Epidemiological and Clinical Profiles of Children Aged 0-71 Months Suffering from Acute Diarrhea at Kalembe-Iembe Pediatric Hospital in Kinshasa City, Democratic Republic of the Congo

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Authors’ contributions

This work was carried out in collaboration among all authors. Author SNMH designed the study. Authors CMM and GKM performed the statistical analysis and wrote the protocol. Authors CMM and GNB wrote the first draft of the manuscript. Authors LLK and OKN managed the analyses of the study. Authors JMB, CKB and TBN performed the survey in the hospital. Authors JMK and TRC managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

**Aim:** The aim of this study was to determine the epidemiological, clinical and etiological profile of children aged 0-71 months suffering from acute diarrhea, admitted at the Kalembe-lembe Pediatric Hospital in 2015.

**Study Design:** This study used a retrospective design whereby medical records of children aged 0-71 months were used.

**Place and Duration of Study:** This survey was carried out at the Kalembe-lembe Pediatric Hospital in Kinshasa, Democratic Republic of the Congo between January 1 and December 31, 2015.

**Methodology:** This study used a questionnaire to collect information whereby 337 cases of acute diarrhea diagnosed at the Kalembe-lembe Pediatric Hospital were recorded, of which 324 cases were selected. The information was collected on a case-by-case basis by consulting the patient records. Data collected were analyzed using Microsoft Excel 10 while the association measures between different qualitative variables were evaluated using Chi-square test and the p-value was 0.05.

**Results:** A predominance of cases (60.49%) was observed in children under 12 months and potentially in males (55.24%) while the majority of deaths was recorded in this same age group. The mean age of admitted children was 12.4 months and vomiting was the most reported symptom associated with diarrhea (75.61%), followed by hyperthermia (70.37%). Most of children emitted liquid stools (65.12%) and the average number of stools issued per day was 6 times with extremes ranging from 3-45 stools/day. However, we recorded high levels of identified etiologic agents in children with diarrhea compared to those reported in other countries. The identification of etiologic agents of diarrhea was performed only in 56.48% of cases. Rotaviruses, bacteria and parasites were found in 48.08%, 32.78% and 26.77% respectively.

**Conclusion:** Further studies are needed to study the antibiotic resistance of these pathogens causing acute diarrhea and identify using molecular techniques new strains of bacteria precisely responsible for acute diarrhea and assess their epidemiological and clinical influence.

Keywords: Epidemiology; clinical profile; acute diarrhea; control; children; Kalembe-lembe; Democratic Republic of the Congo.

1. INTRODUCTION

Acute diarrhea is the emission of at least three soft or liquid stools per day and that evolved not less than 14 days, and diarrhea especially acute diarrhea remains a major public health problem in the world [1].

Each year, 1.3 billion of acute episodes of diarrhea are observed in children worldwide [2]. Acute diarrhea is more serious in developing countries where malnutrition constitutes a major risk factor for many diseases including rotavirus infections. Moreover, children suffering from diarrhea occupy more than one-third of the hospital beds in these countries [3,4]. Sanou et al. [2] reported that in 80% of cases, acute diarrhea is due to infectious agents of which epidemiological characteristics vary according to countries, and even in one country, depending on from one region to another one. In 2012, a survey conducted in the Democratic Republic of the Congo (DRC) reported that diarrhea is the third cause of pediatric consultation after malaria and acute respiratory infections i.e. this pathology is responsible for 31.4% of children death under 5 years old. In 2014, the statistics of the Kalembe-lembe Pediatric Hospital revealed that out of 280 children admitted during this period, only 70 children had suffered from acute diarrhea. Among these children, 42(15%) had various complications such as severe dehydration, undernutrition, etc. This number clearly shows the scope of the problem and the danger that children are facing against this plague. The significance of the current study was to improve the early control of diarrhea in children and to describe the epidemiological, clinical and evolution of acute diarrhea in admitted children under 5 years at the Kalembe-lembe Pediatric Hospital. The aim of this study was to determine the epidemiological, clinical and etiological profiles of children aged 0-71 months suffering from acute diarrhea, consulted and admitted at the Kalembe-lembe Pediatric Hospital in 2015.
2. MATERIALS AND METHODS

2.1 Study Design, Criteria Selection and Data Collection

This is a retrospective study based on the medical records of children aged 0-71 months (5 years and 11 months), admitted for acute diarrhea at the Kalembe-lembe Pediatric Hospital, Kinshasa, DRC between January 1st and December 31st, 2015. We used a questionnaire to collect the requested information. For ethical reasons, the identity of children whose records were the subject of our study was kept confidential. In this study, only children aged 0-71 months admitted at the Kalembe-lembe hospital for acute diarrhea and children whose stool specimens underwent coprological tests were included. Other children older than 71 months and incomplete patient files were excluded from this study.

The procedure was as follows: (1) the identification of number of cases of diarrhea among children aged 0-71 months, admitted, at the Kalembe-lembe Pediatric Hospital during the study period, (2) the description of the epidemiological characteristics (number of cases/month, distribution of cases related to gender and age, isolated causative agent, etc.) and among the clinical and evolutive characteristics of the respondents, and (3) the identification of various complications which occurred in children suffering from acute diarrhea, as well as the rate of mortality.

2.2 Sample Size

During the study period, 337 medical records of children admitted at the Kalembe-lembe Pediatric Hospital because of acute diarrhea were identified. Out of 337 cases, only 324 cases were selected. The sampling was representative of the study population, 96.14%.

2.3 Parameters Studied

The parameters studied were of four types: the epidemiological parameters (monthly distribution of cases, death cases, age and sex of patients), the clinical parameters (numbers of stools emitted per day, stool appearance, signs, symptoms and conditions associated with the diarrhea), the evolutive parameters (distribution of cases per hospitalization duration) as well as the etiological parameters (isolated and identified etiological agents).

2.4 Data Analysis

Data collected were grouped and analyzed using Microsoft Excel 10. The association measures between different qualitative variables studied were evaluated using Chi-square test and the p value was 0.05. The data analysis was performed using R software (version 3.2.2). Considering the descriptive statistics, the frequency was calculated using the following formula:

\[
\% = \frac{n_i}{N} \times 100
\]

Where: \( n_i \) = total number, \( N \) = sample.

3. RESULTS

3.1 Epidemiological Parameters

3.1.1 Monthly distribution of cases

The monthly distribution of children suffering from acute diarrhea and admitted at the Kalembe-lembe Pediatric Hospital is given in Fig. 1 below.

The Fig. 1 revealed a predominance of cases in June (47 cases) and September (43 cases). There are more male children (179 or 55.24%) than female (145 or 44.75%), with a monthly average of 27±10.14 cases i.e. 8.33%). Despite the peaks observed in June and September, the variation in cases of diarrhea in this population is not statistically significant \( (r^2 = 0.0076) \).

3.1.2 Monthly distribution of children aged 0-71 months dead due to acute diarrhea

The monthly distribution of children aged 0-71 months who died as result of acute diarrhea at the Kalembe-lembe Pediatric Hospital during this study is presented in Table 1.

The mortality rate of children aged 0-71 months due to acute diarrhea at the Kalembe-lembe Pediatric Hospital is of 8.95%, of which 18 children (5.86%) were aged less than 12 months old. Of the 29 recorded deaths, 11 (3.09%) are children of 12 months and older.

3.1.3 Distribution of patients according to age and sex

The distribution of cases according to sex and age is presented in Table 2.
Table 1. Monthly distribution of children who died due to acute diarrhea

| Months     | 0-11 | 12-71 | Total |
|------------|------|-------|-------|
| N          | %    | N     | %     |
| January    | 0    | 0     | 0     |
| February   | 1    | 3.45  | 2     | 6.9   |
| March      | 2    | 6.9   | 3     | 10.35 |
| April      | 1    | 3.45  | 2     | 6.9   | 3     | 10.35 |
| May        | 1    | 3.45  | 2     | 6.9   | 3     | 10.35 |
| June       | 4    | 13.79 | 0     | 0     | 4     | 13.79 |
| July       | 0    | 0     | 0     | 0     | 0     |
| August     | 3    | 10.35 | 3     | 10.35 | 6     | 20.69 |
| September  | 3    | 10.35 | 2     | 6.9   | 5     | 17.24 |
| October    | 0    | 0     | 0     | 0     | 0     |
| November   | 1    | 3.45  | 0     | 0     | 1     | 3.45  |
| December   | 2    | 6.9   | 0     | 0     | 2     | 6.9   |
| Total      | 18   | 62.07 | 11    | 37.93 | 29    | 100%  |

Table 2. Distribution of cases according to sex and age

| Age group | Male | Female | Total |
|-----------|------|--------|-------|
| N         | %    | N      | %     |
| 0-11      | 101  | 31.17  | 95    | 29.32 | 196   | 60.5  |
| 12-23     | 57   | 17.59  | 34    | 10.50 | 91    | 28.10 |
| 24-35     | 15   | 4.63   | 8     | 2.47  | 23    | 7.10  |
| 36-47     | 4    | 1.23   | 5     | 1.54  | 9     | 2.8   |
| 48-71     | 2    | 0.62   | 3     | 0.93  | 5     | 1.5   |
| Total     | 179  | 55.24  | 145   | 44.76 | 324   | 100%  |
The monthly distribution of acute diarrhea cases by age group and sex reveals the high prevalence of cases in the age group from 0-11 months (60.49%) and 28.08% in the age group from 12-23 months. As the age increases, the proportions of cases of acute diarrhea decrease: 7.09% (24-35 months), 2.77% (36-47 months), 1.54% (48-71 months), and male children (55.24% of cases) were the most affected. The average age of children admitted for acute diarrhea in this hospital was 12 months and 4 days.

3.2 Clinical Parameters

3.2.1 Frequency of stools

Table 3 presents the distribution of cases according to the frequency of stools emitted per day.

The frequency of stools emitted per day was determined only in 61.42% of cases (i.e. 199 patients) whereby 140 (43.20%) emitted between 3 and 5 stools per day. The average number of stools emitted per day was 6 times per day with extremes ranging from 3-45 stools/day.

3.2.2 Appearance of stools

The distribution of cases according to the appearance of stools is presented in the Table 4.

The stool appearance was described only in 293 cases (i.e. 90.43%); the stool consistency was liquid in 211 children (65.12%), glairy in 30 children (9.26%) and glairo-bloody in 11 children (3.40%).

3.2.3 Signs, symptoms and conditions associated with diarrhea

Different signs, symptoms and conditions associated with acute diarrhea are presented in Table 5.

Vomiting was the most common symptom quoted in the records (75.61%); followed by fever (hyperthermia) (70.37%). The dehydration status of the reported diarrheal children was quoted in only 32.39% of cases, of which 23.45% had moderate dehydration and 8.64% had severe dehydration while 39.81% of cases had physical asthenia.

3.2.4 Duration of hospitalization

The duration of hospitalization of cases recorded at the Kalembe-lembe Pediatric Hospital is presented in the Table 6.
A significant number of children were admitted for 1-7 days (83.95% either 272 cases). The average duration of hospitalization was 5 days and 3 hours with extremes ranging from 1-26 days.

### 3.3 Etiological Parameters

The search for the etiological agents of acute diarrhea (bacteria, viruses, parasites) was only carried out in 183 children (56.48%) out of the 324 admitted children. Bacteria were isolated in 32.78% of cases (60 children) of which 3 species were identified namely: *Salmonella* sp (6 cases), *Shigella* sp (2 cases), and *Campylobacter* sp (1 case). Viruses were responsible of causing acute diarrhea in 128 cases (69.93%) whereby rotaviruses were identified in 48.08% of cases (88 children) and the remaining cases of which 21.85%, viruses could not be identified. The parasitic cause was the major one and the main isolated parasites were roundworms (2 cases), amoeba (2 cases) and other intestinal parasites were not identified and yeasts were found in 11 cases (6.1%).

We have also noticed cases of mixed infections due to two or more pathogens, and it was reported as follows: parasite and rotavirus (17 cases, 9.28%), bacteria and rotavirus (12 cases, 6.55%), unidentified viruses (NIV) and parasites (18 cases, 9.83%), NIV and bacteria (4 cases, 2.18%), *Campylobacter* sp. or *Salmonella* sp. and parasites (3 cases, 1.63%), NIV + bacteria and parasites (3 cases, 1.63%), *Salmonella* sp. and *Shigella* sp. (1 case, 0.54%), *Salmonella* sp. and *Campylobacter* sp. (1 case, 0.54%).

### 4. DISCUSSION

Diarrheal diseases are a leading cause of morbidity and mortality among young children in developing countries. Although oral rehydration has been shown to reduce early child mortality, the diarrhea-specific mortality in children less than 5 years of age in Africa has been estimated at about 10.6 per 1,000 [5]. Causes of diarrhea in areas of endemicity include a wide variety of bacteria, viruses, and protozoa. Poor food hygiene, water, and sanitation are common in communities with high levels of diarrheal disease. Underlying conditions, such as malnutrition, which modify the risk of contracting diarrhea, are also common in many countries of sub-Saharan Africa. These factors combined, facilitate the spread of enteropathogens, and epidemics are common in such settings [27].

#### 4.1 Epidemiological Parameters

Concerning the monthly distribution of cases, it was observed that several cases of acute diarrhea were recorded during June (47 cases, 14.50%) and September (43 cases, 13.23%). These results differ from those of Salou [6], who reported that in Ouagadougou, the highest case rates occurred between December and March with the following frequencies: 19.0%, 10.6%, 13.2% and 12.2% respectively. Meanwhile Tougouma [7], also in Ouagadougou reported that the highest rates of cases were recorded between March and June with the following frequencies: 12.4%, 13.8%, 10.7% and 18.1% respectively. Nevertheless, the studies of Tougouma and Salou, carried out in the same city at two different periods far from 10 years, revealed the persistence of the infantile pathology during 7 months of the year (between December and June). This acute, permanent diarrhea represents, on average, 13.96% of the cases studied. It is well known that more than 80% of cases of acute diarrhea are from infectious origin and the climate offers favorable conditions for the multiplication of infectious agents [6,8].

In respect with the distribution of patients according to sex and age, it was recorded a predominance of male (55.24%) than female (44.76%). These findings are similar to Sanou et al. [2] who reported the frequency of 54.7% for male children and 45.3% of female children whilst Salou [6] recorded the frequency of 58.1% of male children and 41.9% of female children. In Lubumbashi, Kabuya et al. [9] reported the frequency of 52.3% female children and 47.7%
male children. Coulibaly [4], Fohom [10], Konate [11], Bagayoko [12], Reh binder [13] and Sidibe [14] also observed in their study that male children were the most represented with following respective frequencies of 56.7%, 56%, 54%, 55%, 59.2% and 60%. In fact, several studies reported the vulnerability of male children to infectious diseases and among which acute diarrhea. According to Atakore [8], this observation results from social behavior towards children. If the mother, for example, preferred a female birth, the prevalence of diarrhea is higher among males but in households where there is a preference for male birth, females are more likely to suffer from diarrhea than males. In Asian countries, such as Bangladesh, where male children are favored for breastfeeding and care, there is a prevalence of infectious diseases and excess mortality among female children [8]. But the author also raised the issue of genetic factors as the basis for the prevalence of infectious diseases in male children [8].

As to the age of children, the findings revealed that the predominant age range was 0-11 months ca 196 cases (60.49%) where the prevalence of acute diarrhea was high. Kabuya et al. [9] reported this significant frequency of acute diarrhea before the age of one year. Meanwhile Sanou et al. [2] and Salou [6] also reported the high frequency (55.7% and 73.5% respectively) of acute diarrhea in children less than a year. Coulibaly et al. [4] and Maaroufi et al. [15] reported similar observations on the frequency of acute diarrhea in children (51% and 46%) of frequency in Côte d’Ivoire and Tunisia respectively. While comparing the average age of children surveyed in this study i.e. 12 months and 4 days (12.13 months) to those reported by Sanou et al. [2] (13.12 months), Salou et al. [6] (9.92 months) and Kabuya [9] (8.25 months), children identified in the current study, although older than those recorded by Salou or Kabuya and younger than those recorded by Sanou, are in the critical period of growth around 12 months. The child before the age of one year seems to be particularly exposed to diarrhea for two main reasons, which are (i) the period that one develops the immunity peculiar to his body, while there is a decrease of maternal antibodies; and (ii) the child’s dietary diversification begins. When it is badly managed, malnutrition and then diarrhea can occur [2,6].

Regarding the mortality rate, 29 deaths (8.95%) were recorded. The majority of death was observed in children under 12 months (5.86%).

Concerning the stool appearance, this study revealed fewer cases of dysentery (i.e. 3.40%) compared to the results reported by Salou [6] (5.9%) and Sanou [2] (10.4%). The aforementioned studies revealed the highest frequencies of cases of Shigella, an etiological agent of bacillary dysentery. The present study also reports a predominance of liquid stools (211 cases, 65.12%) and this is similar to what Mallan [17] and Haffaf et al. [18] reported i.e. the rates of liquid stools around 71.9% and 78% respectively. The high rate of rotavirus isolated in our study justifies the frequency of loose stools.

As regards to various signs, symptoms and conditions associated with diarrhea, vomiting was the most common sign associated with diarrhea as shown in the current study (75.61%). Fever was observed in 70.37% while 39.81% had physical asthenia and 32.39% of children admitted for acute diarrhea were dehydrated. Our findings are different from those of Jihane [19] who reported fever as the most associated symptom with diarrhea (83.6%). The rate of vomiting was 62.4% of cases and 45% of cases of dehydration were reported as well. Salou [6] reported that hyperthermia (fever) was associated with diarrhea in 75.18% of cases and vomiting was of 66.58% while the dehydration was observed in 58.22% of children. On the other side, our findings are going along with Kabuya et al. [9] who reported that vomiting was associated with diarrhea in 82.4% of cases and
hyperthermia in 81.3% of cases while 93.8% experienced severe or moderate dehydration. Haffaf et al. [18] reported vomiting as a symptom the most associated with diarrhea in 40% of cases, fever in 40% of cases and 14.25% of children were dehydrated. These results are also similar to those of Sidibé [14]. In addition, Konate [11] also reported that vomiting and fever were most frequently associated with diarrhea. Meanwhile, in Rabat, a research carried out at the University Hospital Center of Avicenna reported that diarrhea-vomiting was the most common association with a rate of 87.6% [20].

Concerning the duration of hospitalization, the majority of children diagnosed with diarrhea i.e. 85.95% were admitted for 1-7 days, 14.95% of registered cases stayed in hospital for 8-14 days and 6 patients (1, 85%) more than 14 days. The average duration of hospitalization was 5 days and 3 hours with extremes ranging between 0 and 26 days. Salou [6] reported that 84% of children remained in the hospital more than 7 days and the mean duration of hospitalization was 3.94 days with extremes ranging between 0 and 33 days. It seems that children identified in this research stayed longer in the hospital than those identified in other studies [6]. This observation can be justified as follows: (i) ineffective or inappropriate management of cases, (ii) the fact that admitted patients in DRC did not present the same clinical picture as those recorded by Salou [6]. In addition to diarrhea, the management of conditions or other diseases associated with diarrhea (malaria for example) may be at the root of the lengthening of the hospitalization of different cases recorded in DRC and (iii) the behavior of some parents who are waiting for the deterioration of the child’s condition before driving him to a hospital center.

### 4.3 Etiological Parameters

The present study was able to isolate and/or identify the etiological agents of acute diarrhea only in 56.48% of cases. On the one hand, the search for the etiological agents of diarrhea is not the primary objective while managing diarrhea [6] and the acquisition of adequate laboratory equipment and/or the reinforcement of staff building capacity in recent techniques for the identification of pathogens of diarrhea are extremely required. This pathology constitutes a significant danger to public health at the same time during the year in this fragile age group.

Since 80% of cases of acute diarrhea are due to infectious agents, the identification of these agents is important for better management of children suffering from this pathology. The study by Kabuya et al. [9], found that diarrhea caused by rotavirus increases the risk of bowel movement by 2-fold and leads to more severe/moderate dehydration than diarrhea caused by other viruses and they have suggested an appropriate care in order to prevent deaths. The identification of etiological agents of acute diarrhea is also important for epidemiological studies (risk of spread of the pathogen, emergence of new microbial strains). Among the pathogens isolated and/or identified in children during our study, viruses occupy a prominent place (69.93%) among which rotavirus (48.08%). This explains the frequency of certain clinical signs observed: vomiting (75.61%), fever (70.37%), liquid stools (62.12%). In infants and young children, rotavirus infection causes watery diarrhea with vomiting and fever, which are the clinical signs of gastroenteritis [6].

Rotaviruses were identified and isolated at a rate of 48.08% and 21.85% of viruses were not identified. Sanou [2] and Kabuya et al. [9] reported following rates: 14.4% and 53.8%, respectively for the rotavirus. In Cameroon, Djénéba [21] reported a rate of 42.8% of rotavirus identified as causing agent of acute diarrhea. The frequency of 26.77% of isolated parasites in the present study is higher than that described in other studies [2,6,22,23]. The frequency of bacteria (32.78%) isolated in the current study is higher than that reported by Salou [6] in Burkina Faso (6.20%), Diouf et al. [23] (10.5%), Cowpli-bonny et al. [24] in Côte d’Ivoire (11.2%) and Luki et al. [25] in Kinshasa, (12%) and three bacteria species were partially identified, including: Salmonella sp. (6 cases), Shigella sp. (2 cases) and Campylobacter sp. (1 case) while other bacteria remained unidentified. Thus, the need of using molecular techniques as a diagnostic tool.
As noted above, failure to identify the causative agents of acute diarrhea often results from the fact that (i) the search for the etiological agents of diarrhea is not the primary purpose in the management of diarrhea and (ii) the inadequate laboratory equipment and/or ignorance of recent techniques for identifying pathogens causing diarrhea. The record of cases of mixed infections was also reported in the current study where there were a mixture of two or more pathogens, among which: parasites and rotavirus (7 cases), bacteria and rotavirus (12 cases), unidentified viruses (NIV) and parasites (18 cases), NIV and bacteria (4 cases), Campylobacter sp. or Salmonella sp. and parasites (3 cases), NIV + bacteria and parasites (3 cases), Salmonella sp. and Shigella sp. (1 case), Salmonella sp. and Campylobacter sp. (1 case). Salou [6] in Burkina Faso (at children 0-36 months) reported associations of the following pathogens: E. coli + rotavirus (3 cases); Salmonella sp. + rotavirus (4 cases); Trichomonas intestinalis + amoeba (1 case); E. coli + amoeba (1 case). Djeneba [21] also reported different associations, notably: rotavirus and Hymenolepis nana; Giardia lambia and Trichomonas intestinalis. Orland et al. [26] and Cruz et al. [27], also reported this possibility of co-infection of etiological agents of diarrhea: Shigella sp., Salmonella sp. and E. coli, Giardia lambia and rotavirus.

As to what has been observed above, the health staff of Kalembe-lembe hospital or other hospitals need improve their management of children suffering from acute diarrhea with a particular care on children of less than a year. In addition, they should strengthen their technical platforms for the identification of etiologic agents of diarrhea in particular and promote the training of their laboratory technicians in the identification of the etiological agents causing diarrhea. To make this intervention and management easy, parents should consult health facilities immediately in case of diarrhea for children precisely for children of less than a year, knowing that the mortality rate is high at this tender age. They must also promote compliance with basic hygiene rules (immediate environmental sanitation, hand washing, etc.) and the taking of drinking water.

5. CONCLUSION

The aim of this study was to determine the epidemiological, clinical and etiological profiles of children aged 0-71 months suffering from acute diarrhea, admitted at the Kalembe-lembe Pediatric Hospital in 2015. The findings of this survey revealed that the mortality rate was 8.95% and vomiting was the most associated symptom with diarrhea and no cases of dysentery and cholera were recorded. According to the hospital regulation, the duration of hospitalization was longer than expected. The frequency of the etiological agents identified during this study is greater than that of previous studies.

Further studies are needed in order to: (i) Investigate clinically on the impact of rotavirus infection and other etiological agents of diarrhea (stool frequency, stool appearance and dehydration status), (ii) to study resistance of these agents that cause acute diarrhea (namely bacteria and parasites) to commonly prescribed antibiotics and last (iii) isolate using molecular biology techniques new strains of bacteria responsible for acute diarrhea and assess their epidemiological and clinical influence.

Therefore, we recommend to the political and administrative authorities to promote the rotavirus vaccination for children under 12 months of age and sanitation in urban and peri-urban areas. They must also promote population health education through media awareness of preventive measures and the severity of diarrheal diseases.

ETHICAL APPROVAL

For ethical reasons, the identity of the children whose records were the subject of our study was kept confidential. In this study, only children aged 0-71 months admitted at Kalembe-lembe hospital for acute diarrhea and children whose stool specimens underwent coprological tests were included. Other children older than 71 months and incomplete patient files were excluded from this study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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