Bacterial Enteropathogens Isolated in Childhood Diarrhoea in Kuala Lumpur - The Changing Trend

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Summary

A retrospective review of all stool samples obtained from children aged <16 years with diarrhoea from University of Malaya Medical Centre (UMMC), Kuala Lumpur, from 1978 to 1997 was undertaken to ascertain the pattern of bacterial pathogens causing diarrhoea in children in an urban area in Malaysia.

Of 26444 stool samples processed, 2989 (11%) were positive. The five most common bacterial pathogens isolated were non-typhoidal *Salmonella* (57%), enteropathogenic *E. coli* (EPEC) (14%), *Shigella* spp. (11%), *Campylobacter* spp. (5%) and *Aeromonas* spp. (4%). There was a significant reduction in the average percentage of positive isolation during the last 5 years of the study period as compared to the first 5 years (15.0% vs. 7.2%; r=-0.92, p=0.0001). EPEC and *Shigella* spp. were less commonly isolated in the last five years compared with the first five years of the study (6% vs 21%, p<0.001 for *E. coli*; 7% vs 22%, p<0.001 for *Shigella* spp.).

This information is important for public health education in reducing the incidence of childhood diarrhoea further, and in the selection of appropriate antimicrobials in the management of extra-intestinal complications of childhood diarrhoea.

Key Words: Childhood diarrhoea, Bacterial enteropathogens

Introduction

Diarrhoeal diseases are an important cause of childhood morbidity and mortality, especially in the developing countries[1]. Rotavirus is the single most important aetiological agent of childhood gastroenteritis in both developed and developing countries[2-4]. However, bacterial pathogens causing childhood gastroenteritis in developed countries are quite different from that of developing countries. Non-typhoidal *Salmonella* (NTS) species was the commonest bacterial pathogen isolated from children hospitalized with acute diarrhoea in developed communities such as Italy, Australia and Hong Kong, while enteropathogenic *E. coli* (EPEC) and *Shigella* species were relatively uncommon[5-7]. In developing countries such as Kenya and Nigeria, however, NTS, *E. coli*, *Shigella* and *Campylobacter* species were all common enteropathogens in children[8,9].

There are few comprehensive studies on the bacterial aetiology of acute diarrhoea in children requiring hospital admission in developed countries[6,10]. Little is known about this in developing countries. Two decades ago, both Jegatheson et al[11] and Iyngkaran et al[12] noted that EPEC and *Shigella* species were common pathogens isolated in children hospitalized for acute gastroenteritis (AGE) in Malaysia. Recently, however, NTS was noted to be the commonest bacterial pathogen in children admitted with acute diarrhoea in an urban hospital in Kuala Lumpur, while *E. coli* and *Shigella* species were uncommon[13]. All the above three studies were conducted in the same geographical region in Malaysia. It could be possible that the pattern of bacterial pathogens causing acute diarrhea has changed with the improvement in the standard of living and environmental hygiene within a community.

Knowledge of the predominant bacterial pathogens causing diarrhoea in a community is important in the control of diarrhoeal illness. We report the pattern of bacterial pathogens isolated in children with acute diarrhoea from an urban hospital in Kuala Lumpur and its changing trend over a period of 20 years.

Materials and Methods

The University of Malaya Medical Center (UMMC) is situated at Kuala Lumpur. It is a large tertiary referral center, but also serves the mainly urban population of Kuala Lumpur and its surrounding region. Each year approximately 500 cases of acute gastroenteritis, the third leading cause of all paediatric admissions, were admitted to the Department of Paediatrics of UMMC[14].

The microbiology records of all stool specimens and rectal swabs obtained from children <16 years of age, from 1978 to 1997, were retrieved. These included children with acute severe diarrhoea who required admission to the Department of Paediatrics, and those who were seen at the casualty and outpatient departments for acute diarrhoea but did not require admission. Those reports obtained from children admitted to the oncology ward and special care nursery were not included in the study so that only community-acquired gastroenteritis was studied.

All specimens of stool and rectal swab were routinely processed for *Salmonella, Shigella, Campylobacter, Aeromonas, Vibrio parahaemolyticus and Escherichia coli* by standard bacteriological techniques. Enterotoxingenic *E. coli* was not looked for and *Clostridium difficile* only when a specifical request was made. The age and results of those with a positive bacterial culture were noted. Pathogens that were considered non-pathogenic, such as *Staphylococcus, Klebsiella* species, *Candida* species, and group B streptococcus were not included. The former two were commonly seen in rectal swabs obtained from children who were immunocompromised, such as those with cancer undergoing chemotherapy. Group B streptococcus was commonly seen in rectal swabs from newborns. Similarly, *Salmonella typhi* was excluded as it caused typhoid fever rather than AGE. No attempt was made to retrieve the virological records of stool samples during the study period as they were kept in a separate registry.

The data were analyzed and compared using descriptive statistics, analysis of variance, Student's t-test and x^2 with Yates correction or Fisher exact test where appropriate.

Results

During the study period, a total of 26,444 stool specimens and rectal swabs obtained from patients below 16 years old were processed at the Bacteriology Laboratory, Department of Medical Microbiology, UMMC. Of these, 3602 (14% of total) had a positive culture. Four hundred and eighty nine of these were from newborn infants admitted to the special care nursery of the hospital, most being rectal swabs with group B *Streptococcus* isolate. As these strains were likely to represent bacterial colonization of the infants'

bowel rather than gastroenteritis, they were not included in the study. One hundred and twenty four were *S. typhi*. They were excluded as *S. typhi* caused typhoid fever rather than AGE. Of the remaining 2989 positive results, 2396 (80%) were from hospitalized patients, while the remaining 593 (20%) were from outpatient and casualty units (Figure 1). A small minority (2.8% of total) of these positive isolates consisted of more than one enteropathogens.

Age distribution

Information on age was available for 3014 cases (97%). One thousand six hundred and fifty one (55%) were infants below one year, 920 (31%) were toddlers between one to 4 years of age, 275 (9%) between 5 to 9 years of age, and 168 (6%) were more than 10 years old.

Pattern of isolation

The average number of stool samples obtained annually from children with gastroenteritis had remained relatively constant during the study period (range 1007 to 1667, average 1322 each year). The average percentage of positive isolates during the entire study period was 11.3% (Figure 1). There was a significant reduction in the isolation rate over the years (Spearman ranked coefficient correlation, r=-0.92; p=0.0001, Figure 2). The average isolation rate during the first five years of the study was 15.0%, which decreased to 7.2% during the last five years of the study period (Figure 2). The five most common bacterial pathogens isolated, according to the frequency of isolates were NTS, *Shigella* species, EPEC, *Campylobacter* species, and *Aeromonas* species.

Non-typhoidal *Salmonella* (NTS), the commonest bacterial pathogen isolated (55%) during the entire study, was also the most frequent organism isolated during each year of the study period. This was followed by *Shigella* spp. (13.1%) and EPEC (10.4%). The percentage of isolates positive for NTS over the total stool samples processed had
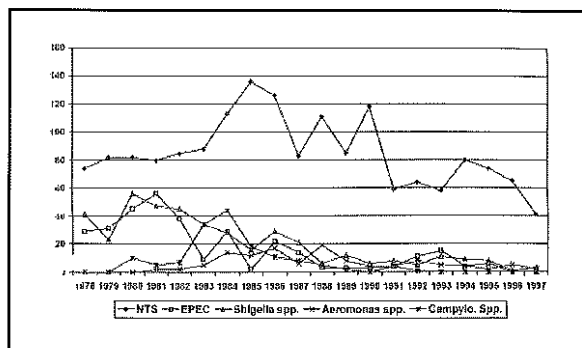

Fig. 1: **Isolation of bacterial enteropathogens from children below 16 years in the Department of Paediatrics, University of Malaya Medical Center, Kuala Lumpur from 1978 to 1997.**
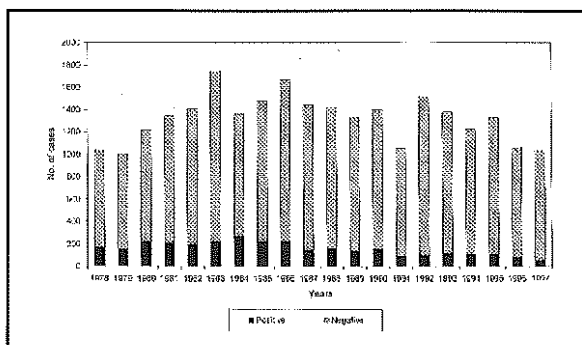

Fig. 2: **The percentage of stool samples positive for bacterial pathogen in children <16 years, UMMC, 1978 - 1997.**

decreased significantly throughout the study period, ranging from an average of 6.7% during the first five years of study to an average of 5.3% during the last five years of study (p-value=0.001; relative risk (RR) 1.27; 95% confidence interval (CI) 1.10,1.47). However, the percentage of NTS

in samples that were positive for any isolate had increased from an average of 43% during the first five years of study to an average of 71% during the last five years of the study (p-value < 0.001; RR 1.27; 95% CI 0.24, 0.39). This was due to the decline of *Shigella* spp. and EPEC, especially during the last five years of the study.

The percentage of positive isolates for *Shigella* spp. and EPEC had decreased significantly during the study period. Both EPEC and *Shigella* spp. were more commonly isolated in the first five years of the study compared with the last five years of the study (*E. coli* 22% vs 8%, p<0.001; RR 3.78; 95% CI 2.53, 5.64; for *Shigella* 23% vs 7%, p<0.001; RR 3.15; 95% CI 2.21,4.49). *Shigella flexneri* constituted 74% of all *Shigella* isolates in the first five years of the study, as compared to 19% during the last five years of the study (p-value <0.001; RR 3.92; 95% CI 1.90, 8.10). There was not a single positive isolate of EPEC during the last two years of the study.

Vibrio cholerae was not common, occurring only as epidemics of cholera in Kuala Lumpur and its surrounding areas. The remaining *Vibrio* isolates were *Vibrio parahaemotylicus* which was only seen sporadically. Similarly, *Aeromonas* species were only seen sporadically. *Campylobacter* spp, which was not uncommon in the early eighties, was not isolated during the last five years of the study.

Discussion

Knowledge of the pattern of bacterial pathogens causing childhood diarrhoea in a community is important for the following reasons. Firstly, it is important in health planning to reduce the incidence and morbidity of childhood gastroenteritis. Secondly, when a young child with acute diarrhea develops extra-intestinal complications such as septicemia, awareness of the predominant bacteria causing acute diarrhoea in a community will enable early institution of appropriate antimicrobial therapy.

This study showed that NTS is the most common bacterial pathogen isolated in children with diarrhoea who required admission or medical attention throughout the study period. NTS, besides being transmitted through contaminated water and by the fecal-oral route, can also be transmitted through contaminated food[15]. *Salmonella* spp. can be found in poultry flocks, and as many as 50% of commercially available chickens may be infected[15]. In addition to the faecal contamination of poultry products that occur during processing, NTS may be passed transovarially, so that even intact eggs may be a source of infection if they are not thoroughly heated[16]. As infections through the fecal-oral route declines, transmission via contaminated food may become relatively important as a source of infection. The proliferation of fast food industry, street-food and illegal hawker stalls in and around Kuala Lumpur may have contributed to this observation.

Another important point regarding NTS as the commonest bacterial pathogen in childhood diarrhoea is when a child with AGE develops extra-intestinal complications such as bacteraemia, it is very likely to be caused by NTS. Thus appropriate antimicrobial therapy should be instituted while awaiting the result of antibiotic sensitivity, thereby avoiding delay in treatment, as NTS bacteramia in very young infants may be associated with significant morbidity and mortality[17].

Twenty years ago, both Jegatheson *et al*[11] and Iyngkaran *et al*[12] noted that EPEC and *Shigella* species were the common pathogens isolated in children hospitalized for acute gastroenteritis (AGE) in Malaysia. However, in the present study, both EPEC and *Shigella* species have become significantly uncommon, especially during the last few years of the study. Furthermore, *S. flexneri*, the predominant subgroup during the early part of the study, had been replaced during the latter part of the study period by *S. sonnei*, which predominates in industrialized countries[18]. This

pattern is very similar to those seen in developed communities, such as in Italy[5], Melbourne[6] and Hong Kong[7]. *Shigella* species is readily spread by direct person-to-person contact because of the low inoculum size needed for initiation of infection[19], while *E. coli* is usually transmitted through faecal-oral route, from contamination of food and water by infected faeces, as well as from person-to-person[20]. Thus, when environmental hygiene improves because of urbanization of a community, enteropathogenic *E. coli* and Shigella species become relatively unimportant as bacterial pathogens causing diarrhoea in children.

This study suggests that in the span of twenty years, there is a trend for the pattern of bacterial pathogens causing childhood diarrhoea changing from that of a developing country to one similar to a developed community. The important route of transmission of childhood diarrhoea has also changed from the faeco-oral route to transmission by contaminated food. Such a trend could occur as a result of improvement in environmental hygiene, resulting in the reduction of mortality and morbidity following acute gastroenteritis in children[13, 21]. A similar explanation may also be possible for the observation that both *Campylobacter* species and *Aeromonas* species, were commonly transmitted faeco-oral route, had become uncommon causes of bacterial diarrhoea during the latter part of the study[22].

This study shows that the percentage of isolates positive for bacterial pathogens has decreased significantly during the latter years of the study period. It is more likely that this trend is a reflection of the change in the pattern of bacterial pathogens causing childhood diarrhoea in Kuala Lumpur and its surrounding area, rather than due to any change in the laboratory methods.

However, the most important limitation in this study was the lack of comparative data on viral pathogens such as rotavirus and adenovirus and other bacterial enteropathogens such as enterotoxingenic *E. coli* and *Clostridium difficile*. Hence it was not possible to compare the relative importance of viral and bacterial pathogens in causing childhood gastroenteritis. In a one-year retrospective study done in the same unit in 1996, rotavirus was the commonest enteropathogen (29% of all diarrheal cases) isolated from stool samples in children admitted with acute diarrhoea, while NTS was isolated in approximately 10% of children[13]. Thus rotavirus was the single most important aetiological agent causing acute diarrhoea in children in UMMC, while NTS was the most common bacterial pathogen. The relative low isolation rate of EPEC and *Shigella* may be due to the rapid urbanization of Kuala Lumpur and its surrounding areas during the last two decades.

Another factor that needs consideration is the increasing trends of mild and moderate diarrhoea being treated at the casualty or outpatients department where stool cultures are not routinely obtained. Hence the pattern of isolation may reflect those with a more severe form of diarrhoea that required in-patient management. Nevertheless, only one fifth of the stool specimens were obtained from children attending outpatient and casualty departments of the hospital for AGE.

This study has shown a changing trend in the isolation of bacterial pathogens causing childhood diarrhoea in Kuala Lumpur and its surrounding areas in the last two decades, from one typical of a developing country to that of a developed one. NTS has become the most important bacterial cause of childhood gastroenteritis. This knowledge is also important in the selection of appropriate antibiotics in the management of extra-intestinal complications in children with AGE. Education of the public regarding the importance of food hygiene is thus important if the incidence of bacterial diarrhoea in childhood in this region is to be reduced further.

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