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ABSTRACT Background: Hepatitis E virus (HEV) infection is a foremost reason of waterborne outbreaks. HEV is transmitted via fecal-oral route through a contaminated water source. Contaminated water caused a massive Hepatitis A outbreak in Shimla town in 2007. Since then sporadic cases continued to be reported due to contamination of drinking water source upstream by the discharge from ill maintained sewerage treatment plant. Though cases were being reported since 2007 but no serious illness/deaths were reported till present outbreak that claimed 33 lives and thousands were taken ill.

Methods & Materials: Integrated Disease Surveillance Project (IDSP) data entry operators informed the Shimla District Surveillance Officer that some cases of jaundice are coming daily. We supervised the trends and found that some clustering (Two or more cases) of cases is happening in Vikasnagar locality where the municipal water tank supplies drinking water lifted from Ashwani River/Khud. Clustering of cases started happening in Vikasnagar and nearby localities rapidly. The DDU hospital doctors were orally alerted for a possible outbreak situation. Some of the patients were referred by the doctors to a private lab for getting their serology for Hepatitis E/A. We tracked the patients and found majority of them suffering from Hepatitis E. As soon as first patient of Hepatitis E was reported by lab and more than five adjoining clusters of cases appeared, we sent a letter to Municipal Corporation and District Administration that there is possibility of Hepatitis outbreak in Shimla Municipality and we need to immediately hyper chlorinate water and check drinking water sources.

Results: The late response of the municipality resulted in 33deaths and more than 6000 people suffering from jaundice and other associated symptoms. Most of the deaths were due to predisposition to alcoholism, pregnancy and medically compromised position that aggravated the illness. Virology for water samples was found to be positive for Hepatitis E/A as the sewerage treated water, upstream, contaminated the drinking water source below that was being routinely chlorinated and the contamination could not be detected due to non availability of virology lab in the municipality.

Conclusion: Early application of epidemiological tools informally helped predict fatal Hepatitis Outbreak in Shimla and these epidemiological tools can be applied in similar situations to avoid such catastrophes in other settings. More waterborne outbreaks are predicted in near future due to climatic disturbances i.e. global rise in temperature and decline in snowfall/rainfall.

KEYWORDS : Outbreak, Hepatitis E, Early warning signals, High mortality of Pregnant women, Hyper-chlorination of drinking water.

Introduction:

Hepatitis E virus (HEV) infection is a foremost reason of outbreaks and acute sporadic hepatitis worldwide. HEV is transmitted via fecaloral route through a contaminated water source and infect human beings and is a causative agent for many water-borne outbreaks.²³It is a virus of public health importance due to its ability to cause sporadic, endemic and epidemic outbreaks. In developing countries it is mostly associated with sewage contamination of drinking water.⁴⁵ Contaminated water poses a considerable risk to public health as 71% of the world's population with 3.4 million symptomatic cases, 70000 deaths and 3000 stillbirths in 2015.⁶⁷ The death rate is higher (as high as 20%–30%) among symptomatic pregnant women than among symptomatic non-pregnant women.⁸

In the absence of an effective vaccine and definitive treatment, interruption of transmission remains the best available strategy against HEV infection. Early detection of warning signs, prompt outbreak investigations and application of specific control measures would check the spread and also reduce mortality due to the disease. Recently, the Government of India has initiated a "National Program on Prevention and Control of Viral Hepatitis in India" under the 12th Five year Plan (2012-2017), which would focus on ascertaining the prevalence, establishing laboratory networks, and support capacity-building activities in outbreak investigation.⁹

In the Indian subcontinent, especially in developing countries epidemics of hepatitis E occur due to poor hygienic conditions and due to recurrent contamination of water supplies.¹³

Annually, numerous outbreaks due to hepatitis virus get reported from across the country, particularly from the "Empowered Action Group

(EAG) States".^{10,11} Shimla is the capital of Himachal Pradesh, a northern hilly state of India. An increase in number of Jaundice cases from municipal corporation (MC) area were noticed by Integrated disease Surveillance Program (IDSP) in the month of Dec 2015. We started the investigations with the objective to (1) confirm the outbreak, (2) assess the magnitude, (3) identify the source (4) investigate the reasons behind its occurrence (5) suggest actions for its prevention in the future.

Materials and methods:

Shimla town experienced a large outbreak of Hepatitis in 2007 (1288 cases) that was later identified due to Hepatitis A virus genotype III A by the National Institute of Virology, Pune. Bharti et al, reported satellite outbreaks²⁴ around Shimla town due to transmission of Hepatitis A virus by the employees coming to Shimla from outskirts of Shimla. In-between sporadic cases of jaundice continued to pour in Shimla Hospitals and we were alert to the situation that outbreak can happen anytime. In Dec 2015, Integrated Disease Surveillance Project (IDSP) data entry operators informed the District Surveillance Officer that some cases of jaundice are coming daily. We supervised the trends and found that some clustering (Two or more cases) of cases is happening in Vikasnagar locality where the municipal water tank supplies drinking water. Clustering of cases started spreading to nearby localities rapidly. The doctors were orally alerted for a possible outbreak situation and report jaundice cases as soon as they come to them. Some of the patients were referred by the doctors to a private lab for getting their serology for Hepatitis E/A. We tracked the patients and found majority of them suffering from Hepatitis E. As soon as first patient of Hepatitis E was reported by lab and more than five clusters appeared, we sent a letter to Municipal Corporation and District Administration that there is possibility of Hepatitis outbreak in

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Shimla Municipality and we need to immediately hyper chlorinate drinking water and check water sources physically for any contamination, before we conclude about the reasons of high number of jaundice cases attending zonal hospital.

As the cases started rising slowly, we collected data related to jaundice cases from district hospital, private hospitals, and the Indira Gandhi medical college (IGMC) situated in the capital for a possible outbreak.

A probable case was defined as any person residing in the Shimla MC area who had dark urination/yellow discoloration of the sclera/skin, between December 2015 to May 2016 onwards and with serum billirubin level above 1.2/ mg/dl. S/he was labeled as confirm case if tested positive for IgM antibodies for HEV by ELISA. On reviewing the surveillance data it was found that five of twenty-five wards of MC were the most affected. We conducted a house to house survey to identify cases and in affected ward. For all cases, demographic information i.e. time of onset of symptoms, sources of drinking water and knowledge about use of boiling water etc was collected. Sentinel surveillance was established in district hospital and the medical college of the area. Serum Samples were tested for IgM antibodies against hepatitis A virus and HEV from early POD (post onset of illness disease) patients. Water sample from available water sources used for drinking, from the household of the family affected, from overhead water tank of a household, which was not used since Oct 2016, from water lifting source (natural stream), Ashwani Khudd, and from Sewerage treatment plant (before and after treatment) which was located about 4 miles upstream to the water lifting source, were sent to National Institute of Virology (NIV) Pune, India for Virus isolation

We discussed with State, District and Shimla MC Officials, Irrigation & Public Health (IPH) Department officials and community leaders about the occurrence of Jaundice, areas affected, investigations undertaken, the water supply and sanitation of affected area and suggested control measures. On inspection of sewerage treatment plant it was found that there was untrained and inadequate staff and no provision of alternate electricity supply (generator) and there was no process of transporting the extracted solid waste (no road). The water treatment plant had leaks from water tank at collection point and the filtered water storage Tank. The flocculation chamber was broken. The chlorination apparatus was at the outlet rather than on inlet of filtered water storage point. There was no provision of adequate chlorination at reservoir tanks or supply tanks of Municipal Corporation. There were no protocols/standard operating procedures available with the staff working both at sewerage treatment plant and water treatment plant.

Line listing of the affected cases and census of the entire municipal area according to age and sex was performed. We constructed an epicurve and a spot map. The data was entered and analyzed in Microsoft Excel. Time, place, and person analysis were performed for all cases patients. Continuous variables and categorical data were summarized in terms of mean and standard deviation, and using proportions, respectively.

Results:

A total of 1681 HEV/ HAV cases out of more than 6000 cases were reported from 11th December 2015 to 25th May 2015 from areas/localities under Shimla municipal corporation wards. However, five of the 25 wards were mainly affected namely Vikas Nagar 238(14%), Khalini 223(13.2%), Kasumpati 207(12.3%) Chota Shimla 201(11.9%) and Panthaghati 151(8.9%) and accounted for 60.6% (1020 out of 1681) total affected cases of jaundice in Shimla town (figure 1). All these affected wards were being supplied water from contaminated Ashwani Khud. Areas supplied by other sources were not affected.



Figure 1: Area wise distribution of jaundice cases in Shimla town.

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There were 33 deaths (case fatality ratio: 1.9%) 90% of them due to HEV. Three out of 8 pregnant women affected with Hepatitis died of Hepatitis related complications post delivery. The most common symptoms among the affected cases were passing of high colored urine (100.0%), fever (90.9%), and yellowish discoloration of sclera (86.4%). The less common symptoms were loss of appetite, vomiting, malaise, fatigue, and upper right abdominal pain.

Out of 1681 affected cases, 552 (32.8%) patients were female and 1129 (67.1%) patients were male. The attack rate in males was 25% per 1000 persons and 10.6% per 1000 persons for females. The disease affected all the age groups but the majorly affected age group was 15-25 years 445(26.4%) followed by 26-35 years, 418(24.8%) and contributed to more than 53% of jaundice cases. (Figure 2).



Figure No.2: Age wise distribution of jaundice cases in Shimla town.

The first case patient developed an illness during second week of December 2015. The outbreak peaked during 13^{th} January 2016 to 25^{th} January 2016.



The main source of water supply to the affected wards was from Ashwani Khad treatment plant. Spot map depicts the affected wards, water supply and clustering of cases in all the five most affected wards during this period (Figure 3).



Figure 3: Spot Map of affected area of Shimla Town.

The laboratory results clearly indicate that the present outbreak is due to Hepatitis E virus as more than 81% are found positive for IgM antibody to HEV, some cases were positive for HAV as well. The high levels of SGOT AS 3527 & SGPT AS1504 are mind boggling and need further research on the early indicators of deaths in HEA outbreak situations.



Figure 3: Malyana sewerage Treatment Plant situated at hill top with Catchment River below since 2006.

Discussion:

The drinking water is provided to all 25 wards under SMC by bulk water supply from Irrigation and Public Health Department (IPH). The supply to the affected areas is through piped water and is from Ashwani Khad/River treatment plant. A sewerage treatment plant is situated four miles upstream to the collection point of water treatment plant on Ashwani Khad. A failure in sewerage treatment and further at water treatment can be a source of water borne diseases. The water lifted from Ashwani Khad is treated at the source itself using rapid sand filters and chlorination is done before transmission to the reservoir for further supply and distribution. The water from reservoir tanks is supplied further to Municipal Corporation distribution tanks for further supply to general public for drinking purpose.

In winters due to shortage of water in streams (Due to less rainfall) the proper water treatment procedures were not followed, especially the 'Contact period' for proper chlorination. The process of measuring residual chlorine before supplying the drinking water was not followed.

The Ashwini Khud treatment plant gets water from the natural sources namely Koti Nalla and Kufri etc. In addition, the treated sewerage effluents released from sewerage treatment plant (STPs) in Malyana and Dhalli upstream also flow into the natural sources and all this ultimately reaches to the Ashwani Khad treatment plant. This water is then treated at Ashwini Khud and then supplied for drinking purposes under SMC areas. The water supply from water treatment plant located at Ashwani Khad under IPH (Irrigation and public Health) department was stopped on 2nd January 2016 on advisory from health department based on the pattern of cases alongwith its distribution areas. The laboratory tests substantiated that proper/appropriate process for treatment of contaminated water was not being followed at the Ashwani Khad treatment plant. Inadequate chlorination and inadequate quantity of alum was being mixed in the untreated water. Further, the corroded and visible pipeline leakages at Ashwini Khud may have led to mixing of contaminated water with the treated water. This may have resulted in the supply of contaminated water to the community settings. Interview with community in the affected areas revealed that they do not boil water before drinking and do not properly practice hand hygiene practices.

Present study confirms the HEV as the prime etiological agent of this outbreak of acute hepatitis. This virus is documented to be a major cause of outbreaks of acute hepatitis in developing countries like India. It is reported as the cause of hepatitis outbreak as early as in 1955-56 from its first detection in Delhi¹⁴ and since then continuously reported from various parts of the country viz., Kanpur, Rajasthan, Kolkata, Hyderabad, Girdharnagar, Ahmedabad, Punjab and Odisha.¹⁵⁻²¹

During this time, the cases appeared within a short span and clustered around particular area indicating a possibility of point source outbreak. The attack rate was more i.e 17.3% to other outbreaks reported from different parts of India (1-15%).²²

Our study showed higher male positivity (67.1%) in comparison to female (32.8%) in present outbreak which is comparable to similar finding documented from various parts of the country.^{5,15,23}

The disease affected all the age groups but the majorly affected age group was 15-25 years followed by 26-35 years in this outbreak as

reported earlier.^{15,23} The reasons of higher attack rate in men than women need further epidemiological investigation. Hepatitis E is reported in urban areas whenever there is break in quality of water supplied including low levels of water chlorination.^{15,20}Direct evidence for a zoonotic transmission of hepatitis E virus from Sika deer to human beings has been reported from Japan and also from Japan, consumption of wild boar meat has been linked to cases of hepatitis E. Mortality of hepatitis A is approximately the same in pregnant versus non-pregnant cases but for unknown reasons the mortality of hepatitis E is much higher (approximately 20%) in pregnant women, compared to on-pregnant individuals. Transmission of HEV from the pregnant mother to her fetus, resulting in fetal wastage, is also common^{25,26}.

The main source of water supply to the affected wards is from Ashwani Khad treatment plant where clustering of cases was reported and complaints of turbid water supply were received from the affected area. As soon as epidemic was noted, the water treatment plant located at Ashwani Khad under IPH (Irrigation and public Health) department was instructed to stop the water treatment services on 2nd January 2016. An intensive IEC campaign to boil water before drinking and to adopt other hygiene practices was launched by health department through print and electronic media. Interestingly all high profile popular water purifiers failed affecting big bigs in administration with jaundice who believed in their high cost filters having membranes and reverse osmotic processes.

Series of review meetings held with stakeholders and active interventions like health education to boil water before drinking, maintaining personal hygiene, media campaign, provision for safe drinking water, interruption of infected water supply and super chlorination helped in subsiding the outbreak. The regular epidemiological and microbiological surveys can contain any future outbreak and associated mortality and morbidity.

Environmental factors make the outbreak fatal: Since 2006 when the Malyana sewerage treatment plant was commissioned the cases of jaundice continue to pour in with a large non fetal hepatitis-A outbreak in 2007 (Jan-March 2007) and subsequently fatal outbreak of Hepatitis-E in 2016. Apart from the fact that there was inadequate treatment of sewerage plant upstream drinking water collection point in the Ashwani river and low contact period of water chlorination tanks, there was less water available in the river and the low dilution factor of the contaminated river water played its role in aggravating the jaundice and made it fatal due to undiluted high dose of contamination in the water. Dose dependent severity has been found with HEV25. The failure of the municipality to have a virology lab to detect any Hepatitis E/A viruses also contributed as 2007 outbreak from the same source should have served municipality a lesson for future to prevent such outbreaks. Consistent rise in temperature and decreasing snowfall/rainfall in Shimla is also contributing to such outbreaks. Analysis of 28 Years of temperature in Shimla district since 1976 till 2004, show that there is a rise in average temperature by $1.1^{\circ C}$. The increase in temperature by 1 degree has caused a sharp decline in average snowfall that is from 272.4 cm in 1976 to 77.2 cm in 2004 seriously jeopardizing the availability of water. Similar outbreaks are predicted elsewhere if all these environmental factors are not kept in mind especially the rising temperature and low rainfall as recorded by meteorological department at Shimla below.

Total Monthly Rainfall of Shimla in mm										
Year	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
January	0.0	80.0	17.8	25.1	15.0	133.3	120.4	51.3	72.1	35.0
February	163.4	49.6	21.3	81.5	55.9	32.7	195.9	88.0	106.1	53.7
March	163.2	2.0	48.9	4.5	37.6	35.6	99.0	142.5	196.4	125.3
April	9.8	56.9	45.9	5.5	37.0	80.5	14.7	82.4	116.5	26.5
May	42.2	146.8	39.6	50.3	93.7	13.8	23.4	68.1	16.1	104.8
June	199.2	535.8	72.4	220.1	196.3	81.3	319.6	235.6	110.5	193.6
July	202.4	204.0	204.3	490.6	296.9	315.9	207.4	561.5	409.2	416.8
August	376.3	389.1	229.5	388.2	338.4	350.6	239.5	160.5	265.5	402.6
September	59.8	315.6	280.4	392.5	159.4	162.0	133.6	108.0	62.9	39.9
October	13.7	26.4	2.2	24.8	19.0	7.9	66.4	29.0	23.0	2.3
November	0.0	7.1	15.8	17.3	0.0	2.7	13.8	0.0	9.4	0.0
December	30.1	10.1	0.6	81.8	17.0	18.7	13.2	97.9	37.5	5.5

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Year	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
September	59.8	315.6	280.4	392.5	159.4	162.0	133.6	108.0	62.9	39.9
October	13.7	26.4	2.2	24.8	19.0	7.9	66.4	29.0	23.0	2.3
November	0.0	7.1	15.8	17.3	0.0	2.7	13.8	0.0	9.4	0.0
December	30.1	10.1	0.6	81.8	17.0	18.7	13.2	97.9	37.5	5.5
Total	103.6	359.2	299.0	516.4	195.4	191.3	227.0	234.9	132.8	47.7
Jaundice	1288	246/	425/	126/	67/0	181/	236/	393/	182/	1681
Patients/	/0	0	0	0		0	0	0	0	/33
Deaths										

Total Precipitation (Snow +Rain) in Shimla from Nov 2006-07 to Nov 2015-16 shows overall declining trend) X axis=year and Y axis =Annual precipitation)



Conclusion:

The Evidence suggested that the outbreak was due to fecal contamination of drinking water supply and improper water treatment procedures (i.e. filtration, flocculation, sedimentation and chlorination) to the affected area especially the 'Contact Period' for proper chlorination. The low rainfall during September to December also contributed by low dilution of the routinely supplied drinking water causing high dose of contamination in drinking water. Early application of epidemiological tools informally helped predict fatal Hepatitis Outbreak in Shimla and can be applied in similar situations to avoid such catastrophes in other settings.

Recommendations:

Community needs to continue practicing personal hygiene practices and boil drinking water before use without believing much on modern purifiers. The collection point of water from natural stream may be shifted before the point of sewerage mixing in Ashwani Khud. Adequate staff must be provided at all the points, sewerage treatment plant, water treatment plant, reservoir tanks and supply tanks. The capacity building and refresher training of field staff working at these points should be regular feature. The necessary repairs of damaged plants needs to be carried with inspection by various stake holders at specific intervals needs to be done. Residual chlorine needs to be checked before supplying the water and facilities of chlorination must be there at supply tanks. Special emphasis need to be given to 'Contact Period' of chlorination. As a long term measure, 'Slow sand filter' system may be adopted.

The recognition of early warning signs, timely investigation and application of specific control measures can reduce the morbidity and mortality due to outbreaks.

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