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Rotavirus infection in Hong Kong: epidemiology and estimates of disease burden

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SUMMARY

Rotavirus gastroenteritis should soon be a vaccine-preventable disease. In a 10-year survey of rotavirus gastroenteritis conducted at the Prince of Wales Hospital (PWH), 2281 cases were detected of which 2213 (97%) occurred in children < 5 years old. A consistent epidemic occurred each winter during the months of December and January. Of all laboratory-confirmed cases, 78% were community-acquired with a mean hospital stay of 4·7 days. The estimated incidence of rotavirus-attributed hospitalization was 2/1000 children < 5 years old. Over the 10 years, rotavirus was responsible for one death, and contributory to three other deaths. On average each year, 195 children < 5 years old were hospitalized for a total of 917 days in PWH, accounting for an estimated expenditure of HK$2·8 (~ US$0·4) million on hospitalization costs. The annual financial burden for rotavirus gastroenteritis for the whole of Hong Kong could be in excess of HK$9·6 (~ US$1·2) million.

INTRODUCTION

Rotaviruses are recognized as a major cause of severe gastroenteritis in infants and have been estimated to be responsible for 20–70% of hospitalizations for diarrhoea among children world-wide [1]. The discovery of rotavirus by Bishop and colleagues in 1973 provided an impetus for research into a rotavirus vaccine [2]. The first vaccine, a live preparation from a bovine strain, was tested in 1983 [3]. Subsequent studies on reassortant live vaccines [4], baculovirus-expressed virus-like particles [5] and naked DNA vaccines [6] have been undertaken with varying degrees of success. Despite the difficulties in measuring the level of protection conferred by various candidate vaccines, and uncertainties in projecting results of animal tests to humans, it is anticipated that a live oral 'Jennerian' reassortant vaccine may soon be approved for human use [7, 8].

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Rotavirus-attributed mortality mainly occurs in the developing countries where the benefit for a rotavirus vaccine would be tremendous. The potential benefit for a rotavirus vaccine in developed countries has been more controversial. In 1985, the Institute of Medicine concluded that a rotavirus vaccine was not a priority for children in the United States [9]. However, Smith and colleagues in a recent report estimated that more than 3 million cases of rotavirus gastroenteritis with over 100000 hospitalizations and 100 deaths occurred there annually, and concluded that a rotavirus vaccine with an efficacy even as low as 50% would be cost-effective if used as a routine childhood immunization in the United States [10]. A similar report by Ryan and colleagues found that 17810 rotavirus-related hospitalizations occurred annually in England and Wales from 1990–4 [11]. With the anticipated availability of an effective rotavirus vaccine in the near future, it is important to document the magnitude of the problem in various countries.

Hong Kong represents an example of a country with rapid economic growth from a previously less developed status, a so-called newly industrialized country. Marked economic improvement has impacted on healthcare and hygienic conditions, resulting in a changing epidemiology and impact of infectious diseases, as has been noted with hepatitis A in Hong Kong over the last 10 years [12]. We set on documenting and assessing the epidemiology and financial burden of rotavirus infection in Hong Kong.

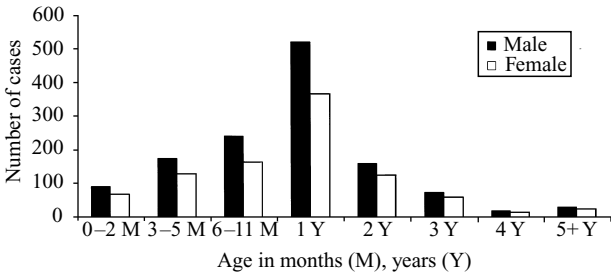

Fig. 1. Rotavirus gastroenteritis by age and sex in the Prince of Wales Hospital, January 1987 to December 1996.

METHODS AND MATERIALS

The study was conducted at the Prince of Wales Hospital (PWH), a 1400-bed acute regional hospital. PWH is the teaching hospital of the Chinese University of Hong Kong, serving the Eastern and Northern New Territories, and the outlying islands with a population of 1·3 million of which 7·6% are children aged < 5 years. This region constitutes about 21% of the total population of Hong Kong. While PWH is the major public hospital serving the region, a portion of residents may utilize private hospitals or public hospitals in the neighbouring regions.

Rotaviruses were detected from patients' faecal samples by using commercial group A-specific indirect enzyme immunoassays Rotazyme (Abbott, USA) from 1987–93 and IDEIA™ Rotavirus (Dako Diagnostics, Cambridgeshire, UK) from 1994–6. Patients who had rotavirus infections were identified through records of the virus laboratory. The time of detection of rotavirus, length of hospital stay and outcome of illness were obtained from the Infection Control Unit of the hospital which documents all rotavirus infections for infection surveillance and control purposes. Using these data, all cases that were positive for rotavirus as a consequence of investigation of a diarrhoeal illness during the period 1 January 1987 to 31 December 1996 constituted our study population.

Clinical information on the study cases were obtained from computerised audit records [13] and included patients' biodata and diagnoses. In addition to recording International Classification of Diseases Codes, hospitalized patients with acute diarrhoeal illnesses were assigned to one of three groups: non-specific gastroenteritis without laboratory confirmation, laboratory-confirmed bacterial gastroenteritis and laboratory-confirmed viral gastroenteritis respectively. Details of all patients assigned to these three groups were abstracted.

The detailed records of the Infection Control Unit for all laboratory-confirmed rotavirus infections in 1996 were reviewed to define the relationship between gastroenteritis as a presenting feature on admission and the time of first detection of rotavirus. Among the 267 positive cases in that year, 212 had gastroenteritis as their major presenting symptom and rotaviruses were detected from their faecal samples on or before day 2 post-admission; while in only 1 of the remaining 55 positive cases who did not have gastroenteritis on admission was the virus detected on day 2 post-admission. Based on this distribution, we defined a rotavirus-attributed admission as one where detection of rotavirus occurred on or before day 2 post-admission. This case definition was used to estimate the portion of rotavirus-attributed admissions occurring over the 10-year study period. Estimates of the impact of rotavirus-attributed admissions seen at the PWH were extrapolated for the whole territory based on demographic data for the region and the rest of Hong Kong.

RESULTS

Epidemiology

Between 1 January 1987 and 31 December 1996, 2281 laboratory-confirmed cases of rotavirus gastroenteritis were detected. Of these, 2213 (97%) occurred in children < 5 years old while only 2 of the remaining 68 cases were in elderly patients > 65 years old. When divided into the age groups 0–2, 3–5 and 6–11 months old, 1, 2, 3, 4 and > 5 years old, the vast majority of cases were found in infants aged 3–23 months. Overall, children aged < 5 years accounted for 97% of cases (Fig. 1), and the male to female ratio was 1·4:1 (range 1·1:1 in > 5-year-old group to 1·5:1 in 6–11 months old group).

A peak incidence of rotavirus infection was ob-

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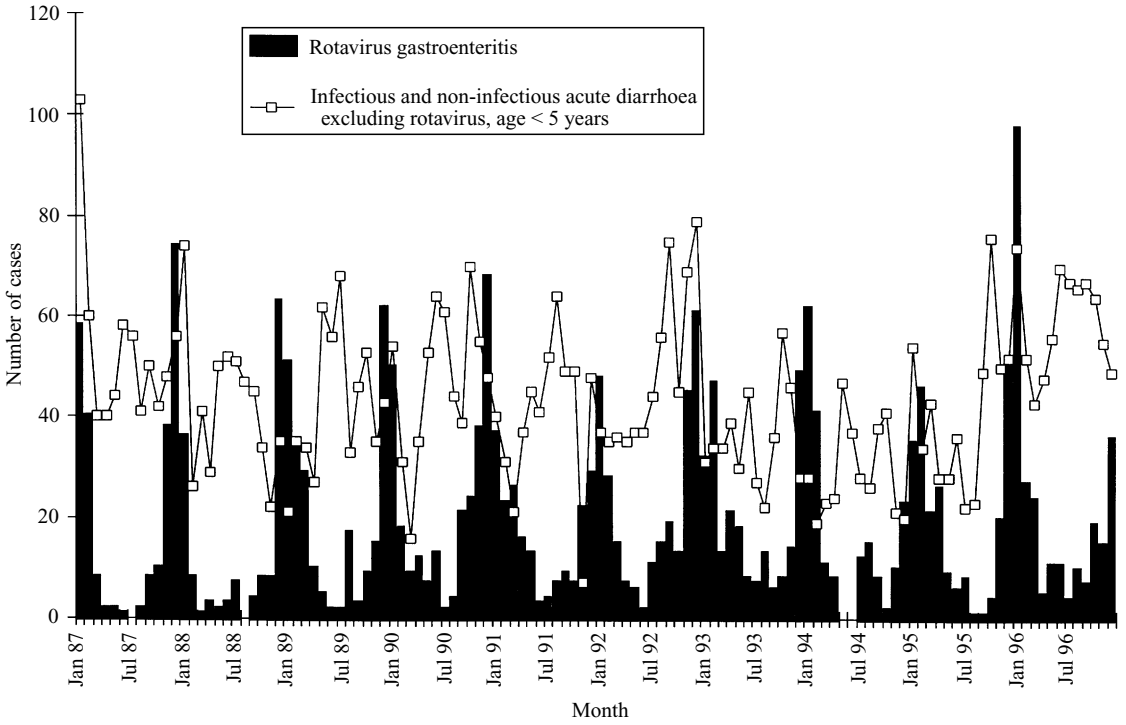

Fig. 2. Rotavirus gastroenteritis and acute diarrhoea by month in the Prince of Wales Hospital, January 1987 to December 1996.

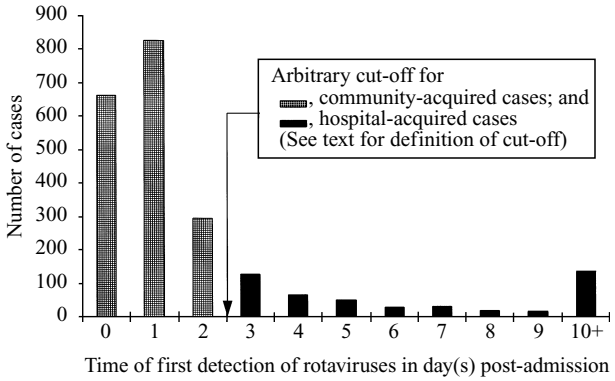

Fig. 3. Community- and hospital-acquired rotavirus gastroenteritis estimated by time of detection in the Prince of Wales Hospital, January 1987 to December 1996.

served in the Hong Kong winter between December and January each year when 45% of the 2281 positive cases occurred. This seasonal variation of rotavirus gastroenteritis and acute diarrhoea other than rotavirus among children < 5 years old is shown in Figure 2.

By extrapolating the 1996 data, an estimated 78% (1779/2281) of cases occurred during the 10-year period were considered to be rotavirus-attributed admissions. The remaining 22% of cases were considered to be hospital-acquired infections. (Fig. 3)

Estimates of disease burden

The mean annual incidence of laboratory-confirmed rotavirus gastroenteritis, irrespective of patient's age, was 228 (range 143–270, S.D. 40), and among children < 5 years old the mean rotavirus-attributed hospital admissions over the study period was 195 per year representing a rate of 2/1000 children of that age group in the region served by the hospital [14]. Rotavirus-attributed admissions represented approximately 26% of diarrhoea-related, and 6% of all admissions of children < 5 years old in PWH. The mean duration of hospital stay for these children admitted for rotavirus gastroenteritis was 4·7 days (range 1–12, S.D. 2·5), accounting for an average of 917 days of hospitalization per year in PWH.

The average daily cost of hospitalization which including charges for bed, medication and laboratory tests in the paediatric wards of PWH as at 1996 was HK$3096 according to the hospital finance department. Based on this figure, the estimated annual cost of rotavirus-attributed admissions to PWH of children < 5 years old is HK$2·8 million, which represented 0·2% of the total annual expenditure of the hospital in 1996. When this is projected to the rest of Hong Kong which has a population of 6·3 million of which 5·3% are children less than 5 years [15, 16] the annual

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financial burden of rotavirus-related admissions would be in the region of HK$9·6 million.

Mortality

Nineteen deaths were recorded amongst the 2281 rotavirus positive cases during the course of hospitalization but in only 4 children could rotavirus infection have been contributory to death. In 3 of these 4 deaths, gastroenteritis persisted along with other ongoing illnesses: one neonate had heart failure due to multiple congenital heart defects, another 2-year-old girl had concurrent *Streptococcus pneumoniae* septicaemia and the third, a 15-month-girl, had concurrent *Haemophilus influenzae* septicaemia. The fourth death occurred in a 14-month-old girl who had no other findings than gastroenteritis to which she succumbed 4 days after admission.

DISCUSSION

Our results confirm previous observations from different parts of the world that rotaviruses are a major cause of hospitalization for children with diarrhoea [17]. There has been no observable change in the epidemiology of rotavirus infection over the 10-year study period. The regular winter epidemics observed in Hong Kong is similar to those observed in temperate climates including Malaysia, Australia, the United States, Japan and the United Kingdom [11, 18–21]. By contrast, in tropical areas the virus is endemic throughout the year, though there appears to be some clustering during the cooler, dry season [22, 23].

While it is frequently stated that rotavirus infection in infants up to 3 months old are either asymptomatic or mild, we found that 7% of our patients requiring hospitalization fall in this age group. This is in agreement with reports from USA and England where the corresponding proportions were 7 and 13% of admissions respectively [20, 24].

We estimated that rotaviruses were responsible for 26% of diarrhoea-related hospital admissions in children < 5 years old. This is lower than those observed in the United Kingdom, Japan and Australia (43–63%) [11, 21, 25], and presumably could be due to the high prevalence of other enteric pathogens particularly *Salmonella* spp. which account for 23% of diarrhoea in hospitalized children in Hong Kong [26]. Socioeconomic status, level of hygiene and the practice of breast feeding are known to affect the prevalence of overt rotavirus infection [17]. We obtained a lower rate of 2/1000 per year rotavirus-attributed hospital admissions for children < 5 years compared to the 5/1000 per year reported in England and Wales [11] and a shorter mean length of hospital stay of 4·7 days than the 5·5 days estimated from the Queen Elizabeth Hospital in London [24]. This may imply the disease burden of rotavirus in Hong Kong is less than that in England and Wales but alternatively, may represent an under-estimation due to utilization of private hospitals and adjacent public hospitals by some of the residents.

The projected direct annual expenditure of HK$9·6 ($\sim$ US$1·2) million on rotavirus-attributed hospital admissions for children < 5 years old in Hong Kong only accounts for part of the total financial burden. The true cost of this infection would include the cost of management at home by ambulatory services and general practitioners, and the parents' lost time from work. Additional costs worth around 25% of the projected estimates will be incurred if infection in patients aged $\geqslant 5$ years are included and the burden of nosocomial infections are considered in the estimates. In addition, the proportion of cases that were admitted to private hospitals should be included to assess the total financial burden for the whole territory. While rotavirus-related mortality is rare in Hong Kong, its contribution to childhood mortality in the presence of concurrent severe illness deserves serious attention whenever it occurs.

It is evident from this study that the true cost of rotavirus infection is enormous. As there is an increasing emphasis on the cost of health provision, there is a need for an in-depth study to determine the true impact and the most cost-effective health policy for rotavirus infection in the community at large. A precise decision on rotavirus immunization policy can only be made when the cost benefit of such a programme has been established; but our findings suggest that a rotavirus vaccine for prevention of severe disease and reduction of treatment costs would be of significant benefit to Hong Kong.

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