

# Children With Hepatitis in a Tertiary Care Center in Nepal: A Prospective Observational Study

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## Abstract

**Objective.** Viral hepatitis is a global problem leading to significant morbidity and mortality in adults as well as children. This study explores Hepatitis A among Nepalese children and their water habits. **Methods.** A prospective observational study was conducted over a period of 10 years among Nepalese children. We included 287 children with hepatitis in our study. **Results.** Among 287 children studied, 266 had Hepatitis A. There were 33 toddlers (11.5%), 121 pre-school children (42.2%), 102 school children (35.5%), and 31 adolescents (10.8%). Ninety-one (32%) children used filtered water, 55 (19%) used boiled water, 23 (8%) used boiled and filtered water, 53 (18%) used jar water and 65 (23%) used direct tap water. Five children had complications. One child died due to complications. The mortality rate in the study was 0.38%. **Conclusion.** Hepatitis A affected pre-school and school children most. Boiled and filtered is safest against transmission of Hepatitis A.

## Keywords

viral hepatitis, hepatitis, Hepatitis A, vaccination, waterborne

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## Introduction

Viral hepatitis is a common problem worldwide. Viral hepatitis accounts for 1.4 million deaths yearly.<sup>1</sup> Among viral hepatitis, Hepatitis A is the commonest hepatitis affecting children.<sup>2,3</sup> As per Global Burden of Diseases (GBD) data, there were 159 million Hepatitis A cases leading to 39 000 deaths in 2019.<sup>4</sup> The severity of clinical manifestations of Hepatitis A is inversely related to age. It is more often asymptomatic and mild in younger age groups. It is more symptomatic as well as more fulminant in the late childhood, adolescents and adults.<sup>2-4</sup> It is caused by Hepatitis A virus (HAV), a RNA virus of the Picornaviridae family discovered by Purcell in 1973.<sup>2</sup>

Hepatitis A is highly endemic in the developing parts of the world. The endemicity is directly correlated with sanitary and hygienic conditions of the particular region. Most of the developing regions, particularly South East Asia, Africa, South America as well as Eastern Europe are particularly vulnerable for this disease. Overall, 66% of Hepatitis A cases and 97% of global mortality occur in these regions.<sup>4</sup> Nepal is a developing country in the Southeast Asia region. Because of sub-optimal drinking

water, hygiene and sanitation issues, water borne diseases like diarrhea, enteric fever, viral hepatitis, are highly prevalent in our region.

Our country lacks sufficient data on hepatitis. Although some research has been done on hepatitis among adults, there is paucity of data on pediatric hepatitis in our region. In view of high endemicity of infectious diseases in our region, the prevalence of Hepatitis A among children could be significant. Therefore, this research was conceptualized to study the clinical profile of children presenting with hepatitis in our center.

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## Methods

### Participants

A prospective observational study was undertaken in a tertiary level teaching hospital in Kathmandu, Nepal. This is a tertiary care center of Nepali Army catering to Army personnel and their dependents. Ethical approval was taken from the Institutional Review Committee (Reg. No. 837) of our institute. The study was conducted for 10 years from July 2012 to June 2022. The study children's parents or caretakers were explained briefly about the study. After explanation, written, informed consent in the local language (Nepali) was taken from each of the patient's caretaker or parents. Those children whose parents or caretakers did not consent to be in the study were excluded. The study participants included children above six months of age and till 14 years of age. Those children who presented to our Out Patient Department with the complaints of jaundice or other features suggestive of hepatitis like abdominal pain, nausea, vomiting, and loss of appetite were included in the study. The children were worked up and those children who had laboratory evidence of hepatitis were included in the study. Non purposive sampling method was used to calculate the sample size. We cater to around on average 100 children daily in our Out Patient Department. On average, we have around three to four children with diagnosis of hepatitis in a month.

### Procedures

The children who had laboratory evidence of hepatitis with raised serum bilirubin more than 1 mg/dL and/or along with raised liver enzymes alanine transaminase (9-25 U/L), aspartate transaminase (18-44 U/L) and alkaline phosphatase (141-460 U/L) were included in the study. Children whose parents did not consent, had alternative diagnosis like obstructive jaundice, Wilson's disease during the course of the illness were excluded. The children with hepatitis were checked for the evidence of Hepatitis A by serum IgM anti-HAV. The positivity of serum IgM anti-HAV was considered as the evidence of acute Hepatitis A infection. They were investigated further as required and managed symptomatically. The children were followed up till discharge. If serum IgM anti-HAV was negative, further evaluation like ultrasonography and other viral markers were carried out to find the etiology. Infants below six months, children with features suggestive of obstructive jaundice, the children with known etiology of non-viral hepatitis, and those who did not give consent were excluded.

### Statistical Analysis

The demographic and clinical profile of the children were entered into excel data sheet. The data was analyzed using SPSS version 22. We analyzed the incidence of Hepatitis A, different age groups and sex of the children affected, the type of water regularly consumed by the participants and the complications.

## Results

### Patient Characteristics

Total 432 children presented to our center with features suggestive of hepatitis. Among them, 311 cases were diagnosed as hepatitis based on their laboratory results. Among these, 24 cases were excluded who were either lost to follow up or did not give consent. Remaining 287 cases were analyzed for our study.

There were total 266 IgM HAV positive cases and 21 IgM HAV negative cases. The incidence of Hepatitis A was 92.7% in this study. There were 162 boys and 125 girls, with sex ratio of M:F of 1.3:1.

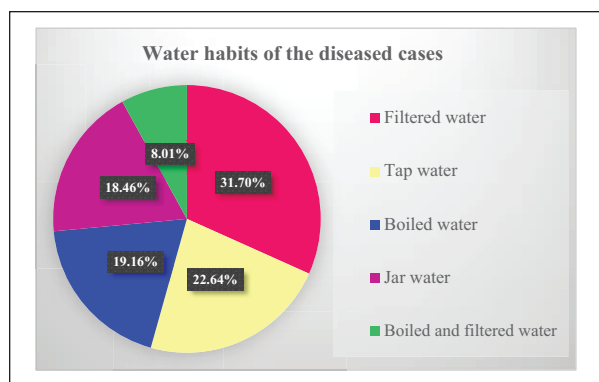
The age distribution of children with hepatitis is shown in histogram in Figure 1. As shown in the figure, majority of the children who were affected with Hepatitis A were of the pre-school and school age groups. The results showed that pre-school (4-6 years) comprised 121 children, school children (7-12 years) comprised 102 children, toddlers (1-3 years) comprised 33 children and adolescents (>12 years) comprised 31 children. The pre-school age group was found to be significantly associated with Hepatitis A with  $P$ -value < .001.

### Sources of Water Type

The source of water in the study children is represented in Figure 2. We had categorized the regular drinking water source as filtered water, boiled water, boiled and filtered, jar water and tap water. Filtered water is the one where the tap or water from source is filtered through the candle type ceramic filters. This type of filters is the commonest variety of water filters used in the most of the middle economic households in Nepal. Boiled water is the water which is obtained from the source and boiled before consumption. Boiled and filtered water is first boiled after getting from the source and further filtered before consumption. Jar water is the commercially available water which is packed by the local water suppliers as drinking water. This is supplied in jars of 20L each and commercially available all over the country, especially in the urban areas. Tap water is supplied by the municipality which is consumed directly from the source without any filtration or boiling. We noted that 91



**Figure 1.** Age distribution of children with Hepatitis A.



**Figure 2.** Sources of water in the diseased children.

children used filtered water, 65 children used direct tap water, 55 used boiled water, 53 children used jar water and 23 used boiled and filtered water. Filtered water was highly significant with Hepatitis A with  $P$ -value of  $<.001$ .

### Complications

In this study, there were significant complications only in five children (1.7%). Two children had hepatic encephalopathy (0.7%), one had enteric fever, one had pneumonia and one had prolonged high fever during the course of illness. Among them, one had septicemia and led to mortality. Thus, the mortality rate with Hepatitis A in this study was 0.38%.

### Discussion

Viral hepatitis is one of the commonest infectious diseases affecting children and adults all over the world. Hepatitis A is the commonest form of viral hepatitis in

children and is highly endemic in developing parts of the world.<sup>1,2,4</sup> Globally, annual estimation of new cases of Hepatitis A is 1.4 million and is variable in different regions of the world. The endemicity is dependent upon the sanitary and hygienic status of the particular region.<sup>4,5</sup> As it is a water borne disease, the disease prevalence is determined by the provision of safe drinking water and uncontaminated food.<sup>6</sup> The disease seroprevalence is correlated with the socioeconomic status of the particular region. Its prevalence is higher in lower socioeconomic regions with no access to safe drinking water and lesser in the countries with higher income and access to safe drinking water.<sup>5-7</sup>

In most of the studies from Southeast Asia Region, the disease seems to be having variable prevalence. According to the study published by Khan et al,<sup>8</sup> the prevalence of Hepatitis A and E were 19% and 10% respectively among adolescents and adults in Bangladesh. According to a review by Abraham P regarding viral hepatitis in India, India is hyperendemic to Hepatitis A. The seroprevalence is showing changing epidemiologic trend in certain geographic regions and various population groups.<sup>9</sup> In a study by Butt and Sharif Hepatitis A accounted for 50% to 60% of cases of viral hepatitis among Pakistani children.<sup>1</sup>

A recent systematic review has been published by Patterson et al regarding Hepatitis A prevalence in Africa. This systematic review in 2019 included 13 out of 54 African countries and concluded that Africa as a whole, should not be considered high endemic zone for Hepatitis A. It also showed that the risk of Hepatitis A was similar in all age groups. The review suggested that some countries, like South Africa, may be shifting from high endemicity to low endemicity.<sup>10</sup> Similarly, a relatively older multi centric study published in 1999 from

South America showed variable prevalence rates in various countries. There was higher prevalence in countries like Dominican Republic (89%), Mexico (81%) and lower in Brazil (64.7%), Chile (58%), Venezuela (55.7%), and Argentina (55%).<sup>11</sup> Similarly, a review published in 2014 regarding seroprevalence of Hepatitis A in Middle East and North Africa region also shows variability according to countries. Higher prevalence was seen in countries like Egypt (86.2%), Iraq (96.4%), and Yemen (86.5%) and lower prevalence was seen in UAE (20.1%), Kuwait (28.62%) and Algeria (12.3%).<sup>12</sup>

There has been relative paucity in research on Hepatitis A in our region. A recent hospital based study from Kathmandu, Nepal showed the prevalence of Hepatitis E as 69.2% and Hepatitis A as 15.3% among 210 Nepalese adults.<sup>13</sup> A mini review by A Shrestha published in 2015 suggested that although Hepatitis A was endemic among children only, it is re-emerging as a problem for young adults.<sup>14</sup> There has been no prior study among Nepalese children regarding Hepatitis A so far. In our study, the prevalence of Hepatitis A among children with hepatitis was 92.7%. Due to lack of adequate resources, the children with non hepatitis A results could not be diagnosed further. This high prevalence of Hepatitis A among our children is highly suggestive that if Hepatitis A is taken care of, then overall hepatitis burden among pediatric population would be significantly reduced.

In our study, there were more boys being affected than girls with hepatitis with sex ratio of 1.3:1. This sex difference could have been resulted because of the higher preference being given to boys in our relatively patriarchal society. While analyzing the involved age groups, among total 287 cases, we had 121 pre-school children (42.2%), 102 school children (35.5%), 33 toddlers (11.5%), and 31 adolescents (10.8%). This shows that Hepatitis A affected the preschool and school children most. As the toddlers are dependent upon their parents for food, hygiene and sanitation, they are relatively safer from Hepatitis A. On the other hand, pre-school children and school children are likely to consume outside food and are more prone to get infected with Hepatitis A. This fact is in congruence with our results where the pre-school age group were significantly associated with Hepatitis A. While adolescents would have seroconverted by their age due to high endemicity, it would affect them relatively lesser.

In regards to the water sources of the children with hepatitis, we had classified the regular water sources into five categories—Filtered water, boiled water, boiled and filtered water, jar water, and tap water. In the present study, 91 (31.7%) children used filtered water, 65 (22.6%) children used tap water, 55 (19.2%) children

used boiled water, 53 (18.5%) children used jar water and 23 (8%) children used boiled and filtered water. In resource limited set ups, safe drinking water is a major issue. As per Globalwaters report, only 27% of Nepalese population have provision of safe drinking water.<sup>15</sup> Most households rely on filtered water for purifying water. Commonly used filters in our country is the candle type ceramic filters. Although this filter is effective in clearing particulate matters and bacteria, it is ineffective in clearing viruses. Hence, Hepatitis A virus can't be removed by the common household candle type ceramic filters. In this study, maximum percentage of children with Hepatitis A had used filtered water. Another method commonly popular to purify water is boiling it. However, almost 20% children in this study had used boiled water but were infected with Hepatitis A. Apparently, boiling and then filtering water appears to be relatively safer method for protection against Hepatitis A transmission, as only 8% of children who regularly consumed boiled and filtered water suffered with Hepatitis A. Another source of water in our set up is jar water. This is more common in crowded urban areas, where Government water supply is scarce. People in these areas depend upon regular supply of jar water from local water suppliers. Although jar water is presumed to be safe, the results show that the risk of jar water consumption and Government supply tap water consumption is almost same (18.5% vs 22.6%).

In regards to complications, Hepatitis A is considered a benign disease in children. Although complications are rare, Hepatitis A is amongst the leading cause of acute fulminant liver failure in children. Various studies have shown that Hepatitis A was responsible for 40% to 80% pediatric acute fulminant liver failure in different countries.<sup>1</sup> In this study, we noted complications in five children (1.7%), including 2 acute fulminant liver failure, one pneumonia, one enteric fever and one prolonged fever. We had two children with fulminant hepatic failure (0.7%). Among them, one was complicated by septicemia and led to mortality, placing the mortality rate at around 0.38%.

Hepatitis A is a water borne disease which is vaccine preventable. The changing epidemiology of Hepatitis A is reflected upon by the improvement in socioeconomic status of the particular region and the provision and coverage of vaccine for Hepatitis A. In USA, there has been dramatic reduction of Hepatitis A incidence by 96.6% from 1996 (11.7 cases per 100 000) to 2011 (0.4 case per 100 000) following introduction of universal immunization from 2006.<sup>16</sup> A systematic review studying the effects of universal mass vaccination in various countries including Argentina, Belgium, China, Greece, Israel, Panama, USA, Uruguay had been published in 2016.



This review concluded that there has been dramatic decline in the incidence of Hepatitis A following immunization in all the countries except Greece.<sup>17</sup> Although WHO has recommended universal mass immunization of children with Hepatitis A vaccine, due to various reasons, this policy has not been implemented in most of the resource limited countries in the world.<sup>4</sup> Even in our neighboring country India, various authors have advocated for immunization with Hepatitis A for children.<sup>18-20</sup> Numerous studies have been conducted which have proven the cost benefit analysis of even single dose Hepatitis A vaccination. Thus, evidence suggests that mass immunization with hepatitis A vaccine is economically beneficial, both in developing and developed regions of the world.<sup>21-26</sup> In this regard, most resource limited countries without access to safe drinking water should consider universal mass immunization with Hepatitis A vaccine for their children.

### Strengths and Limitations

This study is one of the novel studies in the field of pediatric hepatitis in our region. This prospective study has included more than 250 children with hepatitis over a period of 10 years. Hence, the results of this study could have significant impact in the field of pediatric hepatitis. However, being a single centric study and comprising only Nepalese Army dependent families, the results may not represent the common Nepalese children from all over the country. Hence, generalization of these results may not be applicable in the National level.

### Conclusions

Among pediatric hepatitis, 92.7% children had Hepatitis A. The different age groups toddlers, pre-school, school children and adolescents comprised 11.5%, 42.2%, 35.5%, and 10.8% respectively. Most affected children were of the preschool and school children. The water sources of the study population were filtered water (91 i.e. 31.7%), boiled water (55 i.e. 19.2%), boiled and filtered water (53 i.e. 8%), jar water (53 i.e. 18.5%), and direct tap water (65 i.e. 22.6%).

Thus, boiled and filtered water appeared to be safest against transmission of Hepatitis A and children using filtered water were more susceptible to Hepatitis A. The disease was self-limiting in most children with complications only in five children and mortality rate was 0.38%. These study findings need to be corroborated with more elaborate, multi centric studies in the future. In resource limited countries, availability of safe drinking water to children is not easily achievable and hence

it is recommended that immunization with Hepatitis A vaccine should be considered a priority by the Governments.

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### Author Contributions

BS—Principal researcher and author; contributed to conception; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

US—Literature review of the manuscript and critical analysis of the research; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

KK—Literature review and helped the Principal Researcher in the laboratory tests; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

SS—Overview of the research and statistical support to the Principal Researcher; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

### Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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### Ethical Approval

The Nepalese Army Institute of Health Sciences Institutional Review Committee (IRC) approved the study (Reg. No. 837).

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