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An overview of hepatitis A at Tygerberg Children's Hospital

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Introduction. Hepatitis A is a vaccine-preventable infection, common in children in the Western Cape.

Objectives. To describe childhood hepatitis A morbidity and mortality at Tygerberg Children's Hospital, a level two and three referral hospital in the Western Cape, South Africa.

Methods. Serological tests with positive hepatitis A IgM were identified from the Tygerberg Hospital virology laboratory database from 2001 to 2004. Medical records were reviewed if identified sera came from children younger than 13 years. The cases were cross-referenced with the paediatric gastroenterology database. Data collected included demographics, clinical and laboratory information, outcome, notification and primary prophylaxis.

Results. 184 subjects were identified, comprising 117 males and 67 females with a median age of 69 (range 5 - 152) months. Two patients had hepatic failure and both died. Ten (5%) had known hepatitis A contacts but received no post-exposure prophylaxis, and only 31 (17%) were notified. A small percentage of patients were also positive for hepatitis B, hepatitis C and HIV. The median population incidence of serologically proven hepatitis A infection was 45.4/100 000/year, higher than the 20/100 000 advocated as a threshold for introducing vaccination into the immunisation schedule.

Limitations. Incidence data calculated from prospective studies are usually more reliable than those from retrospective studies.

Conclusions. This study confirms that hepatitis A is a serious risk to young children in the Western Cape, with significant morbidity and mortality. In addition, a sizeable number of cases were preventable. In order to determine the burden of disease and make recommendations about vaccination, the national incidence of hepatitis A must be assessed.

Hepatitis A is an RNA-containing virus that causes hepatitis. It is almost always transmitted by the faeco-oral route. Symptomatic hepatitis A causes jaundice, right upper quadrant pain and dark urine and is usually self-limited. In a minority of cases, fulminant hepatitis can occur.[1] The bulk of hepatitis A infection occurs in young children, in whom jaundice is often so subtle that it can only be detected biochemically.

The overall case fatality rate for hepatitis A ranges from 1 to 1.5/1 000, with the highest rates being in under-5s and over-60s. However, mortality may be higher in resource-poor settings. For example, in a study of 12 cases of fulminant hepatitis in children at Chris Hani Baragwanath Hospital, Soweto, 6 were due to hepatitis A and 5 to hepatitis B, the latter being considered a more serious infection.[2] In South Africa there are no recent epidemiological data on viral hepatitis, and the rate of notification is very low.[3]

In developed countries, ageing populations are more susceptible to hepatitis A and outbreaks can be more widespread.[4-9] The majority of studies recommend vaccination.

Hepatitis A vaccination has been associated with a significant drop in the incidence of hepatitis A disease.[10] In South Africa data on hepatitis A are necessary to inform a policy for immunisation.

Objectives

The study aimed to describe the morbidity and mortality associated with childhood hepatitis A at Tygerberg Children's Hospital (TCH), a level two and three referral hospital in the Western Cape, South Africa.

Methods

Sera with detectable hepatitis A IgM were identified by searching the Tygerberg Hospital virology laboratory database for the period 2001 - 2004. Medical records were reviewed if identified sera came from children younger than 13 years. In addition the cases were cross-referenced with the paediatric gastroenterology database.

Data collected included demographics, clinical and laboratory information, outcome, notification and primary prophylaxis. Liver failure was defined as an international normalised ratio (INR) >2 (non-responsive to vitamin K) and hepatic encephalopathy, without pre-existing liver disease, within 8 weeks of the onset of clinical liver disease.[1,11]

The annual incidence of hepatitis A infection in children under 13 years of age over the study period was calculated for TCH's secondary drainage areas using municipal data from the 2001 census undertaken by Statistics South Africa, as well as the

estimated annual population growth rates, also from Statistics South Africa.[12,13]

The Research Ethics committee of the Faculty of Health Sciences, Stellenbosch University, approved the study.

Results

One hundred and eighty-four children with detectable hepatitis A IgM were included in the study. There were 117 males and 67 females, with ages ranging from 5 to 152 months and a median age of 69 months (Fig. 1).

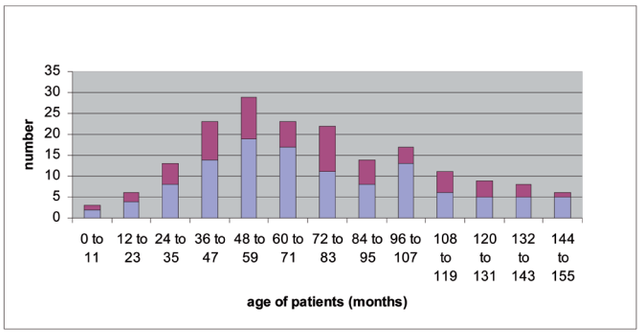

Fig. 1. Age distribution of children with symptomatic hepatitis A.

The clinician made a presumptive diagnosis of hepatitis in 67% (*N*=124) of cases, the diagnosis was not recorded but presumed to be hepatitis in 27% (*N*=49), and in the remaining 6% (*N*=11) the rationale for doing serological testing for hepatitis was either abnormal hepatic signs or abnormal liver function tests. The common symptoms and signs included jaundice (47%), hepatomegaly (33%), nausea and vomiting (33%) and abdominal pain (28%) (Table I). Ninety-two per cent of subjects (*N*=170) were seen in the ambulatory paediatrics clinic and spent less than 1 day at hospital. Fourteen children (8%) required inpatient care and spent a median of 6 (range 1 - 36) days in hospital. Eight subjects (4%) had an INR of over 1.5, including 2 with an INR of more than 2, who both died.

Seventy-one per cent of the subjects (*N*=131) lived in the secondary drainage area of TCH. Of 10 subjects (5%) with known hepatitis A contacts, none had received post-exposure prophylaxis. Only 31 cases (17%) were notified to the Department of Health. Prophylaxis to household contacts was documented in 4 cases. Four subjects (2%) were receiving hepatotoxic drugs at the time of diagnosis: these were antituberculosis drugs (1), antiretrovirals (1) and cytotoxic medication (2).

Of 151 children evaluated for hepatitis B, 4 were surface antigen positive. One of 120 tested had antibodies to hepatitis C and 1 of 12 tested for HIV had a positive enzyme-linked immunosorbent assay (ELISA) (8%) (Table II).

The INR was >1.3 in 95 patients (52%), the activated partial thromboplastin time (aPTT) >45 seconds in 12 (7%), the worst bilirubin level >70 µmol/l in 76 (41%), the worst albumin level <35 g/l in 17 (9%), and the peak alanine transaminase (ALT) level >35 U/l in 162 (88%).

Incidences of hepatitis A over the study period are shown in Table III. The incidence was 102.7/100 000/year in 2001 and 55.4 in 2002. In 2003 a decrease to 18.5 was noted, but the incidence increased to 35.4 for January - August 2004. The median incidence was 45.4.

Discussion

A significant number of children with hepatitis A present to the paediatric emergency department at TCH. It is probable that the experience in other paediatric emergency departments in South Africa is similar.

Recent studies demonstrated that a national strategy of routine hepatitis A vaccination in areas with an incidence of

TABLE I. SYMPTOMS AND SIGNS OF SYMPTOMATIC HEPATITIS A IN CHILDREN <13 YEARS OF AGE*

	N	%
Jaundice	87	47
Hepatomegaly	60	33
Nausea and vomiting	60	33
Abdominal pain	52	28
Loss of appetite	48	26
Fever	34	18
Diarrhoea	19	10
Loss of weight	8	4
Constipation	8	4
Pruritus	4	2
Bleeding tendency	2	1

*Total percentage >100% because patients presented with more than one symptom.

TABLE III. INCIDENCE OF SEROLOGICALLY PROVEN HEPATITIS A IN THE TYGERBERG CHILDREN'S HOSPITAL SECONDARY DRAINAGE AREA*

Year	Population incidence/100 000 children under 13 years of age
2001	102.7
2002	55.4
2003	18.5
2004 (Jan - Aug)	35.4
Median	45.4

*Uitsig, Belhar, Delft, Elsiesriver and Ravensmead - population 38 952 (2001 census).

TABLE II. RESULTS OF TESTING FOR HEPATITIS B, HEPATITIS C AND HIV

	Tested	Not tested	Unknown	Positive		Negative	
				N	%	*N*	%
Hepatitis B	151	16	17	4	2.6	147	97.4
Hepatitis C	120	47	17	1	0.8	119	99.2
HIV	12	156	16	1	8.3	11	91.7

more than 20/100 000/year and selective vaccination in areas with an incidence of 10 - 20/100 000 resulted in a significant reduction in hepatitis A infection over a 15-year period.[14,15] We have documented a high incidence of symptomatic hepatitis A for the secondary drainage area of TCH, as shown by a median incidence of 45.4/100 000. Only the subjects living in the specific drainage area were used in calculating the incidence, although it was not known whether they were all infected in this area. Our calculations of population incidence are impeded by the fact that the last accurate South African population statistics are from the 2001 census. The dramatic change in the population in this specific area over the study years was taken into account by applying the estimated annual population growth rates to the studied population.[12,13] A proposed explanation for the lower incidence in 2003 is the change of laboratory database with loss of information. Data from prospective studies are usually used to calculate disease incidence. The data from this retrospective study may not only have included patients living outside the designated area; it could also have underestimated the true incidence as there was no protocol that determined which symptomatic patients were tested for hepatitis A. In order to determine extent and burden, and to make recommendations about vaccination, the national incidence of hepatitis A must be assessed.

The majority of children with symptomatic hepatitis do not require hospitalisation. In this study 14 children were admitted, of whom 2 died. The overall mortality rate of 11/1 000 is much higher than the 1 - 1.5/1 000 reported for hepatitis A in general. This is probably because sicker children are more likely to present to our service. Both the children who died were under the age of 5 years, emphasising the higher morbidity and mortality in this age group. Hepatitis B and hepatitis C co-infection was uncommon and morbidity was not increased. Owing to this low rate of co-infection, and the fact that the hospitalisation rate is low, streamlining of the battery of unnecessary special investigations that are routinely performed in patients with suspected hepatitis A infection should be considered. However, measuring the INR is probably worth while as >50% of patients required vitamin K.

Notification rates were extremely low, confirming findings in previous South African studies.[3] A low hepatitis A notification rate results in an underestimation of the burden of disease, which in turn is an obstacle to motivating for and recommending interventions such as hepatitis A vaccination. An alternative would be to use laboratory-based sentinel notification.

Few contacts received prophylaxis. This is disturbing, because hepatitis A is a preventable disease. One explanation may be that the contacts presented too late for prophylaxis to be effective. Only 1 patient had HIV infection. Although this patient did not have an adverse course, prolonged excretion of hepatitis A by HIV-infected patients complicates their management.

Conclusion

The burden of hepatitis A infection on both the health service and the population should be assessed nationally in order to make formal recommendations regarding vaccination.

New strategies should be explored in order to significantly improve the notification rate of paediatric hepatitis A. Higher notification rates will allow for appreciation of the extent and burden of hepatitis A.

Hepatitis A also poses a serious health risk to health care workers, and those who are susceptible should be identified and immunised.

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