OUTBREAK OF HEPATITIS-E IN AMANKOT, MINGORA, SWAT, PAKISTAN IN 2013: A CASE CONTROL STUDY

Iftikhar ud din¹, Mumtaz Ali Khan², Muhammad Ishaq³, Muazam Abbas Ranjha³, Jamil Ahmed Ansari², Tayyab Razi Rathore³

¹Bacha Khan Medical College, Mardan
²National Institute of Health Islamabad
³Saidu Medical College, Swat

Correspondence: Iftikhar ud din, Email: dr.iftikhar.uddin@gmail.com

Abstract

Background: Globally, estimated 20 million cases and 70,000 deaths occur annually. A "cluster" was reported from Amankot Swat, during February 2013. Outbreak was investigated to find cases, identify risk factors, infection source and recommend control measures.

Methods: Study design adopted was descriptive followed by case control study. A case was defined as "A person resident of Amankot, with jaundice & any of the following symptoms; malaise, anorexia, abdominal pain, fever, vomiting and dark urine during February-March 2013." Adopting case-control study design, cases and controls were enrolled assuming sampling was independent of exposure. We collected information through a structured questionnaire and data was analyzed through Epiinfo-7. Collected blood samples were tested by ELISA.

Results: Out of 800 surveyed individuals, 299 were found jaundiced. Cases were predominantly male, n=232 (77%) and most affected age group was 16-30 years, n=173 (58%). Apart from jaundice the most frequent symptoms included abdominal discomfort n=247 (82%), malaise n=240 (39%), fever n=197 (32%), anorexia n=266 (37%), and nausea/vomiting n=266 (37%). Identified risk factors included poor sanitation (exposed 274, OR:29, 95% CI: 17-46.6), consumption of municipal water supply (OR 12.3, 95% CI: 7.7-19.8), old pipeline network (exposed 268, OR 8.7, 95%CI: 5.6-13.6), and patient contact (exposed 68, OR 6.7, 95% CI: 3.6-12.4). Water samples were contaminated with fecal coliforms.

Conclusion: Densely populated area with mostly old and rusted pipelines network running alongside sewerage lines, low water flow period (winter) and negative pressure within the pipes probably sucked the sewage which resulted in contamination of water.

Key words: Outbreak, infectious disease, low and middle income country

Introduction

One of the leading causes of acute viral hepatitis globally is hepatitis E virus (HEV) (1) responsible for infecting 33% of the world population residing in developing countries (2). It is responsible for acute hepatitis in vulnerable human population (3). Research suggests that the socioeconomic status of the population is directly associated with the global spread of HEV with seroprevalence reported highest in populations living with poor sanitation conditions. High endemic areas for HEV include Central and South East Asia (4). HEV presents itself as a small non-enveloped single-stranded RNA virus and exhibits high environmental stability. The mode of transmission is the fecal-oral route by the ingestion of contaminated water or food (5). The infection appears like other forms of acute viral hepatitis. Patients may appear jaundiced and complain of fever, malaise, anorexia and generalized body aches. The incubation period varies from 15 to 60 days. A more severe form of the infection is fulminant hepatitis, the fatality rate of which extends from 0.5 to 3% (6).

Recent isolation of a swine virus resembling human HEV has opened the possibility of zoonotic HEV infection. Studies in humans and experimental animals reveal that viral excretion begins approximately 1 week prior to the onset of illness and persists for nearly 2 weeks (7). Immunoglobulin-M antibody to HEV (anti-HEV) appears early during clinical illness and disappears within few months. Immunoglobulin-G anti-HEV appears a few days later and persists for years (8). HEV infection can result in dire consequences for pregnant women increasing the mortality rate to up to 20-25%, while normally the mortality rate is less than 1% (9). According to the World Health Organization (WHO), 20 million HEV infections occur annually, resulting in an estimated 3.3 million symptomatic cases of the infection.
worldwide (10). According to a WHO estimate hepatitis E infection was responsible for approximately 44,000 deaths in 2015 (accounting for 3.3% of the mortality due to viral hepatitis)(11). Supportive treatment is recommended as there is no specific treatment. Ensuring proper sanitation and clean drinking water is the best preventive strategy. A "cluster" of Acute Jaundice cases was reported from Amankot, Mingora, Swat, during February 2013. The outbreak was investigated to ?nd active cases, confirm the diagnosis, identify risk factors, infection source and facilitate control measures.

**Methodology**

**Case Finding**

We reviewed hospital records for admitted patients. The investigation was focused on all residents of Amankot. An operational case definition was formulated to identify active cases. A case was de?ned as "A person resident of Amankot, with jaundice & any of the following symptoms; malaise, anorexia, abdominal pain, fever, vomiting and dark urine during February-March 2013." To describe the outbreak, the clinical and demographic information obtained from cases were recorded between 1st February and 30th March 2013.

**Case-Control Study for risk factors associated with HEV disease**

Adopting a case-control study design and convenient sampling/non-probability sampling technique, cases and controls were enrolled assuming sampling was independent of exposure. As this was an outbreak situation so all reported and searched cases were enrolled. To identify controls, we first verified that the person had not experienced jaundice in the previous 02 years. For the analysis, we defined a control as someone with no history of jaundice during the previous 2 years. Data were collected by house to house survey in the affected locality, using a pretested structured questionnaire by trained Lady Health Workers after informed consent. Using Epi-info-7 software, the risk factors and exposure among cases and controls compared. Persons with evidence of past infection were excluded. Single and multivariable logistic regression was performed to identify the most likely cause of the outbreak and to estimate time and place of exposure. Specific exposures with estimated odds ratios (ORs) >1, p<0.05 were included in a multivariable model.

**Determining the Etiology of the Outbreak**

Blood samples (5ml) were collected and analyzed by ELISA at NIH. Positive samples were analyzed for liver function parameters. Same samples were also tested for hepatitis-A-IgM through ELISA.

**Investigating Water Systems**

Environmental assessment was conducted. The outbreak investigation team observed water distribution systems in the area a total of 05 water samples were collected from different locations and analyzed (Physiochemical and Microbiological analysis). The community persons were also asked about the possible causes/sources of infection.

**Human Subjects Considerations**

All participants provided informed written consent prior to interview and the outbreak was investigated with the approval of the district health department. Suspected cases were referred to Saidu Teaching Hospital where they were provided free of cost lab investigation and treatment facilities.

**Follow-up**

Close contacts were followed upto the maximum incubation period (60 days) for development of any symptom compatible with Hepatitis E.

**Results**

**Description of the Outbreak location/spot map**

Information were collected from hospital record, Local Medical practioners, Lady health workers, municipality workers, community elders and patients. The Union Council is located on the west bank of a water stream and there is no proper disposal system of municipal solid waste which ultimately finds its way into the stream. For drinking water, the union council is mainly dependent on municipal water supplied from water tanks constructed on the top of mountain beside the union council. The water is supplied through old and rusted pipelines running along with sewage system all the way to end user points.

Figure 1. Spot map of cases

In 500 household, 800 individuals were interviewed where 299 cases were identified. The overall attack rate (AR=1.4%). The first case reported in last week of the December 2012 and number of cases gradually increased up to week 6. The interventions initiated on week 6 and the cases started declined in week 10 and after week 17 no case was reported from the affected locality.
Fig 2: Epi curve

Statistical Analyses:
Cases were predominantly male, n=232 (77%) and most affected age group was 16-30 years, n=173 (58%). Out of 67 female cases, 06 were pregnant and fortunately recovered without any complications. They were kept under strict observation for next 4-6 weeks with frequent visits by Lady Health Workers.

Table 1: Age/gender ratio, population composition and sources of drinking water used

<table>
<thead>
<tr>
<th>Male to female ratio</th>
<th>3.7:1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group with most cases</td>
<td>16-30yrs</td>
</tr>
<tr>
<td>Drinking Water source</td>
<td>Municipal Water supply: 92% (n=275)</td>
</tr>
<tr>
<td></td>
<td>Borehole: 08% (n=2)</td>
</tr>
<tr>
<td>Population with most cases</td>
<td>Students: 37% (n=112)</td>
</tr>
<tr>
<td></td>
<td>Teachers: 12 % (n=37)</td>
</tr>
<tr>
<td></td>
<td>Police: 11% (n=35)</td>
</tr>
<tr>
<td></td>
<td>Housewives: 10% (n=29)</td>
</tr>
</tbody>
</table>

Cases presented as per following age group ratio: less than 5 years old were 5%, 6-15 years old were 18% and 16-30 were 58%. The remaining (more than 31years) were 19%.

Apart from jaundice, the most frequent symptoms included fever n=197 (32%), malaise n=240 (39%), anorexia n=266 (37%), nausea/vomiting n=266 (37%), and abdominal discomfort n=247 (82%).

Identified risk factors included poor sanitation (exposed 274, OR29, 95% CI 17-46.6), consumption of municipal water supply (OR 12.3, 95% CI 7.7-19.8), old pipeline network (exposed 268, OR 8.7, 95%CI 5.6-13.6), and patient contact (exposed 68, OR 6.7, 95% CI 3.6-12.4).

Water samples were contaminated with fecal coliforms. Un-ivarriate analysis shows that Poor sanitation, municipal water supply, old pipelines network and contact with known cases were associated with the outcome. Multi-variate analysis also shows that poor sanitation and municipal water supplies are strongly associated with the outcome.

Table 2: Multivariate analysis of the risk factors

<table>
<thead>
<tr>
<th>Term</th>
<th>Odds Ratio</th>
<th>95% C.I.</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor sanitation</td>
<td>18.</td>
<td>11.04</td>
<td>32.51</td>
</tr>
<tr>
<td>Municipal water supply</td>
<td>7.39</td>
<td>4.14</td>
<td>13.22</td>
</tr>
<tr>
<td>H/0 Contact with a case</td>
<td>4.19</td>
<td>1.68</td>
<td>10.45</td>
</tr>
<tr>
<td>Old pipeline network</td>
<td>3.07</td>
<td>1.75</td>
<td>5.41</td>
</tr>
</tbody>
</table>

Environmental Assessment
Water samples from different points collected and analyzed at Microbiology laboratory NIH. Lab. analysis of most of the water sample showed evidence of contamination. Tap water taken from Police station and few houses were un-satisfactory with massive growth of coliform (20counts/100ml) and bore water yielded 4 counts/100ml.

Laboratory
Liver function tests (LFTs) of all the symptomatic cases were deranged with high ALT and bilirubin levels. For confirmation of outbreak, 10 cases with deranged LFTs were confirmed by ELISA at the reference lab at NIH Islamabad.

Community Perceptions about the Cause of the Outbreak
Respondents believed that the illness could have resulted from contaminated drinking water and vegetables grown in field irrigated by dirty water from nearby water stream.

Discussion
This outbreak of jaundice in a densely populated, low-income, urban community was due to HEV, and this investigation suggests that it was spread through fecal contamination of the municipal water system. There is no proper disposal system of municipal solid waste which ultimately finds its way into the nearby water stream. The drinking water source for the entire community is mainly municipal water supplied from water tanks constructed on the top of mountain. The water is supplied through old and rusted pipelines running along with sewage system all the way to end user points probably providing the environment for mixing sewage with drinking water.

The attack rate of acute jaundice is probably higher than the 1.4 % rate recorded, because we recorded only cases with symptoms compatible with acute jaundice. Findings are supported by a study conducted at Darfur, Sudan, 2004(12). There must be more asymptomatic cases in community which could not be recorded through active search. Such a high ratio of asymptomatic to clinical infection has already been described in other studies (12, 13).

Our results suggest that risk of acute HEV infection with jaundice is higher among persons aged 15-30 years and mostly affected gender was male (Table 1). The findings are supported by other similar studies (12). The outbreak started in week 50, the interventions
Initiated on week 6 and the cases started declined in week 10 and after week 17 no case was reported from the affected locality (Fig 2 Epicurve). We assumed that the water sources before the outbreak and some weeks during the outbreak remained the same. We also assume that with the supplies of safe drinking water, chlorination of the water sources and health education, the cases declined after week 8. The same findings were supported by other similar studies (13). The shape of the epidemic curve was consistent with a common source which in this case was probably water. Although person-to-person transmission is likely to have occurred, particularly within families, because of limited resources we did not study secondary attack rates in families. Most of the cases presented with jaundice, fever, malaise, anorexia, nausea/vomiting and abdominal discomfort. These are very common symptoms presented with usually all acute jaundice syndrome (14-16).

The risk factors identified by our study include poor sanitation, consumption of municipal water supply, old pipeline network, and patient contact (Table 2). Univariate analysis shows that poor sanitation, municipal water supply, old pipelines network and contact with known cases were associated with the outcome. Multivariate analysis also shows that poor sanitation and municipal water supplies are strongly associated with the outcome. Poor hygienic practices in households probably caused person-to-person transmission of HEV during this outbreak. The same findings were described in other similar studies (17-21).

Water samples analysis showed evidence of contamination. This presence of fecal coliforms found in water samples has been explained by other studies (14). Water sources had never been chlorinated in the near past. Absence of chlorination and lack of routine verification of the integrity of the distribution system for long time is probably one of the major short comings.

Community members believed that the illness could have resulted from contaminated drinking water and vegetables grown in field irrigated by dirty water from nearby water stream.

**Conclusion**

This outbreak of HEV was likely caused by sewage contamination of the municipal water system. Densely populated area with mostly old and rusted pipelines network running alongside sewerage lines, low water flow period (winter) and negative pressure within the pipes probably sucked the sewage which resulted in contamination of water. Poor sanitation & contaminated drinking water remained the probable cause of the disease transmission. The drinking water was mainly supplied by Municipal Corporation through old & rusted pipelines network running alongside sewerage lines.

**Recommendations**

The response focused on ensuring clean water supplies, improved sanitation and hygiene. Water, sanitation, hygiene (WASH) interventions at community and household levels; replacing damaged pipeline and supply clean water were recommended. Health education and early health-care would improve the outcomes. Ensuring clean water supplies through water tankers as temporary measures and bucket chlorination at the source is vital.

Current recommendations to ensure a safe water supply may have been insufficient to control such epidemics in future. This research highlights the need to evaluate current water sources and supply channels and to take measures accordingly.

**Long term corrective measures**

The following measures were recommended:

- Replacing damaged pipelines
- Improving sanitation and waste disposal systems
- Community mobilization and raising awareness

**References**