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RESEARCH ARTICLE

HYDROELECTROLYTIC IMBALANCES IN CHILDREN'S NOROVIRUS INFECTION

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Abstract: Worldwide, after rotavirus, norovirus (NoV) is the second most important virus that induce diarrheal disease in children and is estimated to be responsible for 17% of acute diarrhea in people of low socioeconomic status. The aim of this study was to establish the prevalence of NoV infection in children admitted to the Emergency Clinical Hospital for Children ,,St. Ioan". During August to December 2021, NoV isolated from feces, as well as the association of NoV with other viral or bacterial digestive infections was retrospectively evaluated. The paraclinical diagnosis was made with the help of immunochromatographic tests, being supported by the haematological and biochemical tests, as well as with clinical data. For a number of 328 patients hospitalized in the Emergency Clinical Hospital for Children ,,St. Ioan", 30 patients were positive to NoV, from which 3% also associated infection with *Clostridium difficile* for GDH-antigen and Toxin A, and 9% presented co-infection with *Campylobacter* spp. This study highlights the local situation regarding the incidence of Norovirus species, co-infections with Rotavirus and Adenovirus, as well as bacterial co-infections. For children infected with NoV included in the study, changes were found regarding the hydro-electrolytic and acid-base balance, observing losses of electrolytes and bicarbonates (43% of the patients showed decreases in the alkaline reserve, as well as 12% decreases in sodium and 10% had elevated levels of potassium) being

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associated with water losses suffered depending on the duration and frequency of diarrheal stools, vomiting. Acute diarrheal disease surveillance is an important tool for updating local protocols and the local strategy for managing these infections.

Keywords: norovirus; children; acute gastroenteritis.

Introduction

The term acute infectious gastroenteritis represents the increase in the frequency of stools (more than 3 stools per day), the decrease in their consistency, often accompanied by fever or vomiting. Infectious pathology is most often caused by viruses, bacteria and less often by parasites or fungi (Ciofu, 2021).

Gastroenteritis is a topical problem due to the high frequency of diarrheal episodes, especially among children under 5 years old, representing the second cause of infant death after respiratory system infections. Norovirus (NoV) is a highly contagious virus. The most common way of transmission is contact with infected persons or fecal-oral route. History plays an important role in the diagnosis of acute gastroenteritis, being able to reveal food mistakes (consumption of contaminated food, food such as green leafy vegetables, fresh fruit and crustaceans, but any food that is served raw that can become contaminated at any time during manipulation). Transmission through contaminated water is less common but may be possible when drinking or recreational water is not chlorinated. Viral shedding occurs mainly 2 to 5 days after infection and is mainly present in stool and vomitus (Minesh, 2019).

Diarrhea of viral origin is the most common cause of gastroenteritis, causing great hydro electrolytic imbalances. The most common viruses involved in the production of acute diarrhea are: rotavirus, norovirus, enteric adenovirus, calicivirus, astrovirus. Diarrhea has a particular impact especially on young children, causing for over two billion deaths annually for 0–5-years-old group. Due to dehydration, 300 deaths have been reported annually in the US in children under 5 years old (Ciofu, 2021).

Globally, after rotavirus infection, norovirus is the second most important cause of viral diarrheal disease in children of 0-5 years old group (Operario, 2017). NoV infections are responsible for 12% of severe diarrhea and up to 200,000 deaths in children under 5 years old in low-income countries (Patel, 2008). However, recent studies estimate that NoV is responsible for

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16-18% of acute diarrhea globally in children under 5 years old (Ahmet, 2014; Nguen, 2017). NoV are non-enveloped viruses, from the family *Caliciviridae*, genus *Norovirus*, with an ssRNA genome in the positive sense, with a particle diameter of >30nm, with a single structural protein (Cernescu 2008; Chhabra, 2019).

Sources of infection include ingestion of contaminated water or food, but also direct transmission from a contaminated surface or from an infected person. The virus is resistant and can survive on surfaces even after disinfection (Esposito, 2020).

The severity of the diarrhea is given by the intensity of the acute dehydration syndrome, loss suffered through the digestive tract. Both water and electrolytes are lost through diarrhea and vomiting, and if the oral intake is not sufficient to compensate for the losses, important imbalances appear. The seriousness of the development of diarrheal disease in children is given in particular by these electrolyte and acid-base imbalances that determine the onset of dehydration, hypovolemia, metabolic acidosis and, in serious cases, central nervous disorders. Rapid treatment is necessary to prevent death (Ciofu, 2021).

The aim of this study is to describe the prevalence of NoV infection in children hospitalised to the Emergency Clinical Hospital for Children „St. Ioan", as well as the association of NoV with other viral or bacterial digestive infections.

Materials and methods

The study carried out represents a retrospective analysis of gastroenteritis caused by NoV infection. The pathological products were collected from children aged between 0-18 years old hospitalized in the Emergency Clinical Hospital for Children „St. Ioan", Galati between August and December 2021.

The collection was made from the spontaneously emitted stool samples. In order to confirm the presence of Norovirus, the stool samples were tested using immunochromatographic tests. The positive result indicates the presence of the virus, but the negative result does not necessarily indicate its absence, but probably the passing of the acute phase of the disease, because the number of virus particles can reach below the detection limit of the test used. The simultaneous presence of other viruses (rotavirus, adenovirus), bacteria (*Campylobacter* spp., *Clostridium difficile, Helicobacter pylori*), was tested with immunochromatographic tests. Parasites (through the

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coproparasitological examination) and the coprocytogram was tested with optic microscopy for the differential diagnosis of acute diarrheal syndromes were monitored in parallel.

The interpretation of the results was carried out in a clinical context, following the dynamics and paraclinical investigations of haematology, biochemistry and immunology. The blood counts were performed on the automatic haematology analysers Celltak MEK 6400K and Mindray BC 6200, which perform the counts of leukocytes, red blood cells, platelets and the leukocyte formula.

Through dry biochemistry (Vitros 4600 analyser), the following parameters were determined: alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline reserve, C-reactive protein, sodium, glucose. The biological reference ranges of the mentioned parameters are the following: sodium 137-145 mmol/L, potassium 3.5-5.2 mmol/L, alkaline reserve 22-30 mmol/L, C-reactive protein 0-0.5 mg/dL, glucose 70-106 mg/dL, ALT 5-25 U/L and AST 14-36 U/L.

The results were collected in the hospital's databases and statistically processed with the help of Microsoft Excel.

Results and discussion

From the total of 328 patients hospitalised in the Emergency Clinical Hospital for Children „St. Ioan", between August and December 2021, tested with norovirus antigen, 30 patients had a positive result.

An increase in the frequency of the present NoV was observed since September to October (Fig.1) for the age groups 1-4 years (70%), the moment that coincides with the period when children enter in the community (nursery, kindergarten) (Minesh, 2019). The age group of 5-9 years shows a decrease in frequency of up to 17%, being followed by the age groups of 10-14 years and children over 15 years of age that show a frequency of up to 3% (Fig.2). The group of patients studied presented a higher percentage for the male sex (57%), compared to the female sex (43%). Similar studies from Mozambique showed that the majority of *Norovirus* positive children were under 2 years old (87.3%), with a higher detection in male patients 57.8% (Chilaúle, 2022).

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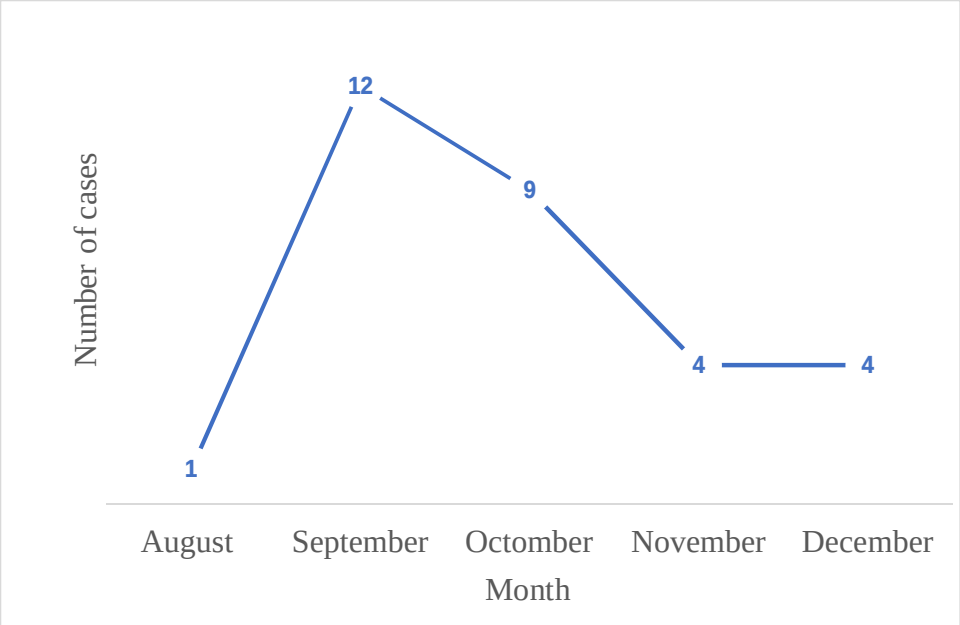

Fig. 1. Distribution of *Norovirus* infection cases by month

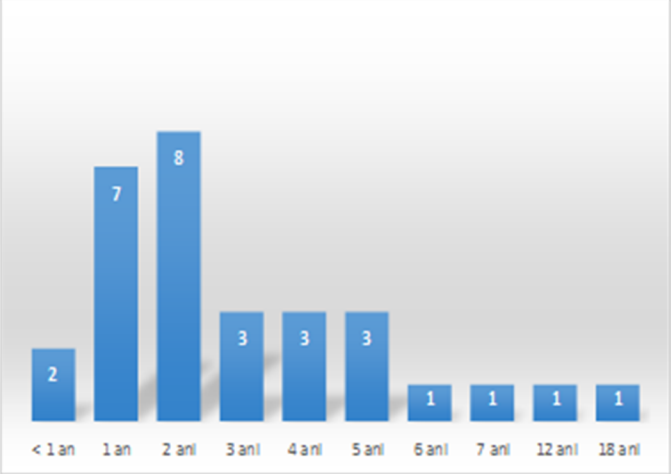

Fig. 2. Norovirus positive cases related to age groups

Compared to the area of origin, male urban patients represented 58%, and female 42%. The male gender had a higher percentage also among the patients from rural areas (55%), compared to the female gender (45%). In Figure 3 it can be seen that of the total number of patients according to the source, 63% are from the urban zone and 37% from the rural zone.

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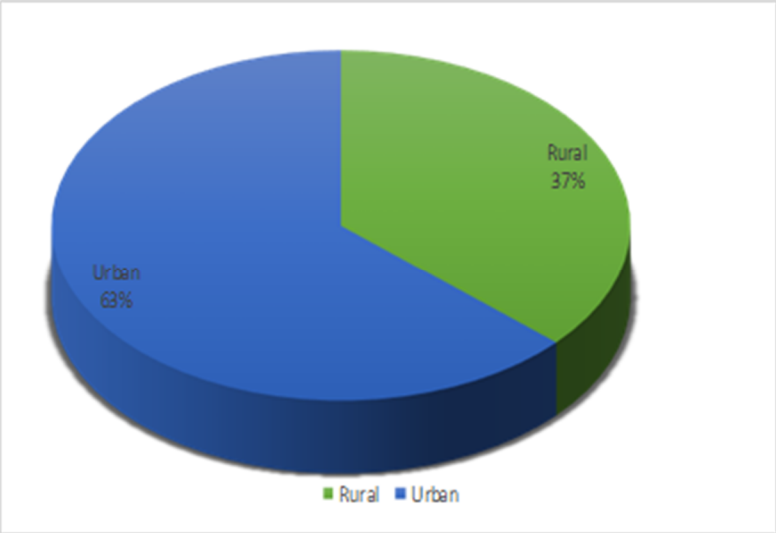

Fig. 3. The environment of origin of patients with NoV infection

The distribution of cases according to the reason for presentation to the hospital showed an increased percentage for digestive system complaints, compared to the symptoms of the accompanying respiratory system and digestive complaints. 67% of the patients presented to the emergency department complained of abdominal pain, fever, diarrhea, vomiting, 27% complained of cough, rhinorrhea, diarrheal stools and 6% had a skin rash accompanied by diarrhea. Out of the total number of patients who complained of abdominal pain, diarrhea, vomiting at admission, 17% presented diarrheal stools with streaks of blood. Similar studies were carried out in Ukraine according to which the basic symptoms were vomiting, diarrhea, hyperthermia. Clinical manifestations of upper respiratory tract symptoms have been described in addition to those of gastroenteritis: acute rhinitis, pharyngitis, tracheitis and tonsillitis (Soloviov, 2022).

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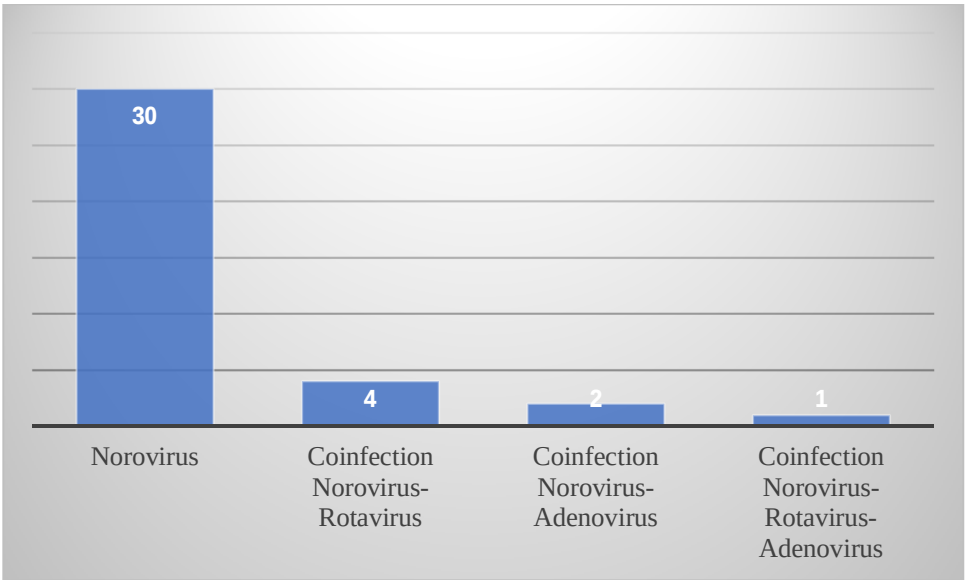

Fig. 4. Cases of NoV and confections with Rotavirus/Adenovirus

For hospitalized patients, immunochromatographic tests were used to determine the presence of Norovirus, Rotavirus and Adenovirus. The simultaneous presence of Norovirus-positive patients was observed, four patients presented NoV-Rotavirus co-infection, two patients Norovirus-Adenovirus, and one patient presenting all three viruses (Fig 4). Of the total number of patients with positive Norovirus, 3% also associated infection with *Clostridium difficile* for GDH-antigen and toxin A, and 9% presented co-infection with *Campylobacter spp*.. Also, 14% of patients were also tested for *Helicobacter pylori*, 5% being positive.

The coprocytogram in 80% of cases showed no changes (rare or very rare leukocytes) and in 20% of cases frequent or relatively frequent polymorphonuclear leukocytes were detected. Coproculture was positive with *Salmonella spp*. in 3% of cases.

An increase in the number of leukocytes (77% of the total) was observed from the blood counts performed on hospitalized patients. The distribution of the absolute values of the lymphocytes revealed a 10% increase over their reference limit and only in 7% of cases were decreased.

Taking into account the fact that white blood cells (WBC) are involved in the body's defense system, these increases recorded in children are in their favour, relevant to the fight against pathogens.

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Laboratory tests were also performed for other inflammatory markers such as C-reactive protein, a protein synthesized by the liver in response to tissue damage, infection and inflammation. In the study, an increase in CRP was observed in 63% of hospitalized patients, reaching a maximum value of 28.44 mg/dL. CRP increases have been reported in patients who had *Salmonella spp*. infections, but also in those with *Clostdridium difficile* and *Campylobacter spp*.

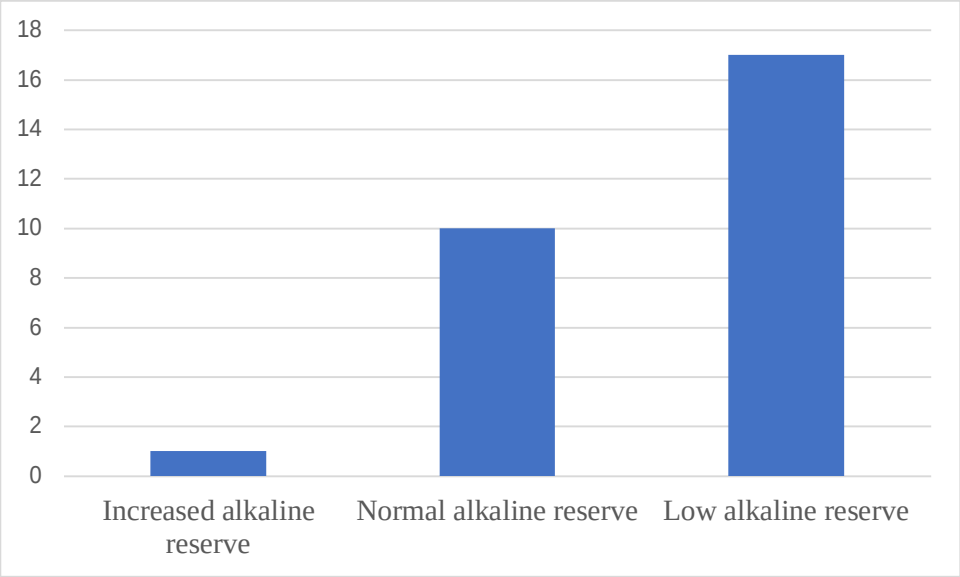

Fig. 5. Alkaline reserve values in patients infected with Norovirus

In Figure 5 it can be seen that from the total of 30 patients, the alkaline reserve at the time of admission had normal values for 15 patients, 13 patients had low values and two patients had high values. A decrease in the alkaline reserve at the time of hospitalization is noted, due to the acid-base imbalances that have occurred, being frequently encountered in infections, acute diarrhea. Along with these losses, a slight electrolyte imbalance is also observed. The sodium values in the patients included in the study varied between 121-144 mmol/L resulting in decreases in 12% of them, hyponatremia found in chronic diarrhea or severe vomiting, dehydration when a large amount of electrolytes including sodium is lost. The body tries to maintain its functionality from the intravascular level, the losses occur mainly from the extracellular space. The electrolyte balance is disturbed due to the loss of water and electrolytes. The ratio between the two allows the classification of dehydration into hypotonic, isotonic and hypertonic. In actual study, the loss of Na is noted, which leads to a hypotonic dehydration, predominantly extracellular. Also, potassium

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varied between 3.81-6.67 mmol/L (10% had elevated levels). Particular attention must be paid to potassium values, both hypo and hyperkalemia can have serious effects such as fatal cardiac arrhythmias. Electrolyte and bicarbonate losses, kidney damage due to severe dehydration, collapse can lead to metabolic acidosis with the accumulation of acids and the loss of bases.

Regarding the value of transaminases, the study revealed an increase in them as follows: TGP/ALT being increased in 10% of hospitalized patients and TGO/AST showed an increase in 38% of them. Glucose increased in 20% of the patients included in the study.

Treatment of gastroenteritis usually begins at home with replacement of fluid losses. Children under 6 months old or with a history of premature birth or chronic medical conditions in which diarrhea and vomiting are persistent require medical evaluation.

A thorough history and physical examination are performed to assess the level of dehydration and possible weight loss. Depending on the degree of dehydration, the treatment includes 2 phases: rehydration (in the first 3-4 hours) and maintenance (refeeding and returning the patient to an age-appropriate diet). Infants continue to be breastfed throughout treatment, plus the use of oral rehydration solutions which contain carbohydrates., sodium, potassium, chloride and bicarbonate to restore electrolyte balance and osmolarity. In cases of severe vomiting that prevents oral rehydration, intravenous fluids can be administered. Adjunctive treatments such as analgesics, antiemetics, antimotility, antisecretory and probiotics are also used.

Conclusions

This study highlights the local situation regarding the incidence of NoV species, co-infections with Rotavirus and Adenovirus, as well as bacterial co-infections. Acute diarrheal disease surveillance is an important tool for updating local protocols and the local strategy for managing these infections. Alkaline reserve values showed significant changes, more than half of all patients included in the study presenting low values. Slightly modified values of sodium and potassium were also recorded. Thus, hydro electrolytic rehydration confirms the urgency it has in the case of diarrhea and vomiting to prevent dehydration that has the power to set in quickly. Parameters such as WBC, CRP showed increased values in most patients, which confirmed the inflammatory and infectious nature of the digestive condition. Corroboration of paraclinical investigations with clinical data could speed up identification and reduce patients' healing and hospitalization time. This retrospective analysis is useful in epidemiology studies and in the

identification of effective solutions for early detection and reduction of the incidence of potentially lethal viral digestive infections.

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