systems. Marked and prolonged intoxication, widespread and deep intestinal damage with constant involvement in the pathological process of the colon and frequent development of hemocolitis. Hospital salmonellosis is characterized by a prolonged course, the development of septic forms, a toxic-dystrophic state and high mortality. Salmonellosis in infants often occurs as a mixed infection in combination with other pathogenic and opportunistic microorganisms (*Shigella*, *Proteus*, *staphylococci*, *Klebsiella*, etc.) [2].

There are multiple etiologies responsible for infectious gastroenteritis causing acute diarrhea which are often under diagnosed. Also acute diarrhea is one of the major causes of morbidity and mortality among children less than 5 years of age. Fecal samples ($n = 130$) were collected from children (<5 years) presenting with symptoms of acute diarrhea. Samples were screened for viral, bacterial, and parasitic etiologies. Rotavirus and Adenovirus were screened by immunochromatographic tests. Diarrhea genic *Escherichia coli* (EPEC, EHEC, STEC, EAEC, O157, O111), *Shigella* spp., *Salmonella* spp., *Vibrio cholera*, *Cryptosporidium* spp., and *Giardia* spp. were detected by gene-specific polymerase chain reaction. Suspecting possible multiple infectious etiologies and diagnosis of the right causative agent(s) can aid in a better pharmacological management of acute childhood diarrhea. It is hypothesized that in cases with concurrent infections the etiological agents might be complementing each other's strategies of pathogenesis resulting in severe diarrhea that could be studied better in experimental infections [16].

Intestinal infections have their own characteristics of course in childhood, and are characterized by a more severe course, rapid development of symptoms of dehydration and complications (hemolytic-uremic syndrome, infectious-toxic shock, hypovolemic shock) Based on the results of the analysis, it was confirmed that the duration of hyperthermia, symptoms of pain, the state of intestinal colic with normal enzymatic activity, as well as the etiological factor and opportunistic flora are the leading factors affecting the consequences of acute intestinal infections. AII is characterized as infections that cause great significant damage to the health of patients. Among the factors determining the consequences of acute intestinal infections in children, the pathogenicity of the pathogen and its dependence on the premorbid state of the patient were determined [17].

Clostridium difficile (*C. difficile*) is a known pathogen associated with diarrhea especially in hospital acquired diarrhea. Yet, it is being recognized as a probable etiology for community acquired diarrhea. The aim of the present study was to detect the presence of *C. difficile* as a pathogen causing community acquired diarrhea in children and to verify the value of different laboratory methods for diagnosis,

namely specific culture, immunoassay for toxin detection, and nested polymerase chain reaction (nested-PCR). From this study, we can conclude that community acquired diarrhea due to *C. difficile* is common among children. It should be sought among the pathogens causing this infection. Rapid laboratory detection of toxin A by a rapid chromatography device is accurate compared to time consuming culture. Moreover, nested PCR for toxin B is an accurate and rapid method when it is available [18].

It is also necessary to take into account the etiological models that are specific to the area. In recent years, the etiological significance of pathogens that cause EII in children has changed. Currently, viral pathogens prevail over bacterial ones. A greater number of bacterial EII (69.7%) were recorded in the summer. Salmonellosis children were ill throughout the year with the same frequency with a slight rise in the disease to 15 cases from April to June. Campylobacteriosis was recorded from March to September, and isolated cases of shigellosis were observed from April to September. Acute intestinal infections caused by CPM did not have a clear seasonality and were recorded throughout all seasons [19].

In epidemiological analysis of the seasonal prevalence of rotavirus diarrhea, the disease was observed mainly in autumn and winter (22.8% and 55.7%, respectively). Bacterial infections, however, were observed in the spring and summer seasons (17.5% and 55%, respectively). From our observations, it turned out that the lesions in children with RVGE mainly increased due to a decrease in temperature. This may be caused by low temperature resistance of rotavirus strains in Uzbekistan [20,21,17].

According to the author's conclusions, seasonal patterns of detection of diarrheal diseases caused by various infectious agents in children under the age of 5 years were revealed. The analysis showed that diarrhea caused by viruses is characterized by registration throughout the year, most often in the autumn period, whereas in the case of bacterial diarrhea, there is a clear summer seasonality (except *Escherichia*). A similar trend is registered for mixed diarrhea, with seasonality depending on the prevailing agent. VVD had a characteristic autumn seasonality, while mixed diarrhea with the presence of bacterial agents prevailed in the summer [22].

The variability of the epidemiological situation, the seasonal increase in severe morbidity, in most cases the invasion of children under 3 years of age, moderate and severe clinical forms of the disease, a comparative assessment of hospital treatment, they are characterized as infections that cause great significant damage to the health of patients [23]. There are a large number of causes of diarrhea. However, the most common cause of diarrhea in children is acute intestinal infections. They take the second place (after acute respiratory infections) among all infectious diseases in childhood. Children account for about 60-70% of all cases of AII, which are registered in different age groups. AII is a large group of human infectious diseases with an enteral mechanism of infection caused by pathogenic and

opportunistic bacteria, viruses and protozoa. The source of infection in AII is the patient or carrier, and the main mechanism of transmission is fecal-oral, implemented by food, water and household contact. Viral intestinal infections are most often found in the cold season, and bacterial infections — in the summer and autumn period [3].

According to the author's conclusions, seasonal patterns of detection of diarrheal diseases caused by various infectious agents in children under the age of 5 years were revealed. The analysis showed that diarrhea caused by viruses is characterized by registration throughout the year, most often in the autumn period, whereas in the case of bacterial diarrhea, there is a clear summer seasonality (except for *Escherichia coli*). A similar trend is registered for mixed diarrhea, with seasonality depending on the prevailing agent. VVD had a characteristic autumn seasonality, while mixed diarrhea with the presence of bacterial agents prevailed in the summer period [24].

The variability of the epidemiological situation, the seasonal increase in severe morbidity, in most cases the invasion of children under 3 years of age, moderate and severe clinical forms of the disease, a comparative assessment of hospital treatment, they are characterized as infections that cause great significant damage to the health of patients [25].

The conducted research has shown the relevance of AII for the Irkutsk region: during the observation period, a significant increase in the incidence AII of established and unspecified etiology was detected; the average long-term incidence rates exceeded the all-Russian data. Among AIIIE dominated infections caused by bacterial agents. At the same time, the long-term aspect revealed a change in the etiological structure of AII: there was a statistically significant increase in the incidence of infection of viral etiology; their growth rates exceeded similar indicators for bacterial AII. Among the bacterial pathogens of intestinal infections, opportunistic bacteria of the Enterobacteriaceae family (*Proteus*, *Enterobacter*, *Citrobacter*, *Klebsiella*, *Morganella*) predominated. The taxonomic spectrum of enter bacteria has undergone significant changes, characterized by a marked increase in the proportion of *Klebsiella* spp. and the decline of *M. morganii* [22].

There are 5 species of representatives of the genus *Proteus*: *R. vulgaris*, *R. mirabilis*, *P. morganii*, *R. retgeri* and *R. inconstans* (*providencia*). Bacteria of each species differ in their antigenic structure, on the basis of which a diagnostic scheme has been developed, including the determination of the number of O-groups and serovars. *R. mirabilis* and *R. vulgaris* occupy a leading position among the proteases of all species. *Klebsiella* cultures often remain viable after treatment with bactericidal soap and disinfectant solutions. 3 species of *Klebsiella* are of clinical significance; *Klebsiella pneumoniae*, *K. rhinoscleromatis*, and *K. ozaenae*. Serological classification is based on differences in K - and O-antigens. 80 capsular K-antigens and 11 somatic O-antigens are known. *Campylobacteriosis* affects mainly weakened people suffering from diabetes, tuberculosis,

hemoblastosis and other oncological diseases. Pregnant women and young children are particularly susceptible. People who are weakened by previous diseases, burned, with immunodeficiency, chronic foci of infection, as well as newborns are susceptible to *Pseudomonas* infection. There is no seasonal incidence of *Pseudomonas* infection. Among children, the highest frequency of *Pseudomonas* infection is observed at an early age. The most susceptible to infection are newborns, weakened patients and patients with immunodeficiency conditions, as well as patients with malignant neoplasms. In these children, infections caused by *Bacillus cereus* are accompanied by persistent bacteremia and often take the form of sepsis [2].

The etiological structure of acute diarrhea in children under 5 years of age was analyzed on the basis of PCR study of stool samples. The obtained data clearly demonstrate that the prevailing etiological agents today are viruses, most often Noro- and rotaviruses, as well as their associations with both other viral and bacterial agents. When analyzing the specific weight of viral agents in the General structure of diarrhea in children, the following data were obtained. Adenoviruses and astroviruses are almost the same frequency as the cause of mono-viral diarrhea, as well as one of the etiologic agents of viral-viral or viral-bacterial diarrhea. At the same time, rotaviruses and noroviruses monoverse significantly more likely to cause diarrhea. Analysis of the specific weight of various bacterial agents in the overall structure of diarrheal diseases in children showed that the causes of mono-bacterial diarrhea are more often *Shigella* (58.1%) and *Campylobacter* (47.6%), while *Salmonella* and *Escherichia* were more often one of the etiologic agents of mixed viral and bacterial diarrhea (less often bacterial and bacterial diarrhea) [18].

Children who die from diarrhea often suffer from concomitant malnutrition, which makes them more vulnerable. Each case of diarrhea, in turn, exacerbates their malnutrition. Diarrhea is one of the main causes of malnutrition among children under five years of age [1].

Rational feeding of infants, when there are intensive processes of growth and development, lays the Foundation of health for the future and is the main factor that ensures harmonious development, a high level of immunobiological protection. Natural feeding at the 1st year of a child's life with mother's milk is the "gold standard" of nutrition that can ensure optimal development and adequate health.. If an infectious disease occurs in a nursing mother she in most cases receives incompetent recommendations to stop breastfeeding for this time [26].

Young age (6-24 mos vs. 24-59 mos adjusted prevalence ratio [aPR] = 1.519 [95% confidence interval: 1.19, 1.91]), maternal HIV (aPR = 1.29 [1.01, 1.66]); and acute malnutrition (aPR = 1.28 [1.06, 1.55]) were associated with higher prevalence of MDNS, as were open defecation (aPR = 2.25 [1.13, 4.50]), household crowding (aPR = 1.29 [1.08, 1.53]) and infrequent caregiver hand-washing (aPR = 1.50 [1.15, 1.95]). Young age, HIV exposure, acute malnutrition and poor sanitation may increase risk of antibiotic

non-susceptible enteric pathogen infections among children in Kenya [27].

Authors were conducted A wide range of strategies have been evaluated for improving delivery arrangements in low-income countries, using sound systematic review methods in both Cochrane and non-Cochrane reviews. These reviews have assessed a range of outcomes. Most of the available evidence focuses on who provides care, where care is provided and coordination of care. For all the main categories of delivery arrangements, we identified gaps in primary research related to uncertainty about the applicability of the evidence to low-income countries, low- or very low-certainty evidence or a lack of studies [28].

Diarrhea can also spread from person to person, which is compounded by poor personal hygiene. Food is another significant cause of diarrhea in cases where it is prepared or stored in unhygienic conditions. Unsafe storage and handling of water in the household is also an important factor. Fish and seafood from contaminated water can also cause this disease [1].

Transmission of the pathogen of typhoid fever is carried out by contact, water, food, as well as by flies. The main importance for young children is the contact-household pathway of infection transmission. Infection can occur both through direct contact with the patient, and through infected household items, toys, underwear, dishes, etc. The waterway of infection in typhoid fever remains important mainly in rural areas. Children can become infected when bathing in polluted reservoirs, when drinking poor-quality water, especially if there are violations in the water supply and Sewerage system (sewage entering rivers, closed reservoirs, wells, etc.). Water outbreaks are easier than food outbreaks, characterized by a long incubation period, the incidence curve has a steep rise and a rapid decline after taking appropriate measures on the water supply, Sewerage, etc. Food outbreaks of typhoid fever occur mainly when eating infected milk and dairy products — in food products, Salmonella tophi can multiply and accumulate in large quantities (especially in milk). Sometimes outbreaks of typhoid fever occur when eating confectionery, ice cream, salads, pates, sea shellfish. Young children are extremely rarely ill with typhoid fever, which is explained by their greater isolation, stricter hygiene, nutrition control, etc [2].

We conducted a systematic review of studies evaluating the effects of WASH interventions on childhood diarrhea in children 0-5 years old. Searches were run up to September 2016. We screened the titles and abstracts of retrieved articles, followed by screening of the full-text reports of relevant studies. We abstracted study characteristics and quantitative data, and assessed study quality. Meta-analyses were performed for similar intervention and outcome pairs. Pooled analyses showed diarrhea risk reductions from the following interventions: point-of-use water filtration (pooled risk ratio (RR): 0.47, 95% confidence interval (CI): 0.36-0.62), point-of-use water disinfection (pooled RR: 0.69, 95% CI: 0.60-0.79), and hygiene education with soap provision (pooled RR: 0.73, 95% CI: 0.57-0.94). Quality

ratings were low or very low for most studies, and heterogeneity was high in pooled analyses. Improvements to the water supply and water disinfection at source did not show significant effects on diarrhea risk, nor did the one eligible study examining the effect of latrine construction [29].

Typhoid bacteria contain thermostable somatic O-antigen and heat-labile flagellar H-antigen. The pathogenicity of typhoid bacteria is determined by endotoxin, as well as "aggression enzymes" (hyaluronidase, fibrinolysin, lecithinase, hemolysin, hemotoxic, catalase, etc.), released by bacteria during colonization and death. The pathogen of typhoid fever is stable in the external environment: in water it persists for up to 90 days, in the soil—about 2 weeks, on vegetables and fruits—10 days, in meat, cheese, bread, milk, oil—1-3 months, in ice—up to 60 days. In an aqueous environment at a temperature of 50°C, the pathogen of typhoid fever can withstand up to 1 h, when boiled (100°C) it dies instantly. Conventional disinfectant solutions kill the microorganism in a few seconds [2].

Cholera is an acute intestinal infection caused by cholera vibrios, characterized by gastro enteric manifestations with acute dehydration of the body due to loss of water and electrolytes with vomit and liquid stool. The special severity of the disease, contagiousness, high mortality, and the propensity to epidemic and even pandemic spread served as the basis for including cholera in the group of particularly dangerous quarantine infections. Cholera pathogens multiply in the small intestine of a person. However, for some time they are able to live, and under favorable conditions, even reproduce in the external environment (biovar El-tor). Cholera vibrios are highly sensitive to temperature increase (at a temperature of 56°C, they die in 30 minutes, and at 100°C — instantly), drying, sunlight and disinfectants [2].

Finding out the cause of diarrhea is sometimes associated with significant difficulties. In acute diarrhea, epidemiological data and the results of bacteriological examination of feces (if intestinal infections are suspected) are of leading importance. In all other cases, a complete examination of the patient is often necessary to establish the diagnosis: finger examination of the rectum, rectoscopy (or colonoscopy as indicated) with a targeted biopsy, x-ray examination of the digestive tract (including irrigoscopy laboratory examination of feces. Diarrhea is one of the manifestations of acute arsenic poisoning (green vomit with the smell of garlic), mercury (mercury stomatitis and gingivitis, acute kidney failure), and poisonous mushrooms. A separate group of diarrhea is dyspepsia, which occurs as a result of digestive disorders when the diet is violated and a sharp change in diet. There are fermentation, putrefaction and soap (fat) dyspepsia. In dyspepsia, there is no General intoxication, than they differ from food toxic infections. Fermentation dyspepsia is characterized by flatulence, sour foamy stools containing a large number of starch grains and iodophil microorganisms (Lugol's solution is colored blue). Fetid putrid alkaline feces with undigested muscle fibers are observed in putrid

dyspepsia. Fat dyspepsia is recognized by the presence of neutral fat in the stool (steatorrhea) [9].

The greatest changes in immunological parameters, namely, the minimum values of secretory IgAs and the maximum concentrations of proinflammatory cytokine (IL-6) were registered among patients in the group with an unidentified etiological agent. The above-described clinical and laboratory signs, as well as the inability to identify the causative agent of infection by routine methods, suggest a high probability of participation of anaerobic flora in the development of the pathological process in the intestine [30].

Apparently, with viral-viral associations, immunodeficiency states develop, and with viral-bacterial ones, a pronounced violation of the microbial - tissue complex in the intestinal mucosa. It is obvious that the data on the combined etiology of AII require systematization. There is a need to develop and implement special approaches to the management of children with such diseases, aimed at improving the effectiveness of therapy and preventing post-infectious disorders [31].

Increased permeability of the intestinal barrier in patients with acute intestinal infection is pronounced, but reversible. Anti-positive changes in the direction of grayer excretion reflect the peculiarities of the mechanism of their transfer through the intestinal wall and confirm the expansion of paracellular transport in conditions of intestinal epithelial damage [5].

Clostridium difficile (*C. difficile*) is a known pathogen associated with diarrhea especially in hospital acquired diarrhea. Yet, it is being recognized as a probable etiology for community acquired diarrhea. The aim of the present study was to detect the presence of *C. difficile* as a pathogen causing community acquired diarrhea in children and to verify the value of different laboratory methods for diagnosis, namely specific culture, immunoassay for toxin detection, and nested polymerase chain reaction (nested-PCR) comparing nested-PCR and toxin detection with culture for detection of *C. difficile* showed an excellent accuracy of both methods. From this study, we can conclude that community acquired diarrhea due to *C. difficile* is common among children. It should be sought among the pathogens causing this infection. Rapid laboratory detection of toxin A by a rapid chromatography device is accurate compared to time consuming culture. Moreover, nested PCR for toxin B is an accurate and rapid method when it is available [32].

Among the epidemiological factors that are important in the development of infection, of great importance are: the age of the patient, the fact of hospitalization in a hospital, his profile, taking antibacterial drugs of various groups. For example, when taking antibiotics of the cephalosporin group in a hospital setting, the risk of developing *C. difficile* infection in children increases to 72.8%. In recent decades, much attention has been paid to the study of intestinal microbiosis, changes in its structure under the influence of antibiotic therapy, and the search for risk factors for *C. difficile*-infections, as well as the study of the long-term

consequences of carrying toxigenic strains in young children [33].

With a detailed analysis of the properties of pathogens of AII, the study of the causes of sudden death syndrome and other severe life-threatening pathological conditions, it becomes obvious that this figure is much higher. In many cases, a direct link between the developed complication and an episode of infectious diarrhea in the anamnesis can only be established by conducting special studies [34].

Allergic diarrhea occurs as an acute enterocolitis. Their distinctive feature is the external manifestations of allergies (Quincke's edema, urticarial, taxidermy). Sometimes occur type abdominal purpura (as in disease Henoch-Schonely purpura) and with symptoms. There are alimentary (milk, eggs, chocolate, strawberries, etc.) and medicinal (antibiotics, phenacetin, PASK, butadiene, etc.) allergic diseases that occur with diarrheal syndrome. Medicinal, as well as food, diarrhea does not always have an allergic pathogenesis. They can occur as a result of individual intolerance. In such cases, there are no allergic manifestations and no enterocolitis clinic. A similar pattern is observed with an overdose of laxatives (drug-induced diarrhea).

1. Senile diarrhea is characterized by sudden urge to stool and bowel movements immediately after taking the food. Liquid excreta is abundant and contains the remains of undigested food.
2. Acute transient character have neurogenic diarrhea (neurogenic diarrhea). Occur after a fright in emotionally labile people.
3. Chronic Diarrhea is observed mainly in chronic diseases of the digestive system. Chronic colitis may be a consequence of dietary infections, protozoan infestations, chronic intoxications. Other causes of chronic diarrhea include helminthiasis, sprue, intestinal lipodystrophy, intestinal amyloidosis (often combined with nephrotic syndrome), terminal ileitis (Crohn's disease), chronic intestinal infections (tuberculosis, actinomycosis, syphilis), non-specific ulcerative colitis, polyposis and colon cancer, small bowel carcinoid, uremic diarrhea, pellagra, gastric and pancreatic achilleic, endocrinopathy (Basedova and Addison's disease) [9].

Assessing the general clinical and epidemiological situation that has developed today with acute intestinal infections, we can note that in recent years, it is in this area of pediatric Infectology that the most noticeable changes have occurred [23]. Gastrointestinal dysfunctions in newborns and infants are successfully corrected by diet therapy and concomitant medication [4]. Our data confirm that gastroesophageal reflux disease is a common disease with a fairly frequent *Helicobacter pylori* infection of the esophageal-gastric junction mucosa and gives a high percentage of paraneoplastic complications in the esophagus in both adults and children [35].

Unfortunately, the nosology of gastrointestinal infection in 50-80% of cases remains unrecognized. Therefore, the

generally accepted classification of AII by etiology is the recommended therapeutic tactics aimed at the treatment of a specific oncological form, usually established in retrospect, they do not currently meet the needs of pediatricians. This is due to the imperfection of the bacteriological laboratory service, as well as to the increase in the specific weight of viral and parasitic intestinal infections in children, the detection of which is not available to many practical laboratories, and differential diagnosis due to the uniformity of clinical manifestations presents certain difficulties for a practical doctor, especially in the initial stage period of the disease [36].

3. Conclusions

In conclusion, we can say that the etiological aspects of acute infectious diarrhea in young children are very diverse. In addition to bacterial etiology, there is a parallel diarrhea of viral etiology and most, especially in young children, prevents food, neurogenic and medicinal. Assessing the overall etiological structure of childhood diarrhea do not forget a number of pathogens that can cause the disease by season. We learned that the variability of the epidemiological situation depends on the regularity of individual climatic conditions. The spectrum of diseases of infants remains in the majority of acute intestinal infections, which has various etiological agents. Therefore, it is very important for us to know the etiological aspects in order to preserve the health of infants and to carry out timely diagnostics, treatment and preventive measures.

REFERENCES

- [1] Basic facts of diarrheal diseases. WHO. May 2017.
- [2] Uchaykin V. F., Shamsheva O. V. Infectious diseases in children. Textbook. Moscow. GEOTAR Media. 2015.
- [3] Babayan M. L. principles of treatment of acute intestinal infections in children. Clinical pharmacology and therapy. 2014. 23(4) p. 42.
- [4] Dumova N. B., Arsentiev V. G., Bogdanov I. Yu., Ivanov D. V. Congenital sodium diarrhea. Pediatrics. 2017; 96(6): bld. 173-176.
- [5] Zhnivina N. E., Dmitriev A. V. Assessment of the status barrier of the colon in de young children with infectious diarrhea. Russian Bulletin Perinatology and Pediatrics. No. 4. 2015 page 150.
- [6] McCormick B. Fundamentals of intensive care. Russian version. Arkhangelsk, 2014.
- [7] Yaghoubi S., Shirazi MH. Profiling of Virulence-associated Factors in Shigella Species Isolated from Acute Pediatric Diarrheal Samples in Tehran, Iran. Osong Public Health Res Perspect. 2017 Jun; 8(3): 220-226. doi: 10.24171/j.phrp.2017.8.3.09. Epub 2017 Jun 30.
- [8] Mahmoudi S, Pourakbari B, Moradzadeh M. Prevalence and antimicrobial susceptibility of Salmonella and Shigella spp. Among children with gastroenteritis in an Iranian referral hospital. Microb Pathog. 2017 Aug; 109: 45-48. doi: 10.1016/j.micpath.2017.05.023. Epub 2017 May 16).
- [9] Lipatov V. A. Differential diagnosis of diarrheal syndrome (<http://drli.h1.ru>).
- [10] Zhou Y, Zhu, Characteristics of diarrheagenic Escherichia coli among children under 5 years of age with acute diarrhea: a hospital based study. BMC Infect Dis. 2018 Feb 1; 18(1): 63. doi: 10.1186/s12879-017-2936-1. 430030, China. zysun@tjh.tjmu.edu.cn).
- [11] Ikumapayi UN. Identification of Subsets of Enteroaggregative Escherichia coli Associated with Diarrheal Disease among Under 5 Years of Age Children from Rural Gambia. Am J Trop Med Hyg. 2017 Oct; 97(4): 997-1004. doi: 10.4269/ajtmh.16-0705. Epub 2017 Aug 18.
- [12] Hawash YA, Ismail KA, Almeahadi M.. High Frequency of Enteric Protozoan, Viral, and Bacterial Potential Pathogens in Community-Acquired Acute Diarrheal Episodes: Evidence Based on Results of Luminex Gastrointestinal Pathogen Panel Assay. Korean J Parasitol. 2017 Oct; 55(5): 513-521. doi: 10.3347/kjp.2017.55.5.513. Epub 2017 Oct 31.
- [13] Grau KR, Roth AN, Zhu S, Hernandez A. The major targets of acute norovirus infection are immune cells in the gut-associated lymphoid tissue Nat Microbiol. 2017 Dec; 2(12): 1586-1591. doi: 10.1038/s41564-017-0057-7 Epub. 2017 Nov 6.
- [14] Levine GA, Walson JL. Defining Pediatric Diarrhea in Low-Resource Settings. J Pediatric Infect Dis Soc. 2017 Sep 1; 6(3): 289-293. doi: 10.1093/jpids/pix024.
- [15] Gorelov A. V., Milutina L. N., Usenko D. V., 2006; Kasymov I. A., Mirismayilov M. M., Valiev A. A., 2006.
- [16] Shrivastava AK, Kumar S, Mohakud NK, Suar M, Sahu PS. Multiple etiologies of infectious diarrhea and concurrent infections in a pediatric outpatient-based screening study in Odisha, India. Gut Pathog. 2017 Apr 11; 9:16. doi: 10.1186/s13099-017-0166-0. Collection 2017.
- [17] Treatment of diarrhea: training manual for doctors and other categories of senior employees. Who, 2006: 57.
- [18] Tuychiev L. H, Eraliev U. E. Etiology of diarrheal syndrome in children. Medical journal of Uzbekistan. 2016. no. 3. Page 42.).
- [19] Akimova V. P., Andreeva L. V., Anisimova T. A., Krasnov M. V. Etiological characteristics of infectious diarrhea in children of Cheboksary in 2017. Journal Acta medica Eurasica. 2019u/ no. 1. Pages 2-4.
- [20] Daminov T. O., Tuychiev L. N., Shukurov B. V., Yusupov M. I., Kodirov S. H. Improving the effectiveness of therapy for rotavirus gastroenteritis in children., Medical journal of Uzbekistan no. 2. 2014, p. 6.
- [21] Osidak L. V., Dondurei E. A, drinevsky V. P. Acute viral infections with combined respiratory and gastrointestinal damage in children (etiology, epidemiology, diagnosis, clinical and laboratory characteristics, treatment). Training manual for doctors. Saint Petersburg, 2007.

- [22] Anganova E. V. et al. Acute intestinal infections in children of the Irkutsk region. *Children's infections* 2013. No. 2. Page 26.
- [23] Tsaregorodtsev A.D., Anokhin V. A., Khaliullina, S. V. Acute infectious diarrhea in children. Modern features of epidemiology and clinical picture of diseases. *Russian journal of Perinatology and Pediatrics* 2015. no. 4. Page 28.
- [24] Eraliev U. E. Seasonal patterns of acute diarrheal diseases in children in Uzbekistan. *Vestnik TMA* 2017. no. 1. page 134.
- [25] Shadjalilova M. S. Differentiated study of factorial analysis and evaluation of the economic efficiency of acute intestinal infections. *Pediatrics*. 2018 No. 4. p. 178.)
- [26] Kotlikov V. K., Kuzmenko L. G. Modern technologies of lactation in nursing mothers// *Pediatrician-2009*. - № 5-p. 81-84. Levine GA, Walson JL. Defining Pediatric Diarrhea in Low-Resource Settings. *J Pediatric Infect Dis Soc*. 2017 Sep 1; 6(3): 289-293. doi: 10.1093/jpids/pix024.
- [27] Brander RL, Walson JL. Correlates of multi-drug non-susceptibility in enteric bacteria isolated from Kenyan children with acute diarrhea. *PLoS Negl Trop Dis*. 2017 Oct 2; 11(10): e0005974. doi: 10.1371/journal.pntd.0005974. eCollection 2017 Oct.
- [28] Ciapponi A. Delivery arrangements for health systems in low-income countries: an overview of systematic reviews. *Cochrane Database Syst Rev*. 2017 Sep 13; 9: CD011083. doi: 10.1002/14651858. CD011083.pub2.
- [29] Darvesh N, Das JK, Vaivada T, Gaffey MF, Water, sanitation and hygiene interventions for acute childhood diarrhea: a systematic review to provide estimates for the Lives Saved Tool. *BMC Public Health*. 2017 Nov 7; 17(Suppl 4): 776. doi: 10.1186/s12889-017-4746-1.
- [30] Zaitseva, L. Yu., Khmelevskaya, and G., Kalutsky, P. V. Clinical and immunological features of the course of viral diarrhea in children. II *Bulletin of modern clinical medicine*. 2017. T 10, no. 2. Pp. 30-33.
- [31] Tkhakushinova N. H. Clinical and epidemiological features of acute intestinal infections of viral and combined etiology in children in the Krasnodar territory. *Epidemiology and infectious diseases*. Topical issue. 2016. No. 6. Page 33.
- [32] Elewa A, Sayed-Zaki ME. Evaluation of Nested Polymerase Chain Reaction and Immunoassay for Rapid Diagnosis of *Clostridium difficile* in Children with Community Acquired Diarrhea. *Clin Lab*. 2017 Feb 1; 63(2): 321-326. doi: 10.7754/Clin.Lab.2016.160606.
- [33] Mazankova A. N, Perlovskaya S. G. Antibiotic-associated diarrhea and *cl. difficile* infection in children: risk factors. *Children's infections*. 2015. №2 page 33.
- [34] Grech V, Calvagna V, Falzon A., MiJ'siul A. Fatal, rotavirus associated myocarditis and pneumonitis in a 2-year-old boy// *Ann Trop Paediatr*. 2001. Vol. 21. P. 147-148.
- [35] Dronova O. B., Tretyakov A. A. and others. Peripheral electrogaster-enterography in the diagnosis of GERD. *Manual for doctors*. M.: ID "MEDPRAKTIKA-M". 2011: 32.2.
- [36] Krivosheev B. I. Pathogenetic mechanisms of diarrhea in children and methods of its treatment. *Zh. Health of the child* 4 (55) 2014. Page 76.
- [37] Cioc A. M., Nuovo G.J. Histologic and in situ viral findings in the myocardium in cases of sudden, unexpected death // *Mod Pathol*. 2002. Vol. 15 (9). P. 914-922.) Samsygina G. A. Intestinal colic in children. M., 2000.
- [38] Stupin V. A., Smirnova G. O., Baglaenko M. V., Siluyanov S. V., Zakirov D. B. Peripheral electrogastroenterography in the diagnosis of disorders of the motor-evacuation function of the gastrointestinal tract. *The attending physician*. - 2005; 2: 60-62.