JMS 2021; 4(3):40-48
UDC:616.33/.34-002-053.2

ACUTE GASTROENTERITIS IN CHILDREN

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Abstract

The aim of the study was to investigate the most frequent etiology of AGE in children admitted at our hospital, and the correlation with severity of clinical manifestation.

The study was designed as a prospective study, and we examined 219 pediatric patients with AGE admitted at the University Children's Hospital–Skopje. The diagnosis of AGE was based by the definition for AGE as a decrease in the consistency of stools (loose or liquid), and/or an increase in the frequency of evacuations (typically >3 in 24 hours), with or without fever or vomiting. The stool specimens were examined using the new multiplex polymerase chain reaction–based rapid diagnostic test–Film Array Gastrointestinal panel test. White blood cell levels (10^3/ul) and hemoglobin levels (g/dL), were determined by using the flow citometry method on Sysmex xs 800i/1000i. Iron levels (μmol/L) were determined by using the biochemistry analyzer Architect c4000 Abbott.

Statistical analysis confirmed significantly different values of stool isolation: viruses and bacteria in the groups $p<0.001$. The stool parasites were insignificant $p>0.05$. Statistical analysis confirmed significantly different values of WBC levels in the groups $p<0.001$. Statistical analysis confirmed significantly different values of iron levels in the groups $p<0.001$. Statistical analysis confirmed significantly different values of hemoglobin levels in the groups $p<0.001$.

Film Array Gastrointestinal panel test is a useful tool in the rapid diagnosis of gastrointestinal pathogens in pediatric patients with acute gastroenteritis.

***Keywords*:** Acute gastroenteritis (AGE), pediatric patients immunocomtentence, pediatric patients, immunocompromised, Film Array Gastrointestinal panel test.

Introduction

Acute gastroenteritis (AGE) is generally defined as a decrease in the consistency of stools (loose or liquid) and/or an increase in the frequency of evacuations (typically 3 in 24 hours), with or without fever or vomiting. Diarrhea typically lasts less than 7 days and no longer than 14 days [1].

The best indicator of diarrhea, especially in the first year of life, is the consistency of the stool, as opposed to the frequency of evacuations. The incidence of diarrhea ranges from 0.5 to 2 episodes per child per year in children <3 years in Europe [2].

The type of etiological agent of AGE varies and depends on the immune competence of the children. Causes of AGE can be: viral, bacterial and parasitic. The most frequent cause of AGE in immunocompetent children from viral agents is the Rotavirus. The incidence of rotavirus AGE is low in countries where oral rotavirus vaccination, Rotarix and RotaTec are carried out. The most common bacterial causative agents in immunocompetent children are Salmonella or Campylobacter, depending on the habitat. While from viral agents in immunocompromised children, the most common are Adenovirus, Rotavirus, Norovirus, Astrovirus and Sapovirus [3-5].

From bacterial pathogens in those children the most common are: Clostridium difficile, Escherichia coli, Salmonella spp, Shigella spp and Aeromonas spp [6]. While the most common parasitic causes are: Cryptosporidium spp, Entamoeba histolytica, Cryptosporidium spp and Giardia lamblia [7].

There is a relationship between the severity of the clinical feature, the etiological factor of diarrhea and immune competence of the children. Moreover, there is a correlation between host risk factors and the occurrence of severe diarrhea.

The risk factors of the host include the age of the children under 3 years, under 6 months of age are especially with dehydration, metabolic disorders of the internal environment, as well as with prolonged hospitalization.

Risk factors also include the presence of other chronic diseases or immunodeficiency in the child. Medical evaluation and treatment should be performed in children with AGE who have another chronic illness, in children less than 6 months of age, children with persistent vomiting, with severe diarrhea with more than 8 stools per day, and in children with clinical signs of severe dehydration.

AGE is common in immunocompromised children and occurs as a result of malnutrition, as a result of an underlying disease, immunosuppression as a result of therapy, and non-infectious etiology, such as mucositis [8].

This group of children often requires prolonged hospital treatment due to the severe clinical presentation, as well as significant morbidity and mortality. In contrast to immunocompetent children with AGE, enteropathogens in immunocompromised children cause severe, disseminated infections, long-term illness, and a prolonged period of asymptomatic shedding [9].

Clinical laboratories use different methods of stool isolation: bacterial, parasitic, and viral causes of acute gastroenteritis, a methodology that suffers from poor sensitivity, potentially long turnaround times, and complicated ordering practices and workflows. We used rapid and accurate diagnostic tools for appropriate management of the diseases.

This way of identifying the pathological causes of AGE, in contrast to conventional techniques, contributes to timely results, greater specificity, greater analytical sensitivity, as well as the ability to quickly detect a wide range of enteropathogens simultaneously [10].

Film Array Gastrointestinal panel test is a PCR based assay that detects 22 different enteric pathogens, including five viruses (Adenovirus F 40/41, Astrovirus, Norovirus GI/GII, Rotavirus A, and Sapovirus (I, II, IV, and V))[11]. These new diagnostic tests offer the opportunity to obtain a more comprehensive picture of the epidemiology of infectious AGE in immunocompromised children.

Most often in children with AGE, proof of a microbiological causative agent is not required, except in certain conditions where microbiological investigations of the causative agent are necessary in diagnosis and treatment [12].

The aim of the study was to investigate the most frequent etiology of AGE in children admitted at our hospital, and correlation with severity of clinical manifestation.

Material and Methods

Study population

The study was designed as a prospective study and we examined 219 pediatric patients with AGE, admitted at the University Children's Hospital–Skopje, during the period from December 2018 until December 2020.

The inclusion criteria for admittance in pediatric patients with AGE were: dehydration, vomiting, seizures, lethargy, tachycardia, electrolyte imbalance, anemia, metabolic acidosis, haemolytic uraemic syndrome. The diagnosis of AGE was based by the definition for AGE as a decrease in the consistency of stools (loose or liquid) and/or an increase in the frequency of evacuations (typically >3 in 24 hours), with or without fever or vomiting.

Diarrhea typically lasts less than 7 days and not longer than 14 days. (ESPGHAN 2008).

The pediatric patients with AGE were divided into two groups. The first group included immunocompetent pediatric patiens with AGE aged 0 to 14 years. The second group included immunocompromised pediatric patients (severe malnutrition, hemato-oncology, cardiologic and neurologic patients) with AGE aged from 0 to 14 years.

Study design

The laboratory tests were done at the Clinical Laboratory at the University Children's Hospital, which included white blood cell (WBC) levels, hemoglobin levels, iron levels, blood gas analysis and stool isolation taken at admission.

White blood cell (WBC) levels (10^3/ul) and hemoglobin levels (g/dL), were determined by using the flow citometry method on Sysmex xs 800i/1000i, iron levels (μmol/L) were determined by using the biochemistry analyzer Architect c4000 Abbott.

The stool specimens were examined using the new multiplex polymerase chain reaction–based rapid diagnostic test Film Array Gastrointestinal panel test. Samples for 200 μl of stool re-suspended in Cary-Blair transport medium, were taken at admission. Samples were diluted in a sample buffer in the sample injection vial.

The Film Array GI Panel test consists of automated nucleic acid extraction, reverse transcription, amplification and analysis, with results available in 1 h per run per specimen.

Statistical analysis

The material was statistically analyzed using the methods of descriptive statistics. Data analysis was performed in a Statistic program 7.1 for Windows and SPSS Statistics 23.0, to compare the means of the variables, one-way ANOVA test. For all analyses, p value < 0.05 was taken as statistically significant.

Results

In our study, we examined 219 (M:F=121:98) pediatric patients with AGE, admitted at the University Children's Hospital–Skopje, during the period from December 2018 until December 2020. There is no significant difference depending on gender between the two groups ($p>0.05$) Friedman ANOVA. There is an equal representation of both genders.

The pediatric patients with AGE are divided into three age groups: 0-1 years, 1-6 years and 6-14 years. There is a significant difference in this parameter between the three groups ($p<0.001$) Friedman ANOVA. The highest average levels (3±2.61) were found in the 1-6 years age group.

There is a significant difference depending on the place of living between the two groups ($p<0.001$) Friedman ANOVA. The higher than average levels were found in the group of pediatric patients from rural living environments.

Statistical analysis confirmed significantly different values of WBC levels in the groups $p<0.001$ (Figure 1).

The highest average levels (16.83±9.64) 10^3/ul of WBCs were measured in the first group of pediatric patients with AGE, in correlation with the second group of pediatric patients with AGE(3.85±4.24)10^3/ul, where they very lower.

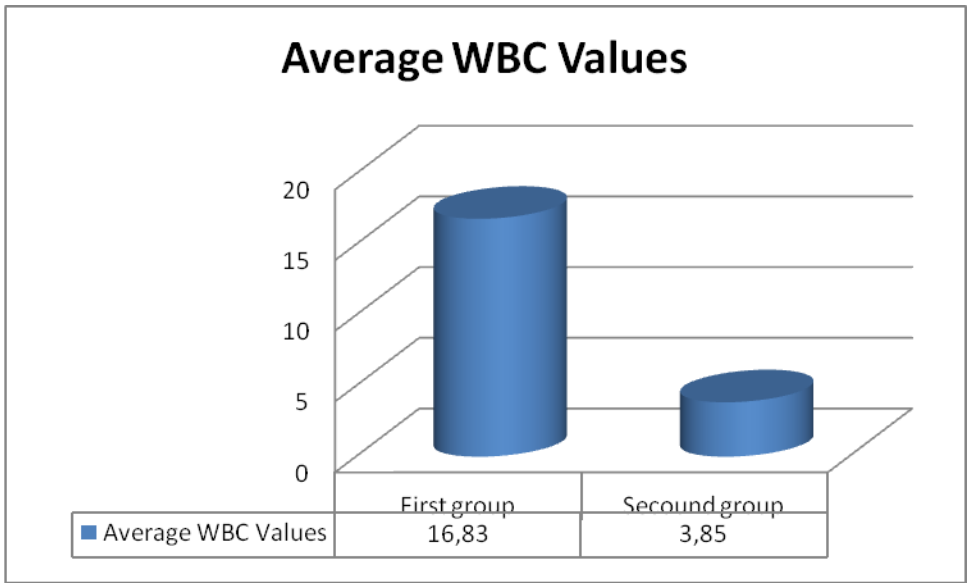

Figure 1. Distribution of average WBC levels in the pediatric patients with AGE proven with stool isolation in both groups.

Statistical analysis confirmed significantly different values of hemoglobin levels in the groups $p<0.001$ (Figure 2). The highest average levels (10.02±2.14) g/dL of hemoglobin were measured in the first group of pediatric patients with AGE, in correlation with the second group of pediatric patients with AGE (9.05±1.24) g/dL, where they were slightly lower.

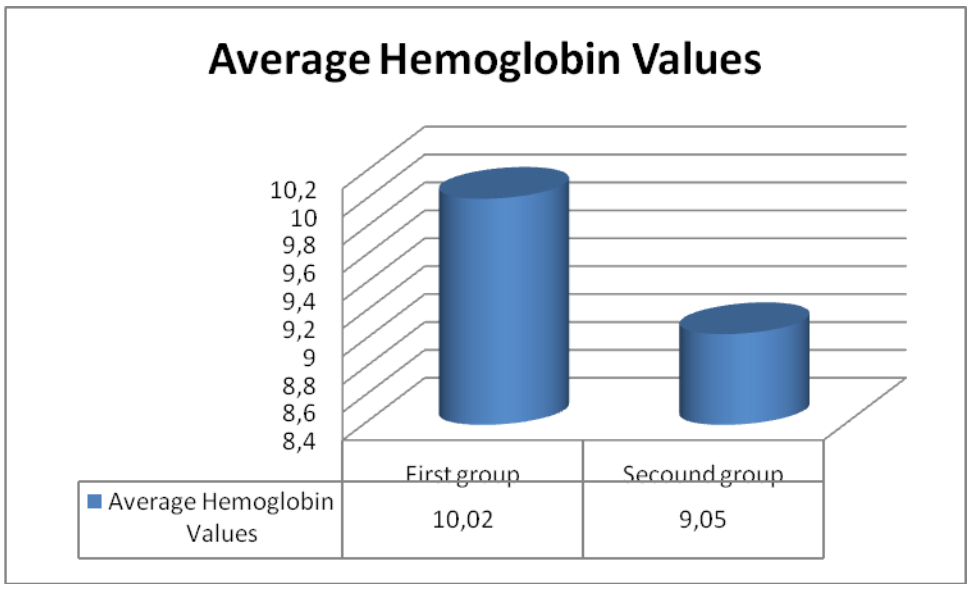

Figure 2. Distribution of average hemoglobin levels in pediatric patients with AGE in both groups.

Statistical analysis confirmed significantly different values of iron levels in the groups $p<0.001$ (Figure.3). The highest average levels (6.12±2.21) µmol/L of iron levels were measured in the first group of pediatric patients with AGE, in correlation with the second group of pediatric patients with AGE (4.15±2.24) µmol/L, where they were lower.

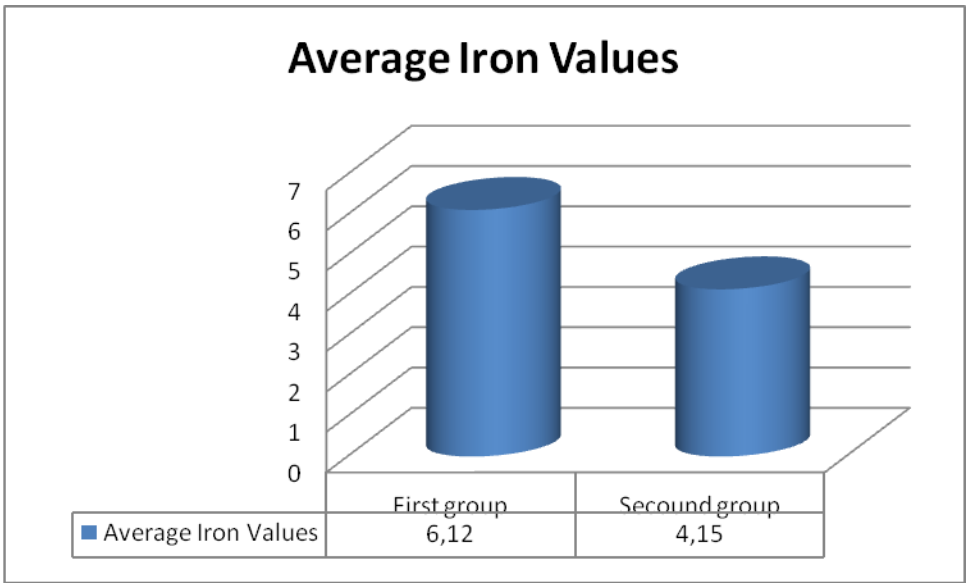

Figure 3. Distribution of average iron levels in the pediatric patients with AGE in both groups.

Statistical analysis confirmed significantly different values of stool isolation: viruses and bacteria in the groups $p<0.001$ (Figure 4). The viruses from stool isolation are most frequent in the first group of immunocompetent pediatric patients with AGE, in correlation with the second group of immunocompromised patients, while the bacteria from stool isolation are most frequent in the second group of immunocompromised patients, in correlation with the first group of immunocompetent pediatric patients with AGE. The parasites from the stool were insignificant $p>0.05$.

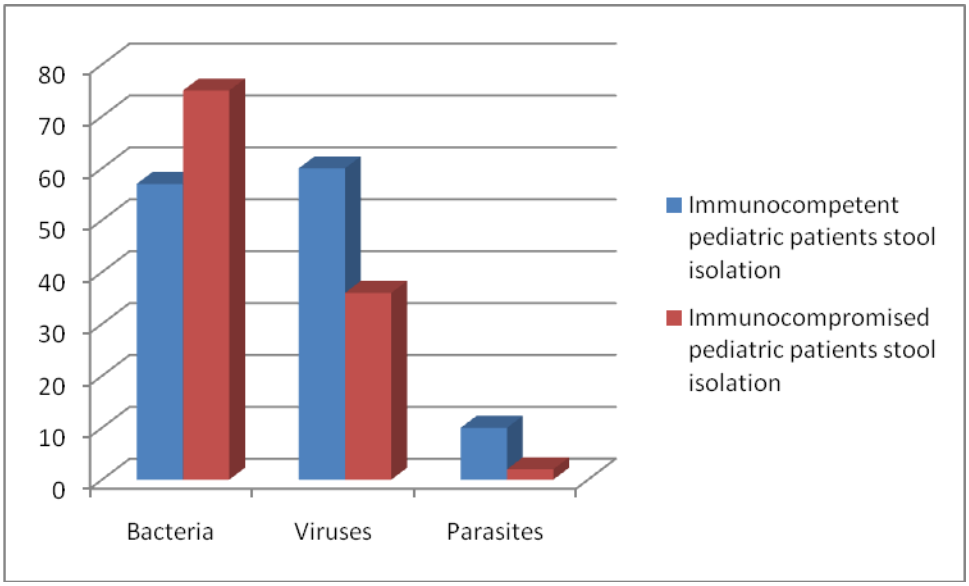

Figure 4. Distribution of stool isolation in the pediatric patients with AGE in both groups.

In Figure 5, we display that Rotavirus was the most frequent stool isolation at immunocompetent pediatric patients with AGE, and the bacteria Clostridium difficile (Toxin A/B).

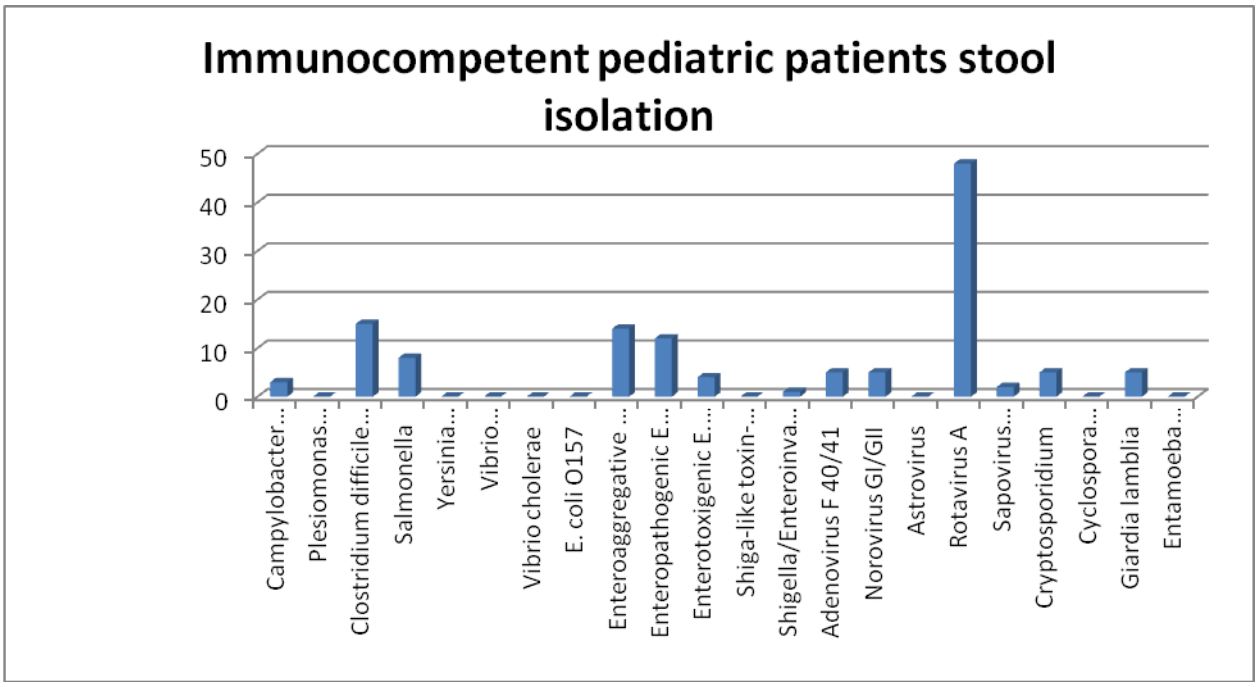

Figure 5. Distribution of stool isolation of the GI panel in the immunocompetent pediatric patients with AGE.

In Figure 6, we show that Norovirus was the most frequent stool isolation in immunocompromised pediatric patients with AGE, and the bacteria Clostridium difficile (Toxin A/B).

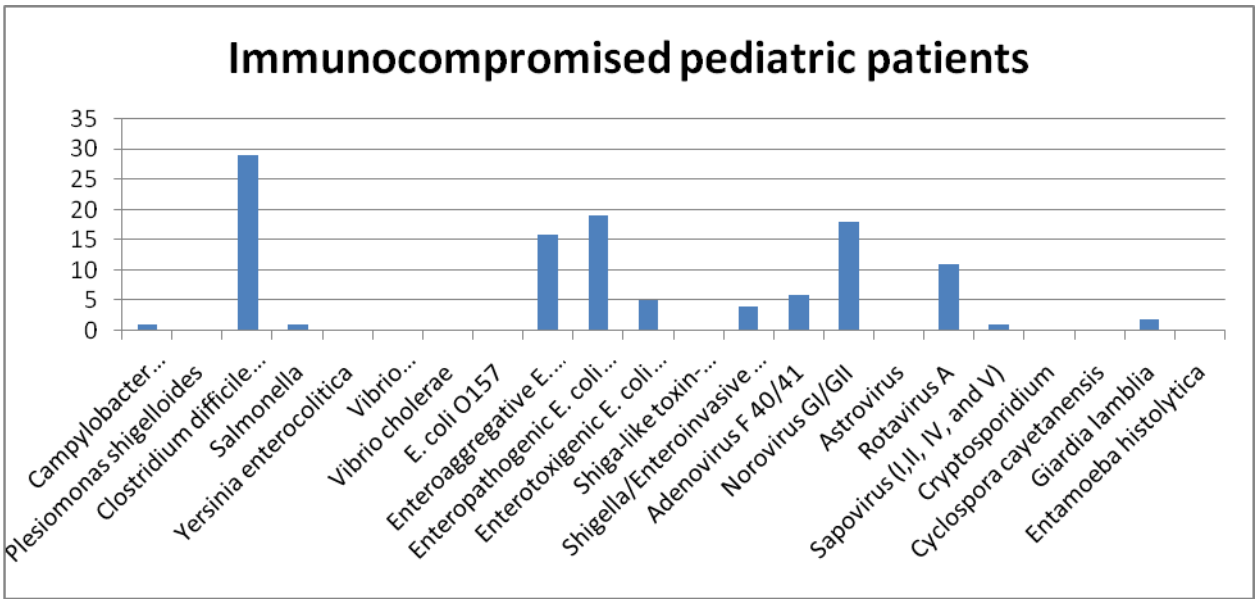

Figure 6. Distribution of stool isolation of GI panel in immunocompromised pediatric patients with AGE.

Capillary blood test findings show lower mean pH and bicarbonates in immunocompromised pediatic patients with AGE, compared with immunocompetent pediatric patients with AGE (7,19±0,18 versus 7,21±0,19).

Average serum albumin values showed lower values in immunocompromised pediatic patients with AGE, compared with immunocompetent pediatric patients with AGE (26,21±3,1g/L versus 33.72±5,4g/L). Average total serum protein values showed lower values in immunocompromised pediatic patients with AGE, compared with immunocompetent pediatric patients with AGE (47,01±5,2g/L versus 50.21±5,7g/L).

Discussion

In our study, we have examined a total of 219 pediatric patients (M:F=121:98) with AGE. Depending on the gender, there was no significant difference in this parameter between the two groups as data from the literature [13].

AGE is still a major cause of mortality and morbidity in children under 5 years of age, especially in developing countries. The pediatric patients were divided into three groups of age: 0-1 years, 1-6 years and 6-14 years.

There was significant difference in this parameter between the three groups of patients. The most frequent group was the group from 1-6 years, as data from the literature [14].

In the study, Abba wrote about risk factors for severe diarrhea that include the age of the child, patients under 3 years, especially under 6 months of age, are associated with dehydration, metabolic disorders of the internal environment, as well as with prolonged hospitalization. Another risk factor for severe diarrhea is feeding, where breastfeeding has a protective role in developing a severe clinical feature [15].

Distribution of pediatric patients with AGE proven stool isolation, depending on their place of living, shows higher levels with pediatric patients from the rural living environment. This is due to the lower living and hygiene standards. Good hygiene, like handwashing and cleanliness are important, but are not enough to control the spread of the disease.

Bacteria, viruses and other pathological agents are transmitted by the fecal-oral route. Socioeconomic factors play an important role in the occurrence of this disease, and is associated with an increased incidence of its occurrence, more severe clinical manifestation and prolonged diarrhea. Statistical analysis confirmed significantly different values of WBC levels in both groups, especially higher values in the group of immunocompetent pediatric patients. Statistical analysis confirmed significantly different hemoglobin values and iron levels in both groups, especially in the group of immunocompromised pediatric patients [16].

In our study, we show that the viruses were more frequent in immunocompetent pediatric patients with AGE, while bacterial isolation were more frequent in immunocompromised pediatric patients with AGE. The parasites were detected in few patients in both group. Viruses are the most common agents for AGE, accounting for >60% of pediatric cases, followed by bacteria and parasites.

The prevalence of individual pathogens varies widely between geographic areas and different age groups, but globally RV infection remains the leading cause of diarrhea in children younger than 5 years [17,18].

Rotavirus is the most common cause of AGE in children in our study, as well as in all European countries. A comprehensive literature search in Western Europe showed an incidence of rotavirus gastroenteritis as high as 1.33 to 4.96 cases/100 persons year.

Hospitalization rates for rotavirus gastroenteritis ranged from 7% to 81% in various countries. The percentage could be higher if stool examination was routine for all patients with AGE (2014). Norovirus, generally considered the second leading agent of AGE, is fast becoming a leading cause of medically attended gastroenteritis in countries with high rotavirus vaccine coverage [18,19].

In our study, in immunocompromised pediatric patient, with AGE, the most frequent agents were bacterial, leading with Clostridium difficile, which is in correlation with literature [20-22].

The most common complication of AGE in children is metabolic acidosis and disturbance of gas blood analysis and electrolyte imbalance [23,24].

Conclusion

Film Array Gastrointestinal panel tests are a useful tool in the rapid diagnosis of gastrointestinal pathogens of pediatric patients with acute gastroenteritis.

Rotavirus is the most common cause of AGE inimmunocompetent pediatric patients in our study, while Norovirus is the most common cause of AGE in immunocompromised pediatric patients. Clostridium difficile is the most common bacterial cause of AGE in pediatric patients.

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