

Investigation of a hepatitis A outbreak in children in an urban slum in Vellore, Tamil Nadu, using geographic information systems

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Background & objectives: An outbreak of symptomatic viral hepatitis in children less than 10 yr of age in Vellore, south India, was investigated and the disease pattern studied using serological and epidemiological methods, supplemented by geographic information systems (GIS) mapping.

Methods: Three cases of hepatitis A were identified during routine surveillance in a birth cohort. House-to-house visits were undertaken to identify other symptomatic cases and samples collected for anti-HAV IgM, ELISA testing. All cases and controls were mapped and geo-referenced using Arc View GIS 3.3. Spatial clustering was investigated using SaTScan 7.0.1 software. Drinking water sources were tested for coliform counts with the most probable number technique.

Results: Of the 965 children surveyed, 26 (2.78%) had jaundice between February to July 2006. From the 26 patients, 11 (42.3%) blood samples were obtained and tested for anti-HAV IgM; 10 (90.9%) were found to be positive. Water analysis showed high coliform counts in all samples. No spatial clustering of cases could be detected.

Interpretation & conclusions: The outbreak was identified because of the symptomatic presentation of the cases. Our study highlighted the increasing detection of symptomatic children with hepatitis A virus infection. Water sources in the area were contaminated and may have served as the source of infection. The lack of clustering in GIS analysis could be due to the common water source.

Key words Geographic information system - hepatitis A - outbreak

Hepatitis A virus (HAV) is a positive-strand RNA virus, classified within the genus *Hepatovirus* in the family *Picornaviridae*¹. The HAV particle was first identified by electron microscopy in 1973. It is a small, non-enveloped virus, and is 27nm in diameter, with a highly stable icosahedral protein capsid containing an RNA genome of 7.5 kb. Hepatitis A is highly endemic in developing countries and most children are believed

to acquire immunity through asymptomatic infection early in life². It has been reported that 70 per cent of children <6 yr of age are asymptotically infected or develop a mild self-limiting illness.

Most hepatitis A outbreaks are due to faecal-oral route of transmission because of contamination of food or water with sewage. In developing countries with poor

living conditions such as inadequate water supply, poor sewage facilities and sanitary conditions, the level of transmission of HAV within the community is high. Improvement in hygienic and socio-economic conditions has resulted in a decrease in the number of natural childhood infections³.

Earlier reports suggest that India is hyperendemic for HAV infection^{2,4-6} with very high infection rates in the first few years of life. A study from north India showed that most of the population acquired antibodies to HAV by the age of 10 yr⁴. However, there are reports of a gradual shift in seroepidemiology of hepatitis A⁷. An outbreak of hepatitis A in adults from Kerala clearly documented that a substantial proportion of individuals were not exposed to HAV till adulthood⁸. Adults are more likely to have symptomatic hepatitis A infection than children. Antibodies to HAV (anti-HAV) can be detected during acute illness. This early antibody response is predominantly of the IgM class, is used to establish a diagnosis of acute infection and persists for 5 to 6 months³. During convalescence and during subsequent life, however, anti-HAV of the IgG class becomes the predominant antibody.

We identified an outbreak of hepatitis A in children less than 10 yr of age in an overcrowded semi-urban community with poor socio-economic and hygienic conditions, from Tamil Nadu, south India, using serotesting for IgM specific antibody to hepatitis A virus from February to July, 2006. Geographic information systems (GIS) mapping and analysis was used to study the spatial distribution of the outbreak and to ascertain spatial clustering. GIS helps to easily process, visualize and analyze data spatially and can assist in understanding spatial patterns of disease distribution^{9,10}. We conducted an investigation of hepatitis A using GIS during this outbreak.

Material & Methods

Study area and population: A birth cohort of 452 children in an urban slum area in Vellore, south India is part of an ongoing Childhood Rotavirus Infection (CRI) study, recruited over a period of 18 months extending from March 2002 to August 2003, as previously described^{11,12}. The study was ethically approved by the Institutional Review Board (Research Committee) of the Christian Medical College, Vellore.

This cohort is based in three urban slums in Vellore, south India: Ramnaickanpalayam, Chinnallapuram and Kaspas, which are geographically adjacent, covering 2.2

km². Vellore municipality had an estimated population density of 1660 per km² in 2001, but density in the slums was higher, approximately 17,000 per km², with overcrowding, many large garbage dumps, open but cemented drains and closely clustered houses¹². Mean annual rainfall is approximately 1054 mm, with peak rainfall between August and November¹³. Water for drinking is supplied at intervals of 2-28 days by the municipality from overhead tanks. During summer, temperatures are above 40 °C and water shortages are common.

The population comprised families resident in the area for multiple generations, as well as migrants who moved into the area in search of employment. The most common occupation was manual production of beedis. Others were employed as unskilled workers in the leather industry, domestic servants, sweepers, and as small traders, with a small number in skilled employment. The diet consisted of mainly of rice, lentils and vegetables.

The children enrolled in the study^{11,12} were visited routinely twice weekly by a field-worker who enquired about diarrhoea and other morbidities and examined the child. As part of the ongoing CRI Study, all children in the area were monitored on a daily basis. A physician-run clinic was held daily in the study area and all children in the study area were given health care free of cost. Three children from the Kaspas slum area presented with jaundice during the month of May 2006. All three were positive for anti-HAV IgM antibodies and were negative for anti-HEV IgM. Following this finding, we conducted a house-to-house survey of children <10 yr of age for jaundice in the study area, also including children who were not part of the study.

All children who reported jaundice in the recent past were interviewed with the help of a validated questionnaire. The questionnaire included their demographic information, family background and an epidemiological case sheet including the name, age, gender, date of onset of signs and symptoms, history of travel, source of water, family history and other topographical information. Active surveillance to identify further cases of jaundice was undertaken, and all children in this area were monitored regularly.

Water samples were collected from the nearby water sources providing water to these houses and were tested for the presence of faecal coliform by standard methods¹⁴.

Anti-HAV IgM testing: Approximately 3 ml of blood was collected per child and tested for IgM antibodies against hepatitis A virus with the ETI-HA-IgMK PLUS Kit (DiaSorin, Sallugia, Italy), at the Department of Virology, Christian Medical College, Vellore.

Water analysis: Coliform count was assessed by the Most Probable Number (MPN) technique by using McCreech's tables¹⁴. Each sample was diluted 1:10, to give 360 coliforms per 100 ml as upper limit of accurate estimation¹⁴. Each water sample was vortexed before dilution and inoculation to ensure that the organisms present in water were uniformly distributed.

Statistical analysis: Data were analyzed using SPSS for Windows 12.0 (SPSS Inc., USA). The cases were divided into subgroups on the basis of age (children <5 vs. children >5 yr of age) and gender (male vs. female) and two-tailed Fisher's exact test was used to compare the differences in the symptoms of hepatitis, between the subgroups. Socio-demographic analysis between children from whom blood samples were collected and those from whom it was not was analyzed was done with Fisher's exact test for categorical variables and Kolmogorov-Smirnov test for continuous variables.

Spatial mapping and analysis: Using the GIS, observations regarding social, economic, political and physical environments were referenced to a common geospatial data framework. All houses in the area where there was a case of jaundice were mapped and geo-referenced using Arc View GIS 3.3 (Environmental Systems Research Inc., California, USA). The waypoints and track points were collected using Garmin GPS V and downloaded as layers using GPS Utility 4.10.4. (GPS Utility Ltd., Southampton, England). Streets and other environmental attributes in that area such as water sources, garbage dumps and faecal contamination points had been mapped previously and were extracted from the CRI database. Socio-demographic characteristics of the cases were collected at baseline. Information regarding safety of drinking water, dietary habit, water sources, animals owned by the household was also obtained. All information collected had a spatial reference by linking to the geographic co-ordinates (latitude, longitude).

The incidence of hepatitis A infections from February 2006 till June 2006 was analyzed to detect any clustering, using SaTScan version 7.0.1 (<http://www.satscan.org/>). To identify spatial clusters for high rates, the Bernoulli model was used¹⁵. The unit of analysis was the house. A house with one or more cases

was considered to be a case house. Control houses were selected by systematically sampling every 10th house in that area. The first control house was the 10th house from the CRI clinic located in the center of the study area, from there on every 10th house was marked consecutively. The maximum spatial cluster size was fixed at 50 per cent of study population, to allow detection of both small as well as large clusters¹⁶.

Results

Clinical features: A total of 965 children were surveyed, of whom 26 were clinically identified to have acute hepatitis. Of the 26 cases, 12 were identified after the end of clinical illness and the remaining 14 were identified while still ill. Among them, 23 cases were icteric, 22 had fever and all of the children complained of anorexia and malaise. Six had abdominal pain and hepatomegaly was noted in two children. None of the children had cholestatic symptoms. There were no case fatalities. Although the outbreak came to our notice when three symptomatic cases visited our clinic, with signs and symptoms of jaundice, on conducting the outbreak investigation we identified the index case as an 8 yr old female child from the same area with the same water source. She had acquired HAV infection in February 2006, following a visit to relatives outside the area.

IgM anti-HAV testing: Eleven (42.3%) of the 26 patients agreed to provide blood sample for testing, 10 (90.9%) out of 11 children who were tested for IgM anti-HAV were positive for IgM antibodies against hepatitis A virus.

Coliform count: Six water samples were collected from the nearby water sources that provided water to these areas. It was also identified that the source of water to this slum area was from a common water tank. All the six water samples had > 180 thermotolerant coliforms/100 ml of water.

Statistical analysis: Epidemiological survey showed that all the affected children were less than 10 yr of age. The median age was 4.5 yr (interquartile range 3 - 7.25 yr), and 13 (50%) cases were aged 5 yr or more. Of the 26 cases, 10 (38.5%) were males and 16 (61.5%) were females. There were no adult cases reported in the area. All the cases were reported from February 2006 till July 2006. No new cases were reported after July 2006. Most of the cases (23, 88.5%) had clinical jaundice (icterus) as their main presenting complaint, irrespective of the age groups.

There was no significant difference in the symptoms of hepatitis between under 5 children and those above

5 yr of age, and between the males and the females (individual data not shown). More patients were seen from March to June 2006, with a peak of seven cases during the month of May 2006 (Fig. 1).

Socio-demographic data of children from whom blood samples were and were not collected, were compared with respect to religion, type of house, education of the head of the household, total number of family members, number of children in the family,

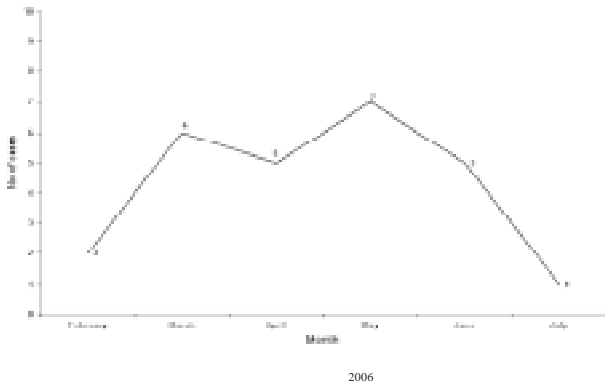


Fig. 1. Monthly incidence of cases of hepatitis in children <10 yr of age in the urban slum areas of Vellore during February-July 2006.

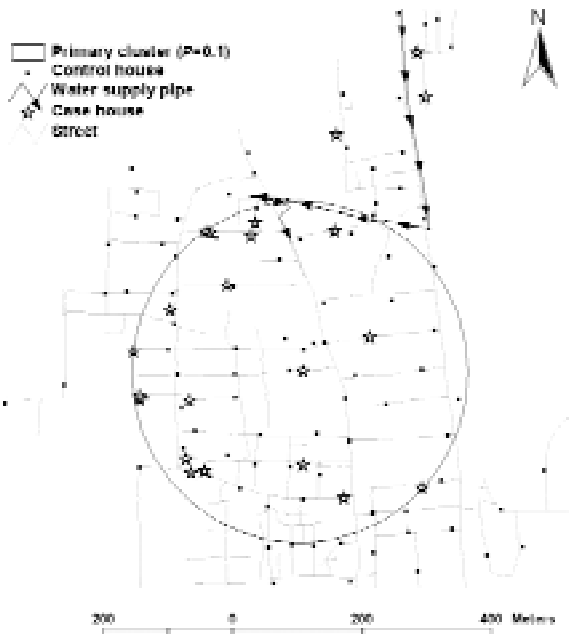


Fig. 2. Geospatial map of the outbreak area showing the number of cases, controls and the primary cluster. The water supply from the overhead tank is shown as lines with arrows indicating the direction of flow.

number of adults in the family, type of family, and were found to be not significantly different.

Spatial analysis: Of the 26 reported cases we were able to obtain only 23 waypoints. One child was not traceable whereas two other children had subsequently moved out of area. Case houses were found to be uniformly distributed. As shown in Fig. 2, the most likely spatial cluster (radius=0.26 km) had 19 case houses as against an expected of 11.07 (RR=5.12). However, this was not statistically significant ($P=0.1$). No particular pattern could be ascertained from the monthly distribution of cases.

Discussion

We identified 26 patients during the period of six months, which was seven times greater than the 22 that were identified during the preceding 36 months in the same area (unpublished data). Since there was a sudden increase in the number, linked in time and space, we considered this an outbreak of hepatitis A.

We established our case definition as all children less than 10 yr of age with clinical symptoms of jaundice. According to the guidelines of clinical case definition of acute viral hepatitis given by the National Institute of Communicable Diseases¹⁷, hepatitis A was confirmed because all the children had classical clinical symptoms of acute viral hepatitis, an epidemiological link (common water source) and laboratory confirmation of anti-HAV IgM. Acute hepatitis A is usually asymptomatic in 70 per cent of affected children younger than 6 yr¹⁸. Therefore, the detection of 26 cases may represent the tip of an iceberg, with many more asymptomatic infections in the community remaining undetected.

Of the 26 patients, 12 were identified after cessation of symptoms in the child. All 12 were identified within a period of three months. Since signs and symptoms of jaundice are easily recognized even by a lay person and parents are unlikely to have forgotten a major illness in a short period, ascertainment and recall bias are likely to have been limited.

The water supply to this area was from a common water source. Water is filled in the overhead tank and then pumped out to the area at varying intervals. All the affected children had the same water source. The primary or index case occurred in February and the subsequent cases did not show any pattern of distribution from this case. The time frame of disease occurrence and the incubation period of hepatitis A infection indicated the

probability of occurrence as a result of water contamination over the entire area. Microbiological analysis of the water samples collected during the outbreak showed that all the samples had faecal contamination. Water samples tested previously in these areas as part of the ongoing CRI study¹² had also shown high confirmed coliform counts. In this study, HAV RNA isolation was not attempted due to lack of laboratory capability. Since all children were from the same area and shared the same water source, the spread of infection could have been due to water contamination.

From the spatial analysis, patients were found to be well distributed in space, with no particular clustering in any location, indicating that the outbreak may be due to a generalized source such as water contamination and not a result of a point-source spread, such as direct spread from the primary or index patient. This also explains the absence of a significant cluster in the spatial analysis. In addition, the spatial analysis used a specific analytic model with a circular pattern. The distribution of case houses did not follow this pattern, as they were located along the streets, and this could be another reason for not getting a significant spatial cluster. Since the control houses for the GIS analysis were selected only from the area affected by hepatitis A, a better analytic framework might have been resulted by including controls from the adjoining areas.

The use of GIS showed the spatial distribution of cases and helped in the ascertainment of any spatial clustering of cases within the study area, which would have been difficult to ascertain using conventional methods. The lack of spatial clustering helped formulate the hypothesis that the outbreak could have been due to contamination of water supply to the entire area.

Geographic information systems have been used for investigations of outbreaks in many industrialised countries, in addition to conventional epidemiological methods. In an outbreak investigation, the use of GIS not only provides useful maps for communication of findings and dissemination of information and for health education, but also gives an insight into epidemiological linkages with potential causes or risk factors. It helps in identifying outbreaks at an early stage and to arrest the spread of the infection^{9,10,19}. GIS can show information on disease occurrence from regions to individual cases⁹. Many studies have used GIS for outbreak investigations²⁰⁻²². In this outbreak, the lack of spatial clustering indicated that the source of infection was probably not a single point source within the

community, but a common risk factor for all residents in the area.

In India, recent studies from northern India indicate that hepatitis A is becoming a major cause of sporadic hepatitis in children, with rates of 64.5²³ and 22 per cent²⁴ in hospital-based studies and 56²⁵ and 78 per cent²⁶ in community-based studies. In our study, given the poor housing and environmental hygiene, it was interesting to note that 50 per cent of affected children were between 5 and 10 yr of age. Our study also highlighted the increasing detection of symptomatic children with hepatitis A virus infection, possibly as a reflection of an outbreak of unknown magnitude. Community based studies may be a more accurate index of the natural history of hepatitis A in Indian populations rather than hospital based analyses, which have intrinsic referral biases. The use of GIS in this outbreak investigation added value by permitting ease of building and testing of a model of source and transmission, and helped in identification of lacunae in data collection.

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