Epidemiological and clinical profiles of acute diarrhea due rotavirus in children aged 0-71 months hospitalized at Kalembe-lembe pediatric hospital in Kinshasa, Democratic Republic of Congo

Clément M. Mbadiko[1], D. Mutambel' Hity S.N.[2], Gracia K. Mbuyi[3], Erick Bukaka[1], Ruth Claudine Tshiama[??], Gédéon Ngiala Bongo[1]

[1]Department of Biology, Faculty of Sciences, University of Kinshasa, Kinshasa; [2]Department of Biology, Faculty of Sciences, National Pedagogical University, Kinshasa; [3]Teaching and Administration in Nursing Care, Nursing Science, Higher Institute of Medical Techniques, Kinshasa, Democratic Republic of Congo

Summary

This research is based on a retrospective analysis of medical records filed in the archives of the emergency departments of Kalembe-lembe Hospital in the provincial city of Kinshasa in the Democratic Republic of Congo. The study involved 324 records of patients aged 0-71 months admitted to the emergency departments and hospitalized for acute diarrhea from January the 1st to December the 31st, 2015. The aim was to inventory the cases of rotavirus diarrhea and/or other germs (individually or in combination) to study their epidemiological and clinical aspects. Thus, the epidemiological and clinical parameters (age, sex, season, symptoms, frequency and physical aspects of stools, dehydration status and duration of hospitalization) of diarrheic children diagnosed as positive for rotavirus were compared with those infected with other germs (individually or in combination with rotavirus or other viruses). The search for the etiological agents of the diarrhea was performed in 56.48% of the cases. The results of this work allowed us to show: (i) a predominance of infections by viruses (69.94%) including rotavirus (48.08%), (ii) high rates of infections by etiological agents of diarrhea including rotavirus in children under 12 months, (iii) a high proportion of vomiting, (iii) a high proportion of vomiting, fever, physical asthenia and restlessness or frequent and liquid stools or moderate dehydration in children infected with rotavirus, (iv) specific clinical pictures according to the etiological agents of diarrhea or their combinations.

Introduction

Acute childhood diarrhea is a global public health problem because it is responsible for significant mortality in developing countries (15). According to the World Health Organization (WHO), 1.5 million children died from acute diarrhea worldwide in 1999 (21); this is significantly lower than the figure reported in 1980, which reported 4.6 million deaths (14). Diarrhea is one of the leading causes of child mortality, especially among children under 5 years of age (14). In industrialized countries, acute diarrhea causes 3 to 4 million medical consultations and is the second leading cause of childhood hospitalization, with 7 to 10% of hospitalizations before the age of 5. The annual incidence of acute childhood diarrhea in these countries is estimated at between 1.3 and 2.3 episodes per child (3,14,1). In developing countries, diarrhea is a major cause of mortality and morbidity (1.4 to 2.5 million deaths in 2000), with an annual incidence of 3 to 9 episodes per child (12,14,23,6), corresponding to 2 to 4 times more than among children in industrialized countries. Children under 5 years of age have 1.5 annual episodes of acute diarrhea (23). Among the main infectious causes of acute diarrhea, viruses including rotavirus are important (26,15).

Globally, rotavirus is the cause of 37% of diarrhea deaths in children under five years of age. It causes more than 450,000 deaths each year, with nearly 95% of rotavirus-related deaths

occurring in developing countries where access to treatment is limited or non-existent. Rotavirus cannot be cured by antibiotics or other drugs (23). Rotaviruses cause up to 25% of diarrheal episodes in children aged 6-24 months; this diarrhea, usually watery, is accompanied by vomiting and fever (22,24). Kabuya *et al.* (15) revealed that rotavirus was responsible for 25% of dehydration mortality in Kinshasa (19). Rotaviruses are most implicated in viral gastroenteritis in young children. About 90% of rotavirus infections occur before the age of two years (12,1,13). Many studies have shown the important role of rotavirus as a cause of diarrhea in children in both developed and developing countries, most of which have occurred in children under 5 years of age (1,2,18,26). Rotavirus is a public health problem in developing countries, where all children under the age of two to three are infected. A similar observation is made in industrialized countries where, however, hygienic conditions are good. The incidence of rotavirus is almost similar in developed and developing countries and varies from one country to another or even within the same country, region to region (7,8).

Kabuya *et al.* (15) in Lubumbashi, Democratic Republic of Congo, confirmed that rotavirus is a major cause of hospitalization for acute gastroenteritis in infants. They also reported that rotavirus diarrhea was 6 times more likely to lead to moderate or severe dehydration; children infected with rotavirus were twice as likely to pass stools more than 6 times a day than those infected with other microorganisms. Another study (15) also reports that vomiting, fever and lethargy characterize rotavirus infection.

Several studies report a correlation between seasonal distribution and rotavirus infection in a population. Indeed, rotavirus infections appear to occur mainly during cold season periods (dry season in tropical countries and winter in temperate climates) (17,27,28,16,13). This study follows the same logic as other publications, particularly that of Kabuya *et al.* (15).

The aim is to describe the epidemiological and clinical characteristics of children with acute rotavirus diarrhea or their association with other causative agents of diarrhea, and to assess whether rotavirus infection or rotavirus and other germs are a major risk factor for dehydration (moderate or severe) associated with stool frequency in these children.

Materials and Methods

Study design

This research is a retrospective analytical study of the medical records of the emergency records of the Kalembe-lembe pediatric hospital in the city of Kinshasa in the Democratic Republic of Congo from January the 1st to December the 31st, 2015.

Study population

As inclusion criteria, the study carried out concerns children aged 0-71 months hospitalized at the Kalembe-lembe pediatric hospital for acute diarrhea. Excluded from this research were children over 71 months of age, ambulatory patients, incomplete or unusable patient records.

Sample size

The search for causative agents of acute diarrhea in hospitalized patients was conducted in 183 children (56.48%) out of 324 hospitalized children in a population of 337 identified children. In addition, although the study is limited to children interned at the Kalembe lembe pediatric hospital, Fisher's statistical relationship indicates that this representative sample is greater than 164 expect-

ed patients. It makes it possible to generalize the results to the population of children aged 0-71 months hospitalized in other health facilities in Kinshasa. This study described the epidemiological and clinical characteristics of acute rotavirus diarrhea or the association of germs and assessed its impact on certain clinical parameters: frequency and appearance of stool, dehydration status, etc.

Parameters studied

This research was based on the following approach:
- Inventory the number of cases of acute rotavirus diarrhea;
- Identify epidemiological (age, sex, seasonality, mortality rate), clinical (frequency and aspects of stool, clinical signs associated with diarrhea, dehydration status), etiological (isolated pathogens) and progressive (duration of hospitalization and complications) characteristics in children 0-71 months of age hospitalized at Kalembe-lembe Hospital, Kinshasa, Democratic Republic of Congo.

For ethical reasons, the identity of the patients whose consultation records were the subject of this study was kept confidential.

Data collection

The data were collected after sorting the medical files (patient records) archived in the movement and statistics section service, using an individual survey form. The study involved 324 children aged 0-71 months admitted to the emergency department and hospitalized at the Kalembe-lembe pediatric hospital for acute diarrhea (Mbadiko et al., 2019).

Data analysis was performed with respect to age, season, month, diarrhea characteristics (appearance and frequency of stool), dehydration status, clinical signs associated with diarrhea, isolated etiological agents, duration of hospitalization, complications that occurred. The idea was to establish and compare epidemiological-clinical profiles of acute rotavirus diarrhea cases with those of diarrhea due to other pathogens or the association of causative agents of diarrhea.

Data analysis

Data collected were analyzed using Microsoft Excel 10 (2010) software.

The measures of association between the different qualitative variables in the study were evaluated by the Chi-square test. The probability threshold used is 0.05. The data analysis was performed using the R software (version 3.2.2). The statistical analysis also used the calculation of the frequency (in %) of the class average.

Results

Epidemiological parameters

Distribution of patients by admission period

The monthly distribution of acute diarrhea cases among children aged 0-71 months in 2015 (Table 1, Figure 1) at Kalembe-lembe Hospital shows a predominance of patients in June and September, two months that do not belong to the same climatic season.

In addition, there are 3 peaks spaced 2 months apart that are higher than the annual average: peaks in March (30 cases), June (47 cases) and September (43 cases). The peaks in June and September are indicative of the changing seasons; indeed, the peak in June corresponds to the beginning of the dry season (cool tem-

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peratures), and that in September at the beginning of the rainy season (warmer temperatures).

Distribution of patients by age and sex

Of the total patient population, 179 sick children (55.24%) were male and 145 (44.76%) female. This study also recorded a predominance of cases in the 0-11 month age group, with 196 cases (60.50%), followed by 28.09% (91 cases) in the 12-23 month age group, 24 cases (7.41%) in the 24-35 month age group, 8 cases (2.46%) in the 36-47 month group and 5 cases (1.54%) in the 48-71 month group. The average age of children hospitalized for acute diarrhea was 12 months and 4 days with extremes ranging from 0-71 months.

Clinical and etiological characteristics

Pathogen relationship and patient age

The search for causative agents of diarrhea was carried out on 183 cases representing 56.48% of the population under study and the isolated pathogens were distributed by age group. Analysis of the distribution of isolated and/or identified etiological agents by age group shows a predominance of virus infection, 128 cases (69.94%), of which 88 cases of rotavirus represent 48.08% of patients. Children under 12 months of age were the most affected by rotavirus diarrhea (61 cases, 33.33%), followed by those aged 12-23 months (23 cases, 12.56%). Bacterial, parasitic and fungal (yeast) infections were also more common in children under 12 months of age.

Distribution of isolated pathogens by sampling period

Analysis of the monthly distribution of pathogens isolated or identified throughout 2015 (Figure 2) shows a peak in March, June and September for rotaviruses.

As observed in the table, there is a peak in June for NIV and bacteria, another peak in January for parasites and March for yeasts.

In general, rotaviruses contribute significantly to the total number of cases recorded, particularly in March and September, two months of the rainy season, but also in June, a month of the dry season (Figure 2).

Relationship between isolated pathogens and clinical signs

Analysis of clinical signs in relation to isolated pathogens reveals, in decreasing numerical order of importance, vomiting, fever probably associated with it, physical asthenia, agitation occurring only in cases of rotavirus infection (Figure 3).

The frequency of the following clinical signs: vomiting, fever, physical asthenia and agitation as clinical signs associated with

Table 1. Monthly distribution of isolated and/or identified etiological agents.

Months	Viruses Rotavirus	NIV	Bacteria	Parasites	Yeasts
January	5	2	3	10	2
February	6	2	0	4	1
March	14	3	4	6	4
April	5	3	2	3	0
May	6	1	2	3	0
June	12	12	14	4	1
July	8	4	12	5	0
August	7	5	8	3	0
September	16	5	8	4	1
October	1	1	6	1	0
November	3	1	1	2	2
December	5	1	1	3	0
Total	88	40	61	48	11

NIV, Non identified viruses.

Figure 2. Evolution of the distribution of patients according to the rotavirus etiological agents identified during 2015.

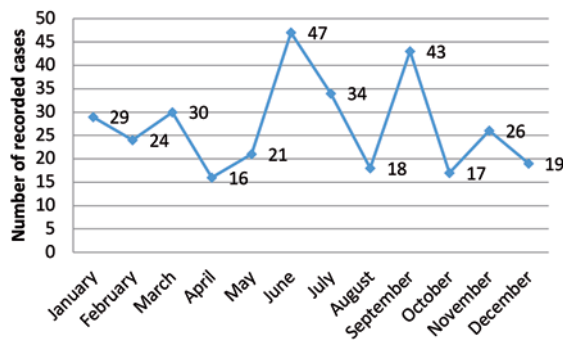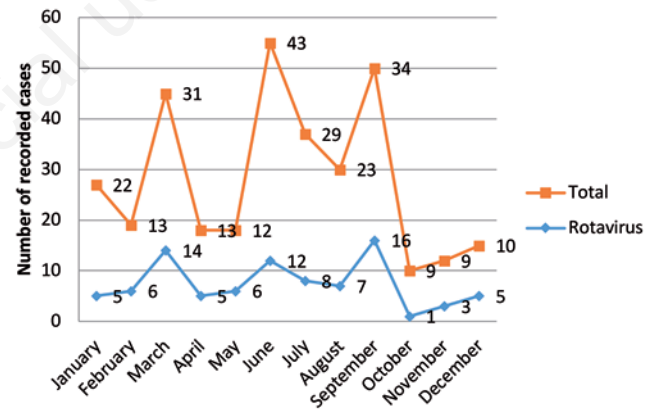**Figure 1. Monthly distribution of acute diarrhea cases reported in 2015 at Kalembe-lembe Hospital.**
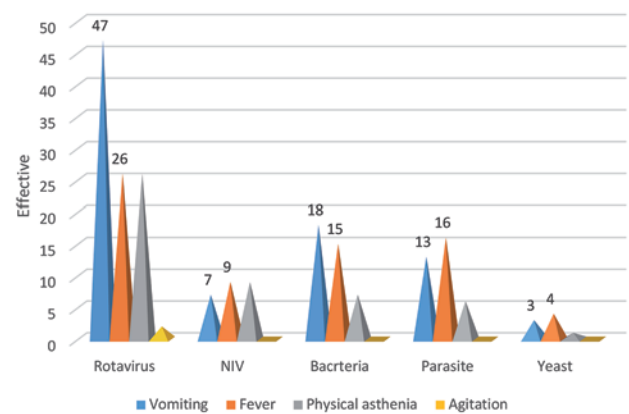
Figure 3. Distribution of patients by clinical signs and germs involved. NIV, non-identified viruses.

diarrhea were more frequent in children infected with rotavirus.

Relationship between pathogen association and clinical signs

The most frequent associations of pathogens in descending order are non-identified viruses (NIV)/bacteria, rotavirus/bacteria and rotavirus/parasites (Figure 4). The associations in which rotaviruses are involved, considering all clinical signs, represent 51 cases (27.87%). There are two distinct classes of pathogen associations: rotavirus or NIVs, associated with other agents. There does not appear to be associations between other pathogens isolated from this population. In general, the clinical signs are distributed in decreasing order as follows: 42 cases of vomiting (23%), 32 cases of fever (17.5%), 21 cases of physical asthenia (11.5%), no case of agitation.

Relationship between isolated pathogens and stool frequency

The results of the relationship between isolated pathogens and stool frequency are shown in Figure 5.

Statistical analysis does not provide a statistically significant relationship between isolated pathogens and stool count/24h ($X^2=3.4352$, df=8, p value = 0.9042). However, the prevalence of

rotavirus infections can be observed on the frequency of stool in 24 hours, a value that does not exceed 13 times. Overall, considering all stool classes/24 hours, 54 cases associated with rotavirus (29.51%), 18 cases associated with bacteria (9.84%), 12 cases with parasites (6.56%), 5 cases with NIVs (2.73%) and 4 cases with yeasts (2.19%) are observed. The only case reported with a 24-hour frequency greater than 14 hours is associated with rotaviruses (Figure 5). The frequency classes of stool/24 hours are distributed in decreasing order according to: 3 to 6 times, 82 cases (44.81%), 7 to 13 times, 10 cases (5.5%), 14 times and more, 1 case (0.55%).

Analysis of this parameter (Figure 6) also reveals, in general, the distribution of stool frequencies in 24 hours in the following decreasing order, all associations combined: 3 to 6 times, 62 cases (33.88%), 7 to 13 times, 18 cases (9.84%), 14 times and more, 3 cases (1.64%). This last frequency class of stool/24 is entirely attributed to rotavirus. Similarly, pathogen associations, taken in isolation, reveal the predominance of stool cases (65 cases) due to rotavirus alone or in association with other isolated pathogens (33.88%), 18 cases due to NIV alone or in association with other pathogens (9.84%). The presence of rotavirus or unidentified viruses at the time of infection in patients may justify the high rate of persistent fever in the sample (Figure 7). The presence of more pathogens indicates a highly significant relationship between stool
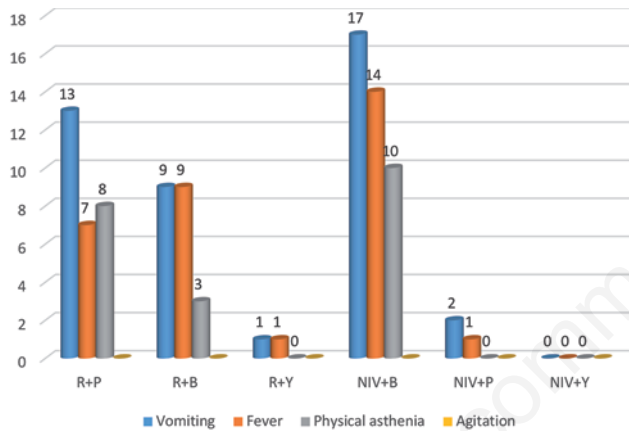

Figure 4. Distribution of cases according to clinical signs and associations of the germs involved. NIV, non-identified viruses; R, rotavirus; P, parasytes; B, bacteria; Y, yeast.
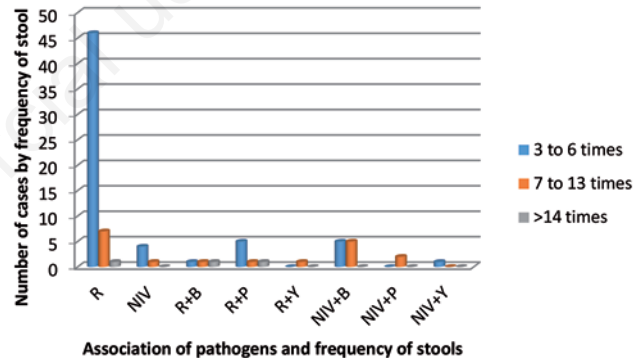

Figure 6. Distribution of cases according to the association of pathogens isolated and the number of stools/day. NIV, non-identified viruses; R, rotavirus; P, parasytes; B, bacteria; Y, yeast.
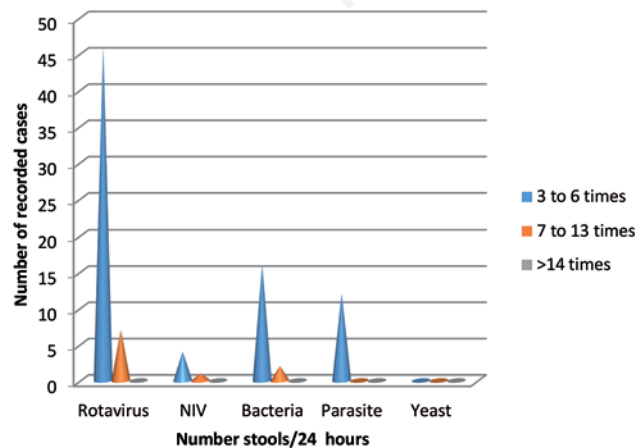

Figure 5. Distribution of cases according to the pathogens isolated and the number of stools/day.
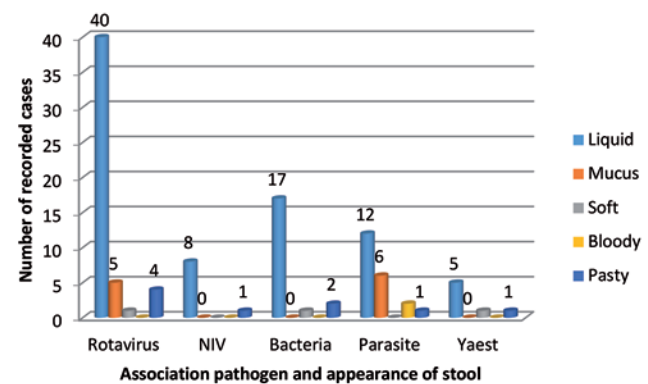

Figure 7. Distribution of cases by isolated pathogens and stool appearance. NIV, non-identified viruses.

count/24h and associations of isolated pathogens (X²=30.004, df=14, p value = 0.007621).

Relationship between pathogenic agent and aspect of stools

There is a statistically significant relationship between the different aspects of stool and isolated pathogens (X²=24.58, df=12, p value=0.01694). Most stools are liquid (Figure 8), regardless of the pathogen isolated, the other aspects being poorly represented (<10%).

The results do not show a significant relationship between the different aspects of stool and pathogen associations (X²=23.55, df=32, p value = 0.8603). However, it can be noted that the liquid aspect of the stool predominates in all associations of isolated pathogens, while the other aspects of the stool remain very weak (Figure 8). It can be noted, once again, that the liquid aspect of the stool of patients infected with rotavirus alone, 40 cases (21.86%), or associated with other pathogens, remains significantly more important than the other aspects of the stool: rotavirus + bacteria, 8 cases (4.37%), rotavirus + parasites, 12 cases (6.56%), rotavirus + yeasts, 1 case (0.55%).

Regardless of the association of pathogens, the presence of viruses is clinically observed, particularly rotavirus at 9.83% of isolated cases, and 31.69% of cases in which rotavirus occurs. The NIV associated with bacteria has a significant soft stool frequency, 14 cases (7.65%).

Relationship between isolated pathogens and state of dehydration

Severe dehydration (C) in hospitalized patients appears to be mainly associated with the presence of bacteria, while moderate dehydration (B) with rotavirus (Figure 9). Moderate dehydration by viruses accounts for 13.85% of cases compared to 4.92% of severe cases due to bacteria and parasites combined; severe dehydration is observed at 1.64% and 3.28%, respectively due to viruses and bacteria and parasites. The Chi-square test does not provide a statistically significant relationship between isolated pathogens and dehydration status (X²=3,402, df=3, p value = 0.3337).

In general, there are more cases of type B dehydration, 27 cases representing 14.75%, than of severe dehydration, 3 cases (1.64%). The low rate of severe dehydration can indicate good patient management during hospitalization.

The results (Figure 10) indicate that there is no statistical relationship between dehydration status and the associations of the isolated pathogens (X²=7.6444, df=6, p value = 0.2653).

Discussion

Epidemiological, clinical and etiological findings

Monthly distribution of isolated pathogens

The results of this study show that pathogens were isolated throughout the year. However, there is a peak in March, June and September for rotaviruses, June for NIVs and bacteria, January for parasites and March for yeasts. The dry season (January and June) provided conditions conducive to the multiplication of the causative agents of diarrhea (rotavirus and other viruses, bacteria and parasites) compared to the rainy season (March, September). This justifies the peak during the dry season. Many publications attest that in hospitals or daycare centers, the frequency of rotavirus infections can range from 50-80%, especially in winter, which corresponds to the dry season in the Democratic Republic of Congo (17,27,28,16,9, 24).
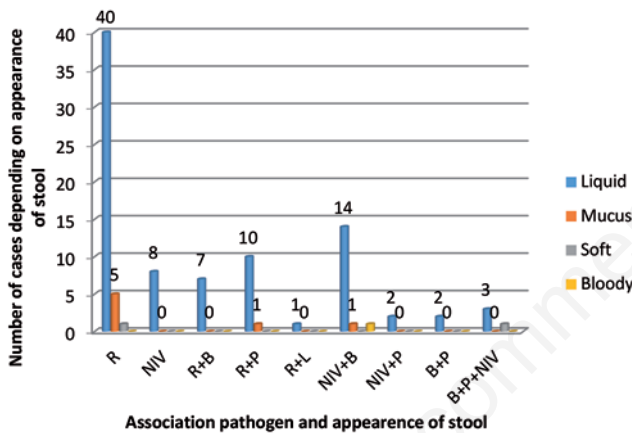

Figure 8. Distribution of stool appearance cases by association of isolated pathogens. NIV, non-identified viruses; R, rotavirus; P, parasytes; B, bacteria; Y, yeast.
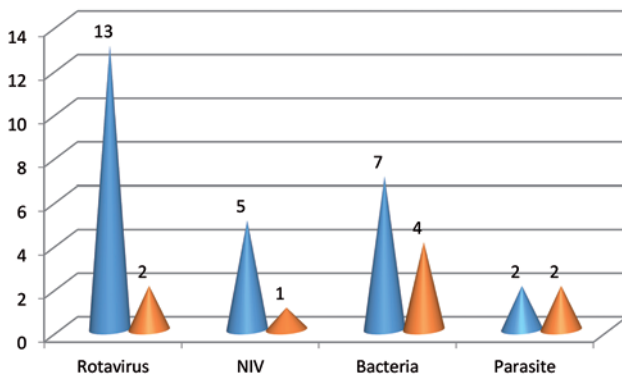

Figure 9. Distribution of acute diarrhea cases by isolated pathogens and state of dehydration. NIV, non-identified viruses.
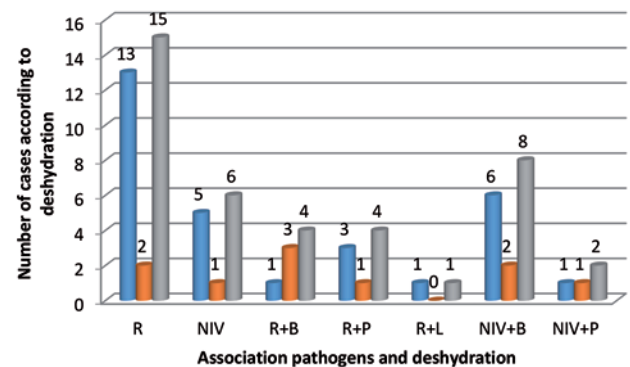

Figure 10. Distribution of acute diarrhea cases according to the association of isolated pathogens and state of dehydration. NIV, non-identified viruses; R, rotavirus; P, parasytes; B, bacteria; Y, yeast.

Distribution by age and germs involved

The search for diarrhea agents was carried out in only 56.48% of cases (183 cases). However, there is a predominance of viral infection (128 cases, or 69.94%), including rotaviruses, which have been isolated and identified in 48.08% of cases (88 patients). Children aged 0-11 months were the most affected by rotavirus diarrhea, with 61 cases (33.33%). The same applies to infections with other causative agents of diarrhea. As age increases, the proportion of infections with the causative agents of diarrhea decreases. This could be explained by the development of the child's immune system and the introduction of antibodies specific to the germs responsible for diarrhea after repeated infections (24,25,5). This would explain the decrease in rotavirus incidence in children aged 12-24 months observed in the findings.

The results of this investigation are similar to those of Kabuya *et al*. (15), who found a rate of 49.22% rotavirus infection in children aged 0-12 months. The maximum number of cases reported in children aged 0-12 months (76.1%) was also reported by Huilan (11); Offit *et al*. (20), Jiang *et al*. (14), Salou (24). These studies reported that rotavirus infection mainly affected children under 2 years of age with a peak incidence in children aged 6-11 months. They justified this observation by the protective effect of maternal antibodies in 6-months-old breastfeeding children and the development of natural immunity after repeated infections in children over 2 years of age.

Djénéba (5) also reported that the incidence of diarrhea due to rotavirus was higher in children aged 2-11 months (38.71%) compared to those aged 12-24 months (12.5%). The same observation was made by Cardoso *et al*. (4), who reported that rotavirus detection is high in children under 12 months of age compared to those 24 months of age and decreases sharply after 2 years.

Distribution of patients according to clinical signs and germs involved

This study revealed the following most common clinical signs in children from whom rotaviruses were isolated: vomiting, fever, physical asthenia and agitation were significant (Figure 3). Kabuya (15), also reported high proportions of vomiting, fever and lethargy in infants infected with rotavirus compared to those infected with other germs.

Distribution of patients according to clinical signs and association of germs involved

Vomiting was more frequent in virus and bacteria and rotavirus-parasite combinations, while fever and physical asthenia were more common in virus-bacteria combinations (Figure 4).

Vomiting (1st symptom preceding diarrhea), watery stools, moderate fever (of very variable intensity), dehydration, electrolyte imbalance and metabolic acidosis often characterize rotavirus infection (10,15). It should be noted, however, that this clinical picture is not specific to rotavirus infection; other etiological agents of diarrhea, such as bacteria (*Salmonella, Campylobacter, Yersinia enterolitica*, enteropathogenic *Escherichia coli, Staphylococcus aureus*, etc.) or parasites may reflect the same picture.

Frequency of stool and germs involved

By comparing the group of children infected with rotavirus and the group of children infected with other germs, the children in the first group passed more stool (Figure 5) than those infected with other germs. Nevertheless, the analysis of the Chi-square test does not reveal a different significant statistical relationship (X^2=3.4352 ; df=8 ; p value = 0.9042).

The fact that the Chi-square test did not establish a significant statistical relationship suggests that in addition to rotavirus, other germs may also be responsible for more frequent stools.

Kabuya *et al*. (15), reported 59.6% of children infected with rotavirus and having passed a number of stools ≥6 compared to 41.6% in the group of children infected with other germs and having passed the same number of stools.

Relation of stool frequency and association of isolated pathogens

Groups of children infected with rotavirus alone had more stools (3-13 stools/day) (Figure 6) compared to those of cases of germ associations. When comparing data on the relationship between the association of germs and stool frequency, it is observed that the virus-bacteria association caused frequent stool (7-13 stools/day) compared to other associations. Analysis of the X^2 test indicates a highly significant relationship between the number of stools/24h and associations of isolated pathogens. Analysis of these results suggests that in addition to rotaviruses, the combination of rotaviruses or other viruses and bacteria can also cause frequent stools.

Relationship between the physical aspect of the stool and the germs involved

Liquid stools were very common in the group of individuals infected with rotavirus (40 cases), followed by those infected with bacteria (17 cases) (Figure 7), while mucus stools were predominant in parasite infections. Statistical analysis showed a significant relationship between the different aspects of stool and isolated pathogens (X^2=24.58; df=12; p value = 0.01694). Indeed, infection with rotaviruses or certain bacteria (*Salmonella*, *Campylobacter*, and *Yersinia enterolitica*) is often characterized by watery stools (10,15).

Relation of physical appearance of stool and association of isolated pathogens

This study shows that liquid stools characterize rotavirus infections (40 cases), virus-bacteria association (14 cases) and rotavirus-parasites (10 cases) (Figure 8), whereas mucus stools are characteristic of rotavirus infections. Statistical analysis does not show a significant relationship between the different aspects of stool and associations of isolated germs (X^2=23.55; df=32; p value = 0.8603).

Relationship between the state of dehydration and the germs involved

Moderate dehydration characterizes rotavirus infections, followed by bacterial infections, while severe dehydration characterizes bacterial infections (Figure 9). Nevertheless, the Chi-square test does not provide a statistically significant relationship between isolated pathogens and dehydration status (X^2=3.402, df=3, p value = 0.3337). Kabuya *et al*. (15), reported that children were 6 times more likely to experience moderate or severe dehydration than those infected with other germs.

Relationship between dehydration status and association of the pathogens involved

Moderate dehydration was much more common in rotavirus infections or virus-bacteria combinations, while severe dehydration is characterized by rotavirus-bacteria combinations (Figure 10). The Chi-square analysis indicates that there is no statistical relationship between dehydration status and associations of isolated germs (X^2=7.6444; df=6; p value = 0.2653).

Conclusions

Acute rotavirus diarrhea is present in the city of Kinshasa province and particularly affects children under 12 months of age. Infections by the causative agents of diarrhea are endemic throughout the year and do not appear to be exclusively reserved for the dry season as described elsewhere. The higher proportion of vomiting, fever, physical asthenia and agitation was higher in rotavirus infections; in addition, vomiting was more common in bacterial-virus and rotavirus-parasite combinations, while fever and physical asthenia were more common in virus-bacterial combinations.

Cases of rotavirus infections were more likely to pass stool compared to those of infections due to other germs; however, statistical analysis did not show a significant relationship. In addition, virus-bacteria associations caused abundant stools (7-13/day) compared to other associations, with the analysis showing a highly significant statistical relationship. Moderate dehydration characterized cases of rotavirus and bacterial infections, while severe dehydration was more common in cases of bacterial infections, although the chi-square test did not indicate a significant statistical relationship. In addition, virus-bacteria associations were characterized by moderate dehydration while rotavirus-bacteria association was characterized by severe dehydration; as in the cases of previous associations, the Chi-square test showed the absence of a significant statistical relationship.

Subsequent studies should establish a relationship between the etiological agents of diarrhea and the identification of bacterial species and rotavirus strains.

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