EPIDEMIOLOGY OF INTUSSUSCEPTION IN MALAYSIA:
A THREE-YEAR REVIEW

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Abstract. This study aimed to document the baseline incidence and epidemiology of intussusception (IS) in Malaysia. This retrospective surveillance examined hospital discharge data from three hospitals in Malaysia to identify IS cases over a 3-year period (2000-2003) in children <5 years of age. Identification of definite cases of IS was done through a search of computerized hospital discharge records (ICD-9-CM code 560.0) followed by confirmation of diagnosis through medical record review. The definition of IS was based on the clinical guidelines from the IS Brighton Collaboration Working Group, version 2002. During the 3-year study period, there were 62 cases hospitalized due to IS, of which 74.2% were <1 year of age. The incidences for hospitalization due to IS in children <1 year old and <5 years old averaged 17.8 and 4.8 per 100,000 person-years, respectively. No IS-associated deaths were recorded and all IS cases had a favorable outcome. No distinct seasonality with IS occurrence was observed.

INTRODUCTION

Rotavirus (RV) has been identified as the most common cause of severe gastroenteritis (GE) in infants and young children throughout the world (Salinas et al., 2004), leading to more than 600,000 deaths per year in the developing countries (Parashar et al., 2003, 2006). Of these deaths, 90% occur in the poorest countries of Africa and Asia (Parashar et al., 2003; Bresee et al., 2005; Glass, et al., 2005).

In Southeast Asia, RV is estimated to cause death in 1 out of every 111-203 Bangladeshi children (Unicomb et al., 1997) and up to a staggering 100,000 deaths in India every year (Jain et al., 2001). A recent study conducted in Malaysia showed that RV disease is the cause of one-half of all hospitalizations for acute GE. Approximately, 23,000 inpatient and outpatient visits for acute GE were caused by RV annually. These data show the significant burden of RV disease in Malaysia (Hsu et al., 2005).

In the United States severe RV disease is associated with 500,000 physician visits per year, with 60,000 hospitalizations, 20-40 deaths, and annual costs exceeding $1 billion (Glass et al., 2005).

These alarming figures led the World Health Organization (WHO), the Institute of Medicine, and the Global Alliance for Vaccines and Immunization (GAVI), to identify RV vaccines as a priority for development (Glass et al., 2006). However, the first licensed rotavirus vaccine, RotaShield™ (Wyeth-Lederle), which was highly efficacious in preventing severe GE and hospitalizations due to RV infection, was suspended 9 months after introduction due to reports of a temporal association between...
the vaccination and the development of intussusception (IS) (CDC, 1999). However, the exact risk, which was estimated to be about one case of IS in 10,000 RotaShield™ vaccine recipients, remains controversial (Peter and Myers, 2002). As new rotavirus vaccines are becoming increasingly available in Asian countries, there is a need for effective surveillance of IS in the countries where these vaccines may be introduced as a part of the routine childhood immunization schedule (Glass et al, 2006; Phua et al, 2006). Two oral rotavirus vaccines are now available in Malaysia, Rotarix™ (GlaxoSmithKline Biologicals, Rixensart, Belgium) available since July 2006 and RotaTeq™ (Merck and Co), available since July 2007.

Intussusception is the most common cause of abdominal surgical emergencies in infants and children and is characterized by a palpable abdominal mass, colicky abdominal pain, vomiting and passage of bloody stool in children 3 months to 5 years old (Parashar et al, 2000; Nakagomi et al, 2006). Some IS cases resolve spontaneously and, if treated early, almost all can be reduced by enema or surgery; if untreated IS may be fatal.

In Asian countries, such as Vietnam, Singapore, Japan and Taiwan, 71-302 cases of IS/100,000 infants <1 year of age have been reported annually, while mortality varied between 0-58% (WHO, 2002; Ho et al, 2005; Bines et al, 2006; Nakagomi et al, 2006).

There are only limited data reporting the incidence of IS in the Malaysian population. Hence, this hospital-based retrospective surveillance study assessed the incidence, clinical presentations, management and outcomes of IS from cases reported in three hospitals (Hospital Ipoh, Perak; Hospital Pulau Penang, Penang; and Sarawak General Hospital, Sarawak) in Malaysia.

MATERIAL AND METHODS

This retrospective review using data extracted from the medical records of children <5 years of age who were diagnosed with having IS was conducted over a 3-year period (June 2000-June 2003) in Malaysia. The study was approved by the ethics review committee and International Conference of Harmonization Good Clinical Practice (ICH/GCP) guidelines were complied with throughout the study.

Malaysia is a federation of 14 states (WHO, 2004) in Southeast Asia comprised of various ethnic groups, including Chinese, Malays and Indians. Three hospitals (Hospital Ipoh, Hospital Pulau Penang and Sarawak General Hospital) were chosen to conduct the study and ascertain the number of IS cases. These three study sites cover about 20% of the Malaysian population of both peninsular and East Malaysia (States of Malaysia, 2006), and are the representative locations chosen to conduct the study (Fig 1).

Identification of definite cases of IS was done through a search of the computerized hospital discharge and death records, followed by confirmation of the diagnosis through a medical record review. An initial check of hospital records using the International Classification of Diseases (ICD), Ninth Revision, Clinical Modification code IS (560.0) was followed by a review of the discharge diagnoses logbook kept for patients who presented to the emergency department. To avoid potential missed cases, records of the radiology, surgery and pathology departments of all participating hospitals were also reviewed.

A case-subject was defined as a child <5 years of age who fulfilled level 1 diagnostic certainty by the criteria of the Brighton Collaboration IS Working Group (Table 1). Once a potential case-subject was identified, the child’s medical records were reviewed to ensure that the case met the inclusion criteria. If the diagnosis of IS was solely based on clinical signs and symptoms, the case-subject was excluded.
Level 1 of evidence (Definite)

**Surgical criteria**
The demonstration of invagination of the intestine at surgery, and/or

**Radiological criteria**
The demonstration of invagination of the intestine by either gas or liquid contrast enema, or
The demonstration of an intra-abdominal mass by abdominal ultrasound with specific characteristic features\(^a\) that is proven to be reduced by hydrostatic enema on post-reduction ultrasound and/or

**Autopsy criteria**
The demonstration of invagination of the intestine.

\(^a\) target sign or doughnut sign on transverse section and a pseudo-kidney or sandwich sign on longitudinal section

The chart review of IS cases was performed using a standardized case report form. Variables obtained included demographics, past medical history, clinical signs and symptoms, diagnostic procedures, laboratory results, medical and vaccination history, treatment and outcome of admission.

To compute the incidence of IS cases, the numerator comprised all cases of definite IS. The denominator was calculated as the size of a one year birth cohort in the study site areas multiplied by the duration of the study (in years) and by the estimated overall proportion of that cohort who would visit the study hospitals should they have an IS. For the person-year incidence rate, the denominator was multiplied by 5, as all subjects <5 years of age were considered. All statistical analyses were...
performed using the SAS software program, version 8.2.

RESULTS

For a period of three years, beginning June 2000, a total of 67 patients with a discharge diagnosis of IS were identified from the hospital database. Five patients were excluded from analysis since their date of birth was unknown. Therefore, the final analysis was performed on 62 cases in children age <5 years. Of these, 46 cases (74.2%) occurred in infants (<1 year old).

The mean age of the children was 11.4 months (standard deviation: 10.4 months), and ranged between 2 and 52 months. Of the 62 children diagnosed with IS, 58.1% occurred in males (male vs female = 1.4: 1). The ethnic distribution was 62.9% Malays, 19.4% Chinese, 3.2% Indians, with the remaining 14.5% from other ethnic groups (Bidayuh and Iban).

The incidences of hospitalization due to IS in children age <1 year and <5 years averaged 17.8 and 4.8 per 100,000 person-years, respectively. The IS-associated hospitalization rates ranged between 14.48-21.26 per 100,000 person-years for the <1 year age group, and 3.31-8.5 per 100,000 person-years for the <5 years age group during the study period (Fig 2).

IS-associated hospitalizations showed a distinctive peak in the 6-11 months old age group, accounting for 45.2% of the total (Fig 3). Hospitalizations in the <6 months old age group accounted for 29%, while there were no hospitalizations in the 0-1 month old age group. Only one-fourth of the IS hospitalizations occurred in children age >1 year old (25.8%).

There was no evidence of seasonally related variability in the rates of IS-associated hospitalizations over the 3-year period. However, the quarterly distribution of cases indicates 29% of cases occurred between March and May and another 29% between June and August, different from the expected 25% per quarter (Fig 4).

Vomiting (80.7%) and abdominal mass (45.2%) were the most common presenting clinical symptoms. Co-existing diarrhea was present in 40.3% of cases (Table 2).

A diagnosis of IS was made in the majority of cases by barium enema (67.7%), followed by surgery (17.7%). Reduction of the IS occurred mostly by surgery (56.5%) followed by reduction through radiological methods (37.1%) (Table 3).

There were no reports of deaths during the study period and all definite IS cases had a favorable outcome.

DISCUSSION

We expect there is minimal underestimation of cases for the following reasons. First, since IS is an acute illness, patients are less likely to travel to another state to seek
Due to the small number of cases, great variability in the incidences was observed. During June 2000-June 2003, the estimated incidence rate averaged 17.8 per 100,000 in infants <1 year old and 4.8 per 100,000 in children <5 years old. Over the 3-year duration of the study, there was a 2-fold difference in the incidence, indicating notable variation from year to year. The hospital-based IS incidences reported in this study rank lower than...
the incidences reported from various other Asian countries, such as Vietnam, Singapore, Japan and Taiwan (WHO, 2002; Ho et al, 2005; Bines et al, 2006; Nakagomi et al, 2006) where the incidences have been estimated at 71-302 cases of IS/100,000 in infants <1 year of age.

It is worth noting that the number of IS cases at each center varied: 23 cases in Ipoh Hospital, 8 cases in Hospital Pulau Penang and 36 cases in Sarawak General Hospital. This variation in the distribution of IS cases could be due to the management of cases at each center. The three hospitals differ by the type of population they serve. In Penang, much of the population seek treatment at the numerous private hospitals. There are no published statistics on the percent of patients seeking private hospital treatment in Malaysia, but it is a minority (less than 20%) since patients seek treatment at public hospitals. To reconfirm and clarify this lower incidence rate for IS in Malaysia compared to other countries in the region, a prospective surveillance system involving all private hospitals should be put in place.

An underlying cause for the lower incidence rate in this study may also be due to improved sanitation, ethnic, genetic or nutritional factors (Justice et al, 2005). In very young infants, this low rate may occur due to persisting maternal antibodies, breastfeeding or the low antigenic diversity of infant diets (Parashar et al, 2000).

We found that age and gender distributions in Malaysia were consistent with the known epidemiological profile of IS elsewhere (WHO, 2002). There were no seasonal variations in the incidences of IS in the study, which is reasonable for a country like Malaysia where there are no distinct seasons. Previous studies have demonstrated that IS occurred either consistently throughout the year or peaks during the summer (Hsu et al, 2005).

Vomiting was the most common clinical symptom. Its absence makes the diagnosis of IS unlikely (Eshel et al, 1997). Other commonly reported symptoms included on abdominal mass and diarrhea, which are consistent clinical features is IS (Meier et al, 1996; Nelson, 2007). This is in line with several studies showed the diagnosis of IS is carried out conservatively (barium, air or saline enema). In our study, most of the children were diagnosed with barium enema (WHO, 2002; Justice et al, 2006).

The majority of the children in this study were treated for their IS using surgery. The high rate of surgery (56.5%), instead of using an enema, may be attributed to a longer delay in seeking treatment and less access to other treatment tools. A lack of experience

<table>
<thead>
<tr>
<th>Variables</th>
<th>No. of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td></td>
</tr>
<tr>
<td>Air enema</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Barium enema</td>
<td>42 (67.7)</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>7 (11.3)</td>
</tr>
<tr>
<td>Other radiographic procedure</td>
<td>7 (11.3)</td>
</tr>
<tr>
<td>Laparotomy/surgery</td>
<td>11 (17.7)</td>
</tr>
<tr>
<td>Others</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Unknown</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Reduction procedures</td>
<td></td>
</tr>
<tr>
<td>Resolved without treatment</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Resolved by radiological reduction</td>
<td>23 (37.1)</td>
</tr>
<tr>
<td>Failed radiological reduction, sent to surgery</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Surgery</td>
<td>35 (56.5)</td>
</tr>
<tr>
<td>Others</td>
<td>4 (6.5)</td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
</tr>
<tr>
<td>Recovered</td>
<td>62 (100.0)</td>
</tr>
<tr>
<td>Deceased</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

N = Total number of intussusception cases

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The majority of the children in this study were treated for their IS using surgery. The high rate of surgery (56.5%), instead of using an enema, may be attributed to a longer delay in seeking treatment and less access to other treatment tools. A lack of experience
with non-surgical treatment is another probably factor (Huppertz et al, 2006). Successful outcome is less common in children with IS treated in the developing world, where patients present late in the course of the disease and are usually treated operatively with mortality rates reported as high as 25% (Meier et al, 1996). The treatment outcomes in this study were favorable for all patients with no fatalities.

This study provides an estimate of the incidence rate and baseline data regarding the epidemiology of IS in children <5 years of age in Malaysia. Age and gender distributions of IS in Malaysia are in line with previously reported data. No seasonal associations were observed in the occurrence of IS. The incidences of IS in children <1 year old and <5 years old were 17.8 and 4.8 per 100,000 person-years. These estimates are lower than other countries in the region. More studies are needed to provide a clearer understanding of IS in the Malaysian population.

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REFERENCES


