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Original Article

Assessment of risk factors associated with outbreak of hepatitis A in Shakrial, Rawalpindi, Pakistan

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Abstract

Introduction: Two patients with jaundice reported to the National Institute of Health (NIH), Islamabad from Shakrial, Rawalpindi in April 2017. An outbreak investigation team was formulated to assess the disease magnitude, risk factors and control measures.

Methodology: A case-control study was conducted in 360 houses in May 2017. The case definition was: onset of acute jaundice with any symptom including fever, right upper-quadrant pain, loss of appetite, dark urine, nausea and vomiting among Shakrial residents from March 10 - May 19, 2017. Four age and gender matched controls were selected for each case. Blood samples were sent to the NIH for laboratory confirmation. Frequencies, attack rates (AR), odd ratios, and logistic regression were computed at 95% confidence interval and $p < 0.05$.

Results: A total of 25 cases (23 new) were identified with mean age 8 years and male to female ratio 1.5:1. Overall AR was 1.39% and the most severely affected age-group was 5-10 years (AR of 3.92%). Multivariate analysis revealed that raw vegetable consumption, lack of awareness and poor handwashing practices had significant association with disease spread. All blood samples were positive for hepatitis A, and no resident was previously vaccinated. Lack of awareness of disease spread among the community was the most probable reason for the outbreak. There were no new cases during follow up until May 30, 2017.

Conclusions: Healthcare departments should implement public policies towards the management of hepatitis A in Pakistan. Health awareness sessions and vaccination for children ≤ 16 years age is recommended.

Key words: Hepatitis A; outbreak; threats; unawareness; poor handwashing.

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Introduction

Hepatitis A is a highly contagious disease of the liver and is caused by the hepatitis A virus (HAV) which belongs to the genus *Hepatovirus* of family Picornaviridae [1]. HAV infection causes mild to severe illness and is rarely fatal. Almost everyone recovers from it and develops lifelong immunity. A small proportion of cases (< 1%) may die due to fulminant hepatitis [2,3]. About 90% of the cases in children do not develop clinical symptoms of the disease [4]. The time period between infection and appearance of symptoms in the cases is between 2 to 6 weeks, with an average of 28 days [5]. The major route of transmission for HAV is the fecal-oral route. This happens through ingestion of contaminated food or water, through a person preparing food with contaminated hands, or through physical contact with infectious persons. It is rarely transmitted through blood and blood byproducts, and intravenous transfusion. Approximately 50% of the cases do not have an identifiable source of infection [6].

According to a World Health Organization (WHO) report, a total of 1.34 million deaths occurred due to viral hepatitis in 2015. This death toll was higher than the number of deaths due to HIV or malaria while it was on par with deaths due to tuberculosis (excluding HIV-associated tuberculosis). The global burden of disease due to typhoid and para-typhoid fever in 2017 was 14.3 million cases [7], while it was estimated that there were 20.1 million hepatitis-E virus infection with 3.4 million symptomatic cases, and 70,000 deaths in 2005 in nine regions of Asia and Africa [8]. Similarly, in 2015 it was assessed that globally 677 million cases were caused by

Norovirus, 233 million by enterotoxigenic *E. coli*, 188 million by *Shigella* spp., and 179 by *Giardia lamblia* [9]. The WHO also estimated that in 2015 out of the total deaths due to viral hepatitis, approximately 11,000 (0.8%) deaths occurred due to hepatitis A [10]. The circulation level of the hepatitis A virus is high in developing countries, while it is low in developed countries. Most of the adolescents and adults get exposed to the disease in developing countries and develop immunity to it, whereas in mid-level countries, they are at a risk of disease and may cause outbreaks if they get exposed to it [11].

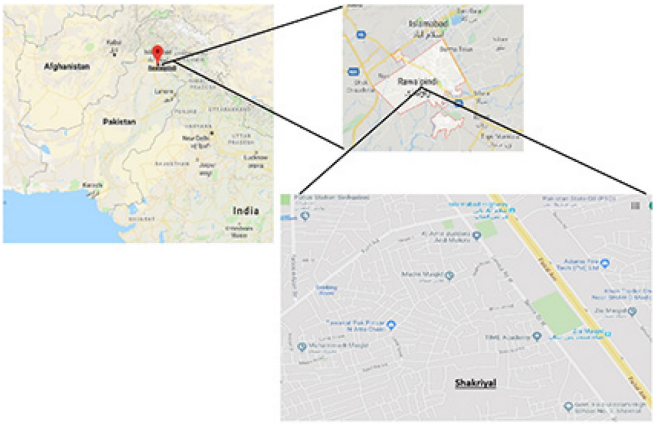
The United States (US) has faced many localized outbreaks of hepatitis A since early 2017. The Los Angeles Country Department of Public Health (LOC DPH) has identified 7 major outbreaks of hepatitis A from October 2018 to January 2019 [12]. By January 2019, there were 11,500 cases of hepatitis A in the US with 100 deaths caused by HAV [13].

Hepatitis A is an endemic disease in Pakistan. Poor hygiene and sanitation conditions and practices may be the reason for hepatitis A infection in approximately 90% of the children before they reach the age of 10 years. Hepatitis A accounted for approximately 50 to 60% of acute viral hepatitis cases among the pediatric population [14]. In contrast to the children, approximately 5.4% cases of acute hepatitis in the adult population were attributed to the hepatitis A virus [15]. However, it is likely that actual rate of hepatitis A in the population might be higher than the reported rate because of reasons such as limited access to secondary and tertiary care hospitals, non-availability of laboratories in remote areas, and variability in clinical presentation of cases [16]. Many outbreaks of hepatitis A occur in low socio-economic settings, and in urban slums but scarce published data is available in this regard. In 2003-04, an outbreak of acute viral hepatitis occurred in two schools of Nowshera, KP. A total of 626 cases from the local community and affected schools were tested, out of which 40.57% were found to be positive for hepatitis A virus antibodies (HAV-IgM) with age range of 3-27 years [17]. A few community-based studies had been carried out to assess its incidence and prevalence.

In 2009, the Hepatitis Sentinel Surveillance System was developed by the Pakistan Field Epidemiology and Laboratory Training Program (FELTP) in collaboration with the Ministry of Health, Pakistan and Centers for Disease Prevention and Control (CDC), USA. Five public sector tertiary care hospitals were identified across Pakistan for this purpose. Analysis of sentinel site data from June 2010 to March 2011 indicated that out of a total of 712 cases of viral hepatitis, 19.8% had acute hepatitis A, which was more common in males (69.5%). Age distribution analysis of this study revealed a change in disease pattern as compared to previous studies. In this study, the highest prevalence of hepatitis A virus was found in the 20-29 years age group (41.2%), followed by 30-39 years (16.3%), and 6-19 years (12.8%) [18]. In contrast, previous studies reported that approximately 90% children get infected by the hepatitis A virus before reaching the age of 10 years [14]. Therefore, it can be deduced from previous literature that although Hepatitis A is endemic in Pakistan, some changes in the disease pattern especially with reference to the age of those affected by the virus has been observed over the span of time.

A local practitioner in Shakrial, Rawalpindi reported 2 cases with acute jaundice to the National Institute of Health (NIH), Islamabad on 28th April 2017. The NIH conveyed this information to the local health authorities. Later on, the local health authorities requested the NIH and the FELTP to conduct an outbreak investigation in that area, and recommend control measures. An outbreak investigation team comprising of FELTP fellows was formulated to carry out epidemiological investigations with the aim to find out about the affected age groups of the community, assess the magnitude of the disease, assess the risk factors associated with the spread of the disease in the community, and to recommend control measures.

Figure 1. Map of study area (Shakrial, Rawalpindi).



Methodology

Study design

An epidemiological investigation of the outbreak was conducted. This was followed by a case-control study to assess the risk factors associated with the outbreak of the disease.

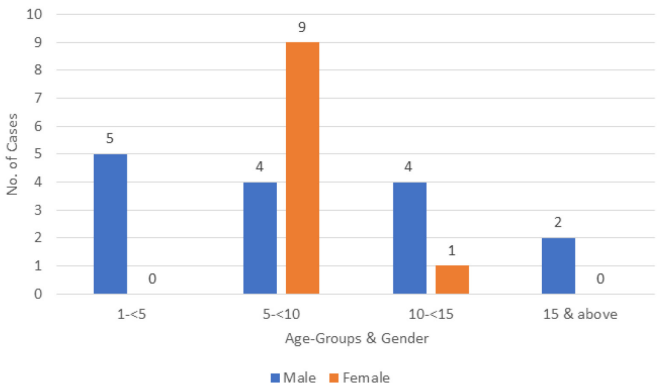
Study population

Outbreak investigation was carried out in Shakrial, located in Rawalpindi city, the capital of Rawalpindi district located in the Punjab province of Pakistan (Figure 1). Rawalpindi city covers 259 km^2 and is the twin city of Islamabad (capital of Pakistan). It has humid subtropical climate with hot and wet summers, and cooler and drier winters. According to the 2017 census, the population of Rawalpindi district was 5.4 million and that of Rawalpindi city was 2.1 million people. The population density of the city is 8100 people per km^2. Shakrial is a densely populated residential area with medium socio-economic level located in Rawalpindi city. This area was initially visited to assess the suspected areas of disease outbreak. A total of 360 houses were surveyed from door-to-door to find active cases. Age and gender matched controls were also taken from the same geographical area.

Case definition, inclusion and exclusion criteria for cases and controls

Case definition formulated for the outbreak investigation was "Onset of acute jaundice characterized by yellow discoloration of scelera/skin in the residents of Shakrial from March 10 - May 19, 2017 with any of the symptoms such as fever, right upper quadrant pain, loss of appetite, dark urine, nausea and vomiting". The inclusion criteria for cases were residents of all ages from the suspected outbreak area of Shakrial, while exclusion criteria was any person who was not a resident of the suspected outbreak area of Shakrial. Similarly, the inclusion criteria for taking controls were residents of Shakrial who had no signs and symptoms of the disease as per case definition, while who were not residents of the outbreak affected area, and had any signs and symptoms of any enteric disease were not taken as controls. Two age and gender matched controls were taken for each case.

Figure 2. Age-wise and gender-wise distribution of hepatitis-A cases in Shakrial, Rawalpindi in May 2017.



Data collection Tool

A semi-structured questionnaire with both open and close ended questions was prepared to collect data from cases and controls. The questions were formulated to collect data on demographic information, clinical features, laboratory testing, and risk factors. A consent form was also prepared and administered along with the questionnaire to take consent of study participants.

Laboratory testing

Blood samples were taken from epidemiologically linked and clinically confirmed cases of hepatitis. A total of 9 blood samples (5 mL each) of the suspected cases were taken, and sent to the NIH, Islamabad, to confirm the presence of IgM antibodies for hepatitis A and/or E virus through Enzyme Linked Immunosorbent Assay (ELISA) testing method. A total of 6 water samples (500 mL each) were taken from different water sources of the affected community i.e., bore water, municipal filtration plant, and municipal water supply, and sent to the NIH to confirm presence of coliform micro-organisms. A high level of coliform contamination was observed as a result of this analysis.

Data collection and analysis

Data was collected from cases and controls by employing the case definition. The data was tabulated and analyzed by using Epi-Info (version 7). The Epi-curve for the outbreak was prepared. Gender-wise age groups were formed for cases to determine the most affected age group of the community. Attack rates per age group were calculated. Frequencies for clinical signs and symptoms were calculated. Risk factor analysis was carried out by computing odd ratios for different risk factors, and Chi-Square was applied as test of significance at confidence interval of 95% and p value < 0.05. Multivariate analysis was also carried out by employing binary logistic regression at confidence interval of 95% and p *value* < 0.05.

Results

A total of 2 cases with jaundice were reported to the NIH, Islamabad by a local practitioner from Shakrial, Rawalpindi on 28th April 2017. An outbreak investigation was carried out at the request of the government health administration by a team of FELTP fellows. An active search was carried out in the suspected community comprising of 360 houses with a population of approximately 1800 people. During this activity 23 new cases were found (total number of cases = 25). The mean age of the cases was 8 years, ranging from 3-16 years. The cases were distributed into age-

groups and the greatest number of cases (n = 13, 52%) were found in the age-group of 5-10 years. The male group was more affected (n = 15, 60%) as compared to females, and the male to female ratio among cases was 1.5:1. The data for age-wise and gender-wise distribution of hepatitis A cases in Shakrial, Rawalpindi during May 2017 is presented in Figure 2.

The attack rates were calculated, and it was found that the overall attack rate for the affected population was 1.39% (n = 25/1800), while the age specific attack rates were; 1.53% (n = 5/327) for age-group of 1 to < 5 years, 4.25% (n = 13/306) for 5 to < 10 years, 1.73% (n = 5/289) for 10 to < 15 years, and 0.23% (n = 2/878) for 15 years and above age group. The attack rates confirmed that 5-10 years was the most affected age-group. The distribution of hepatitis A cases by date of onset of symptoms indicated that index cases developed symptoms on 10th April 2017, and the infection spread over a period of more than 3 weeks. However, the peak in cases was observed on 2nd May 2017. The epi-curve showed that it was a continuous common source outbreak (Figure 3). The distribution of cases over more than 3 weeks period showed that there was some source of hepatitis A virus contamination which was continuously infecting the population. The source was later found to be contaminated water in that area.

The most common symptoms found in these cases (n = 25) were jaundice (25 cases, 100%), fever (24, 96%), dark urine (24, 96%), vomiting (21, 84%), anorexia (21, 84%), and pain in the right hind quarter (n = 16, 64%) (Figure 4).

All the blood samples taken from suspected cases were found to be positive for hepatitis A-IgM, and negative for hepatitis-E IgM. The history of hepatitis A vaccination was recorded from the residents of the affected area and it was found that no resident had received vaccination against hepatitis A.

Similarly, the laboratory test results for water samples showed that 4 out of 6 samples were unfit for drinking, and had a heavy load of coliform organisms, and only 2 out of 6 samples were fit for drinking. The presence of coliform organisms was indicative of fecal contamination in water, and was a possible source of the outbreak.

Risk factor analysis was carried out and odd ratios were computed to find the risk factors significantly associated with the spread of the disease. It was concluded that poor hand washing practice after toilet use (OR: 13.4, 95% CI: 4.8-37.3, $p < 0.00$), use of shared toilet (OR: 13.3, 95% CI: 4.5-39.5, $p < 0.00$), lack of awareness about disease spread (OR: 7.5, 95% CI: 2.4-23.7, $p < 0.00$), and consumption of raw vegetables (OR: 6.4, 95% CI: 1.4-28.9, $p < 0.00$) had significant associations with the spread of disease in the outbreak affected community. The results of the analysis of risk factors associated with the outbreak of hepatitis A is presented in Table 1.

Figure 3. Distribution of Hepatitis-A cases according to date of onset of symptoms in Shakrial, Rawalpindi in May 2017.

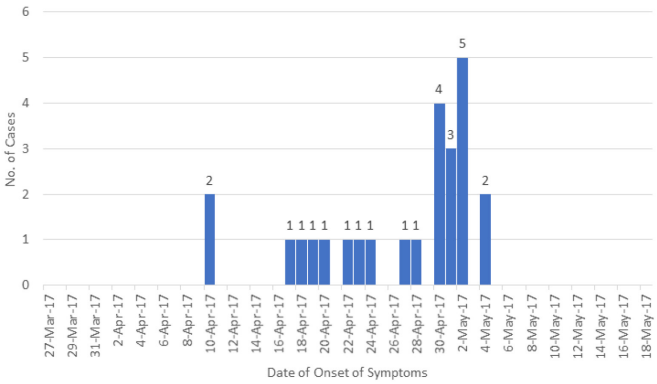


Figure 4. Most common signs and symptoms of hepatitis-A cases in Shakrial, Rawalpindi during May 2017.

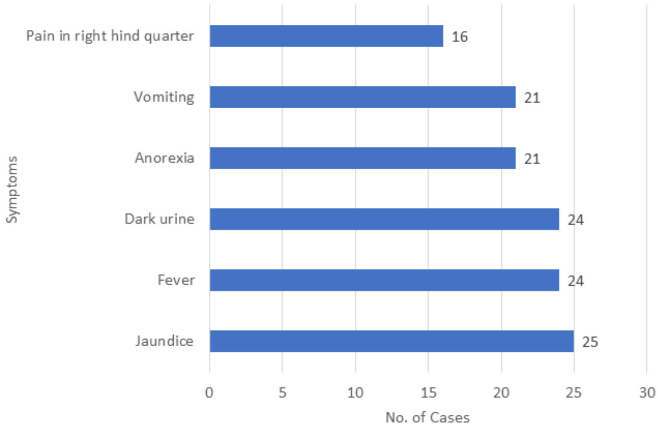


Table 1. Analysis of risk factors associated with outbreak of hepatitis A in Shakrial, Rawalpindi during May 2017.

Risk Factors	Cases exposed (n = 25)	Controls exposed (n = 95)	OR / (95% CI) / *p* value
Poor hand washing practices after use of toilet	17 (68%)	13 (14%)	13.40 / (4.81-37.32) / $p < 0.00$
Use of shared toilet	20 (80%)	22 (23%)	13.27 / (4.46 - 39.47) / $p < 0.00$
Lack of awareness regarding disease spread	21 (84%)	39 (41%)	7.54 / (2.40 – 23.68) / $p < 0.00$
Consumption of raw vegetable	23 (92%)	61 (64%)	6.41 / (1.42 – 28.86) / $p < 0.00$

Multivariate analysis for the risk factors was carried out by applying binary log regression. The results of this analysis indicated that consumption of raw vegetables (OR: 9.4, 95% CI: 1.2-72.2, $p < 0.05$), lack of awareness of spread of disease (OR: 7.5, 95% CI: 1.2-22.8, $p < 0.05$) and poor hand washing practices (OR: 7.1, 95% CI: 1.9-26.7, $p < 0.05$) had significant associations with the spread of hepatitis A.

The actions taken to control the outbreak were change of filters at the municipal filtration plant, chlorination of water tanks, and distribution of water chlorination tablets among the residents of the outbreak affected area. Health awareness sessions were carried out in the community to educate the people regarding basic hygiene practices, water chlorination practices, and use of clean drinking water. The health staff of the local administration were advised to monitor the drinking water quality of the area on a regular basis and change municipal water filters frequently. It was recommended that the health staff of local administration should distribute water chlorination tablets among the residents on a monthly basis to ensure the safety of the drinking water. The local administration was also advised to replace all damaged water and sewerage pipes immediately. The outbreak affected area was monitored for 4-6 weeks and no new cases of hepatitis A were reported from that area.

Discussion

Hepatitis A is an acute viral disease of the liver, and it is well established that it spreads through the oro-fecal route. The results of this study demonstrated that poor sanitation and hygiene practices, including poor hand washing practices were a significant risk factor for the spread of disease in the affected community. These results are in alignment with a report of World Health Organization (WHO), which includes poor sanitation practices as a risk factor for the transmission of hepatitis A [2]. Poor sanitation and hygiene are most commonly associated with HAV infection [19]. The results of the current study also showed that the use of shared toilets was a risk factor for the outbreak due to contamination from an infected person to a healthy person. A study conducted on hepatitis A infection among Amazonian children in Brazil concluded that one of the risk factors for hepatitis A infection is poor toilet condition and the use of shared toilet facilities by the affected population [20]. Similarly, it was demonstrated that infection can spread within a household through oro-fecal route due to poor hygienic practices and sharing of objects [21]. These studies support our conclusions. Lack of awareness serves as a risk factor for the spread of infectious diseases. The results of our study showed significant association between the lack of awareness among the people in the community about the spread of hepatitis A and its outbreak in that area. A study in Iraq assessed the risk factors associated with hepatitis B in patients attending the Hepatitis Unit and found that 90% of the patients did not know about the risk factors of hepatitis B virus transmission [22]. This clearly showed that lack of knowledge about a disease, and its mode of transmission leads to infection and subsequent spread of the disease. Another study in China assessed the impact of health education in students and concluded that health education had a positive impact on awareness about infectious diseases and promoted behavior that led to prevention of the disease [23]. Consumption of raw vegetables was also found to be a significant risk factor for disease outbreak in our study. Previous reports have demonstrated that the use of contaminated water for irrigation of fruits and vegetables leads to presence of disease-causing micro-organisms in the produce and can become a source of disease for consumers [24]. Similarly, it was also reported that use of contaminated water containing different micro-organisms during the pre-harvest stage in the farm can result in contamination of fruits and vegetables, and this risk can be further amplified during the post-harvest and processing stage [25]. A food-borne outbreak of hepatitis A was investigated in the US and it was found that contaminated green onions were responsible for this outbreak [26]. Therefore, these reports support the results of our study.

Conclusions

It was concluded that poor hygiene and sanitation practices, use of shared toilets, and use of raw vegetables particularly those washed with contaminated water were the most probable factors linked with the hepatitis A outbreak in the area. Moreover, lack of awareness about the mode of transmission and spread of disease in the community also played a significant role in the disease outbreak.

Therefore, it was recommended that health awareness and education sessions should be conducted in the community on a regular basis. This would help improve knowledge of the community about the mode of transmission and spread of the diseases, especially in the case of food and water borne diseases, and would also improve hygiene and sanitation practices where shared toilets are used.

It was also recommended that the district health authority should carry out water testing in the area on a regular basis. If the quality criteria are not met, then all

the filters should be changed immediately, water should be decontaminated in all municipal storage tanks, and chlorine tablets should be distributed to all the households of the community for decontamination of water storages located in the houses. The community members were also advised to avoid consumption of raw vegetables, particularly those washed and processed with contaminated water, and to avoid food cooked by any ill person. A further recommendation was to improve community awareness regarding vaccination against hepatitis A. Vaccination camps and campaigns should be arranged in the identified hotspots to vaccinate the eligible population.

Additionally, it was also recommended to the district health authority that a comprehensive monitoring and evaluation plan should be prepared for the entire Rawalpindi city which would encompass regular testing of water, repair or replacement of damaged water and sewage pipelines, regular replacement of water filters, and conduction of health awareness and education sessions in the community. This would help in the prevention and control of food and water borne diseases, and would also improve the health indicators of the community.

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