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ORIGINAL ARTICLE

Epidemiological Investigation of Hepatitis E outbreak in a Northern city of India

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ABSTRACT:

Background: Shimla city has been observing outbreak of hepatitis A/E every year since 2007. An unusual rise in the number of jaundice cases was reported in the first fortnight of December 2015. **Objectives:** To study the distribution and determinants of hepatitis cases, to find the source of infection, and to initiate the control measures in the affected area. **Materials and Methods:** A case of acute hepatitis was defined as a person who had acute jaundice with at least one of the following symptom: dark urine, anorexia, malaise, fatigue and right upper quadrant tenderness between December 2015 and March 2016. Line listing of cases was done and analyzed according to time, place, and person distribution. Blood samples were tested for IgM antibody for hepatitis A & E virus. Water samples were also collected for the bacteriological examination and residual chlorine. **Results:** A total of 6080 cases (attack rate 35.9/1000) were reported in this outbreak. 1132 serum sample were found positive for HEV IgM antibodies out of 1988 samples tested randomly, which confirmed a hepatitis E outbreak. The attack rate was significantly higher in males ($P < 0.05$) and in age groups 25-34 years ($P < 0.001$). Case fatality rate was found to be 0.4% among general population and 21% among pregnant females. Extensive IEC was done through electronic and print media. More than one lakh chlorine tablets were distributed. Environmental investigation confirmed sewage contamination of drinking water. All 6 STP were found to be working sub optimally. Ineffective chlorination was found at all 4 WTP. The relative risk of developing hepatitis E among people using contaminated water supply against those using other sources was 5.68 (95% CI 4.81 , 7.14). **Conclusion:** HEV was confirmed as the major etiological agent in this outbreak which was transmitted by contaminated drinking water. **Keywords:** Epidemiological investigation, Hepatitis E, Attack Rate, Relative Risk, Serological examination.

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Introduction

Hepatitis E virus (HEV) is a significant public health problem and it is estimated that 2.3 billion people are infected globally.[1,2] It is a major cause of acute, self-limiting hepatitis transmitted by the faeco-oral route and frequently results in epidemic, as well as sporadic, hepatitis.[3] Epidemics of hepatitis E are generally restricted to developing countries where the disease is endemic because of poor sanitation and hygiene.[4,5]

Contamination of drinking water by sewage has frequently been the cause of such outbreaks, which tend to occur both during rainy and summer seasons and display a unimodal and short course.[6] However, some multimodal and protracted outbreaks have occurred and these may result from continuing person-to-person transmission.[7] They vary from single to multi-peaked epidemics, lasting for a few weeks to a year and affect thousands of people. The incubation period ranges from 2 weeks to 2 months, usually 1 month to 45 days.[8]

HEV primarily affects young adults aged 15–40 and fewer cases are seen in children. Person to person or secondary transmission is inefficient.[9] HEV results in 20-30% mortality in pregnant women in certain geographic regions of endemic countries.[10]

In India, HEV infection is responsible for 30-70% of the cases of acute and sporadic hepatitis. Over the past two decades a large number of well-documented and careful studies have been conducted of HEV epidemics and many sero-epidemiologic and cross-sectional studies have assessed the prevalence of antibodies to HEV from the northern, western and south central parts of India .[11]

Many outbreaks of hepatitis E have been reported in Shimla city in the state of Himachal Pradesh since 2007 but none of them were documented or characterized thoroughly.[12] Also

the sporadic cases of HEV infection keep occurring in the city, usually during periods between outbreaks .In December 2015, we received information that several people were presenting to the hospitals with acute hepatitis in Shimla city.[13-16]Therefore, we planned to investigate the outbreak.

The objectives of our study were to: (i) perform a detailed epidemiological investigation to determine the incidence of the disease in the population, (ii) to confirm the cause of the outbreak, (iii) to identify the aetiological agent (iv) to identify the source of the infection and (v) to institute appropriate control measures and(vi) to suggest preventive measures for future.

Materials and Methods

Descriptive epidemiology

An epidemic investigation was carried out in the Shimla city having a population of 169,578 distributed in 25 wards of Municipal Corporation (census 2011) by the team consisting of a an epidemiologist and other survey staff from CMO Shimla & IGMC Shimla in December 2015 through March 2016. We determined the existence of an outbreak by comparing the incidence of jaundice cases during the investigation period with the background rate through IDSP.

We searched cases by defining a case of acute hepatitis as "a person who had acute jaundice with at least one of the following symptom: dark urine, anorexia, malaise, fatigue and right upper quadrant tenderness between December 2015 and March 2016 in the households of the city." Data were collected through (1) a door-to-door survey and (2) hospital records. We prepared a line list of cases - collected data on: demographic characteristics – age and sex, Place of residence and work, date of onset, symptoms & duration of illness, complications and laboratory investigation, exposures to common water and food sources using a pre-tested semi-structured questionnaire. We described the outbreak in terms of time, place and person characteristics to generate hypothesis.

Analytical epidemiology

We conducted a retrospective cohort study to test the hypothesis regarding the cause of the hepatitis outbreak. We divided the area into two cohorts on the basis of suspected exposer-- (a) the area which was supplied drinking water through contaminated water supply (b) the area which was supplied drinking water through uncontaminated water supply. Then we identified people who had developed the disease and who did not, among the exposed and non-exposed and compared the attack rates from two different sources.

Laboratory Methods

Plasma samples from Hospitalized patients were tested randomly for anti-HEV/anti- HAV IgM antibodies using ELISA for determination/confirmation of the causative agent of the outbreak.

Environmental investigations

An investigation team visited houses and collected information regarding water quality, source of water supply, and drainage system. Information regarding any public gathering, exposure to outside food and local food vendors between December to March was also collected through a questionnaire. The available blueprint of the water supply pipelines and drains was examined. Water samples were collected and analyzed in laboratory from outlet of STPs at Malyana, inlet and outlet of water treatment plant at Ashwani Khad (both raw and treated water), and seven consumption units by investigation team for testing presumptive coliform count using standard techniques to assess the water quality in the city during the outbreak,

Statistical methods

Data was entered in MS Excel and analyzed using Epi-Info 2007 software. We calculated overall attack rate and stratum-specific Attack rates (age groups, gender & place of living) and Risk ratio (95% confidence interval) for the analytic component of the study.

Ethics

This study was approved by the institutional ethics committee of IGMC Shimla. Participants were informed about the study and written consent was obtained from all participants before the use of their samples and clinical records. All data were securely stored in the study database.

Results

Survey findings

The annual incidence of viral hepatitis as per the IDSP data ranged from 0.3 to 7.6 per 1000 in the Shimla city from 2007-2014.(Table 1)

Table 1: Annual numbers of viral hepatitis case in Shimla city as per IDSP Report

Name of disease	2007	2008	2009	2010	2011	2012	2013	2014
Viral hepatitis	1288	246	425	126	67	181	236	393

The index case reported to the district hospital Shimla on 11/12/2015 from the Kusumpti Area. Then there was a sharp rise in cases in the first week of December followed by a peak in the fourth week of January. (Figure 1)

The sample survey covered 33,590 households consisting of 167,955 individuals, with 92576 males and 75,368 females. A total of 6080 people were found to have jaundice between December 2015 to March 2016. The overall attack rate was 3.6 % (36 per 1000 population). Out of the total cases, 67.4% were males (4096 cases) and 32.6% females (1984). Men had a higher attack rate of 4.4 % (44 per 1000 population) than women 2.6 % (26 per 1000 population), and were at 1.9 times greater risk of getting infected than women ($P < 0.05$). Out of the total affected females, 24 were pregnant. Children under 5 years of age had a lowest attack rate of 1.47% while highest attack rate was seen in age group 25-34 years 46.63% ($P < 0.001$).

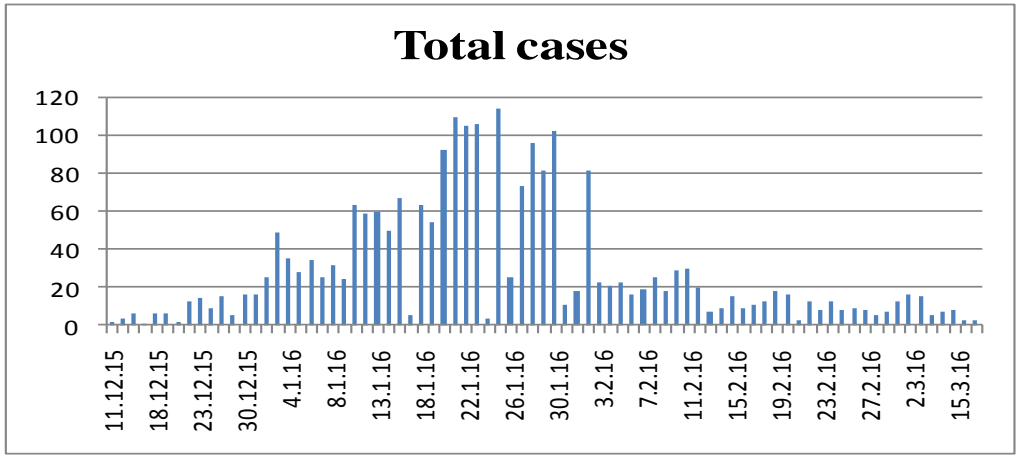

Figure 1: Epi curve of jaundice cases reported in affected wards of SMC (December 2015 to March 2016)

Age Group	Population	Cases	Attack Rate	Male	Cases	Attack Rate	Female	Cases	Attack Rate
All age	169578	6080	35.85	93152	4096	43.97	76426	1984	25.96
0—4	8854	13	1.47	4626	9	1.95	4228	4	0.95
5—14	25847	180	6.96	14286	138	9.66	11561	42	3.63
15—24	36903	1666	45.15	20148	1018	50.53	16755	648	38.68
25-34	31461	1467	46.63	16856	979	58.08	14605	488	33.41
35-44	27818	1185	42.60	14734	785	53.28	13084	400	30.57
45-54	21205	1051	49.56	12379	737	59.54	8826	314	35.58
55-64	10907	454	41.62	6634	381	57.43	4273	73	17.08
>65	6583	64	9.72	3489	49	14.04	3094	15	4.85

Table 2: Age wise distribution of jaundice cases in shimla city and at their attack rates

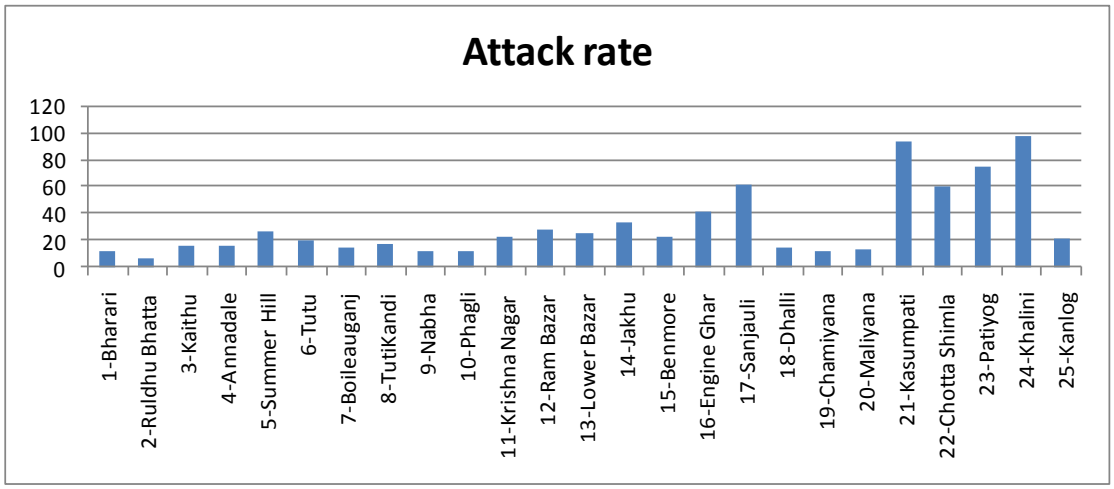

Figure 2: Area wise distribution of attack rates in the all wards of SMC Shimla

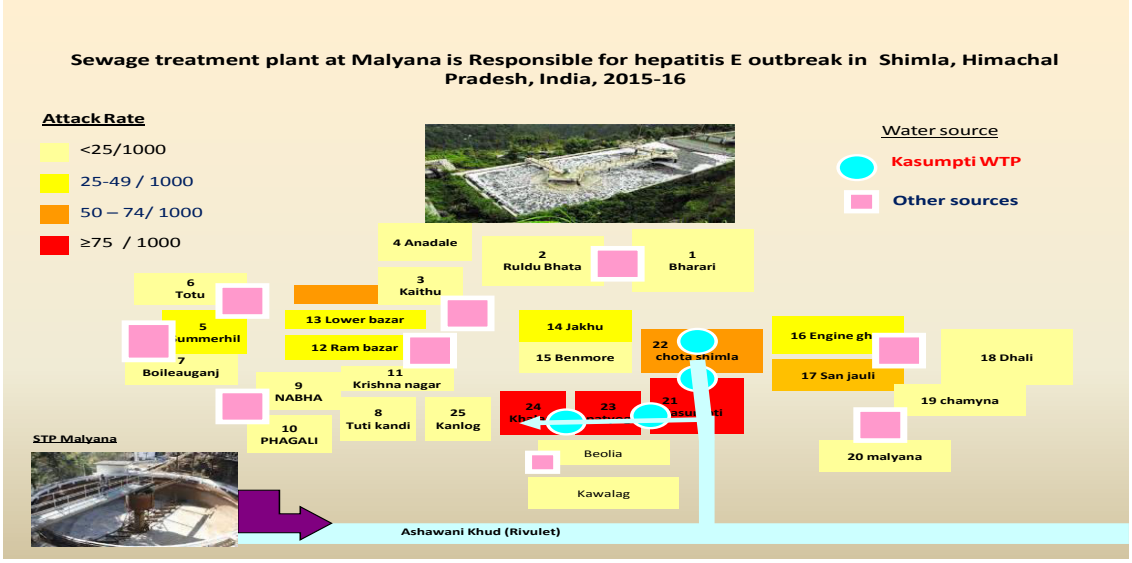

Figure 3 - Spot map of areas affected with contaminated water supply in SMC

The epi curve (Figure 1) indicates a continuous point source outbreak and large number of community being affected due to consumption of contaminated water from a common source i.e. Ashwini Khud water supply.

A total of 6080 jaundice cases were reported during December 2015 to March 2016 from areas/localities under SMC wards. However, four of the 25 wards were mainly affected namely Chota Shimla (914 cases), Kasumpati (862 cases), Patiyog (905 cases) and Khalini (819cases). These four wards accounted for about 3/5th of all the reported cases of jaundice (3500/6080 cases i.e. 57.6%) while the overall attack rate was 35.8 per 1000 person. The highest attack rates were found in wards of Kasumpati (95.48 per 1000 person) and lowest in Ruldhu Bhatta (6.43 per 1000 person).

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

There were 24 deaths because of hepatitis in the survey, with a case-fatality rate of 0.4%. CFR was very high among 5 out of 24 (21%) pregnant females.

Virological investigation

Of the 1988 blood samples tested for anti-HEV /anti –HAV IgM antibodies (ELISA), 1132 were positive for anti-HEV IgM, which confirmed a hepatitis E outbreak. The laboratory results clearly indicate that the present outbreak was due to Hepatitis E virus as more than 57% are found positive for IgM antibody to HEV.

Attack rates and water source

On sanitary survey, Malyana sewage treatment plant (STP) from where sewerage was being directed to Ashwani Khud Rivulet was found to be functioning poorly. Outdated machinery at sewage plant required cooling after every hour of work, subsequently letting the untreated liquid portion of sewage being disposed to the Ashwini khad directly for an hour.

The Ashwini Khud treatment plant gets water from the natural sources namely Koti Nalla and Kufri etc. In addition, the treated sewage effluents released from sewerage treatment plant (STPs) in Malyana and Dhalli also flow into the natural sources and all this ultimately reaches to the AshwaniKhad. This water is then treated at Ashwini Khud WTP and then supplied for drinking purposes.

It was substantiated that 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. Flocculation chamber and clarifier were not working properly and contact period for chlorination before distribution was not found adequate. 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.

There was no laboratory facility at Ashwani, Gumma and Chairh WTPs. The testing of water samples of water treatment plants and city water supply was done in the Central Laboratory located at Dhalli WTP, Shimla

Families who received water from Ashwini Khad pumping station (Kusumpti, Patiyog ,Khalini) had the highest attack rates among all wards.The difference in attack rates in comparison with families who received their drinking water from other pumping station like Gumma –giri (Sanjauli, Choda maidan, Chamyana) was significant ($P < 0.001$). The relative risk of developing hepatitis E among people using contaminated water supply against those using other sources was 5.86 (95% CI 1.79 , 3.37). (Table 3)

Area	Population Suryed	Cases	Attack Rate	Risk Ratio(95% Ci)
Kusumpti	9884	862	93.85	5.86 (4.81-7.14)
Dhalli	7327	109	14.88	

Table 3: comparison of cases and attack rate in two wards having different water supply

Table 4: Clinical symptoms present among cases investigated

Symptoms	%age	Frequency
Malaise	95.02	458
Dark urine	90.46	436
Yellow Sclera	87.97	424
Anorexia	82.6	398
Fever	63.8	306
Pain Rt Upper Abd	53.11	256
Vomiting	51.25	246
Pruritis	36.25	184
Joint pain	33.33	160
Clay coloured stool	19.58	94
Diarhoea	12.03	58

Duration Of Illness	Frequency	Percent	Cum. Percent
< 1Week	82	17.01	17.01
1-2 Weak	225	46.68	63.69
>2 Weak	175	36.31	100.00
Total	482	100.00	100.00

Table 5: Duration of illness among most of the cases of Hepatitis E.

Most common symptoms found among cases were malaise (95%), dark urine (90%), yellowish sclera (88%) and anorexia (82%). Fever and pain abdomen were noticed by 63% and 53% of cases investigated respectively. Pruritis and athralgia were found among 36% and 33% of cases respectively. Duration of illness among most of the cases was from 1 to 2 weeks.

Water analysis data

Water samples were collected and analyzed in laboratory from outlet of STPs at Malyana, inlet and outlet of water treatment plant at Ashwani Khad (both raw and treated water), and seven consumption units were sent for faecal contamination to microbiology lab of IGMC Shimla. All of these samples tested were found unsatisfactory with presumptive coliform counts >180/100 ml which on further investigation were positive for Hepatitis E virus in the final report of national institute of virology, Pune.

Community awareness

Communication with the community in the affected areas revealed that most of them didn't use boiled water for drinking and observed poor hand hygiene. Some of the community members also revealed that they have started consuming water from baweris as piped water was contaminated, despite the fact that signage on the baweris had clearly mentioned that the water is unsafe for consumption. Few vendors were also found selling beverages near baweris. A part of the community households had septic tanks and open disposal too was observed at some places.

Actions Taken by the State/District administration

Commissioner Municipal Corporation was informed about unusual increase of jaundice cases, with a request to monitor the quality of water supply from natural resources and as well as IPH supply. It was also requested to chlorinate the water supply in order to prevent any impending outbreak of other waterborne diseases.

The study findings were also reported to the other authorities of the city who then directed maintenance of STP and proper chlorination at WTP which supply water to the affected areas. Extensive IEC was done through electronic and print media. Daily newspapers and local radio stations reported our findings to educate the public about control measures like consuming boiled water and observing hand hygiene. More than one lakh chlorine tablets were distributed.

Discussion

District Shimla lies in the north western ranges of Himalayas, located 31.6ºN 77.10ºE with an average altitude 2397.59 mt. above mean sea level. The average temperature during summer is between 19 and 28º C and between -1 and 10º C in winter.[17] Shimla Municipal Corporation(SMC) is divided in to 25 wards;it resembles an irregular crescent having eastern portion toTotu andextends to western portion up toDhalli. SMC has a population of about 1.6 lakh (2011

census) and population density of 4197 per sq km (area 35.34sq km).[18]

During hepatitis E outbreaks, the overall attack rates among general population range from 1% to 15% as per literature.[19] We report an attack rate of 3.6% (6080 cases) in shimla during the study period. The largest epidemic reported was in Kanpur in 1991, which affected an estimated 79 000 individuals.[20]

Many epidemiological features of this outbreak resemble previous hepatitis E epidemics. Outbreak was a unimodal with a single peak suggestive of a point-source, common-vehicle epidemic. Similar outbreak of hepatitis E has been reported Ghirdarnagar, Ahmedabad.[21] The age specific incidence was highest among 25-34 years age group (46.63/1000), similar to what was reported by another study.[22] Men had higher attack rates than women, attack rates in children were low and young adults showed high attack rates which is consistent with other studies .[9,23]

There were 24 pregnant women who suffered from HEV in the survey population and out of them 5 died during the study period. This is similar to reports from north India where a high case fatality has been reported in pregnant women. [24] A study on sporadic disease conducted in Chennai, south India showed a very low incidence in pregnant women.[10] It has been proposed that a subgenotypic shift in the northern Indian strains may contribute to virulence, while the strains in the south might be stable and less virulent.[10,25]

Study revealed the occurrence of recurrent outbreak during the winter months since 2007. Climatic conditions, soil leaching caused by heavy winter rainfalls after a long period of dry spell, and the use of unsanitised sludge as crop fertilizer, are factors that may explain the intensity of the epidemic during the winter.[26,27] According to ONAS, several factors may affect the efficiency and reliability of the treatment process in the STPs, namely, hydraulic and organic overloads of the STP, an antiquated state of equipment and structures, retension time, lack of experienced operating staff.[28] With the increase in urban populations in shimla, sewage treatment plants do not have the capacity to process such large volumes; consequently, retention times for wastewater treatment become too short to be effective.

HEV is shed in high numbers in the feces of infected individuals, whether symptomatic or not, and ends up in large quantities in raw sewage. Contaminated treated wastewater discharged in the environment is one of the main sources of viral diseases and is considered the major vehicle for viral transmission , since enteric viruses entering the STP are released to the environment and can reinfect susceptible populations.[29,30] Due to its high infectivity with low doses and greater resistance to usual wastewater treatments and the ability to survive for long periods in several environments, HEV can contaminate soil, food, and natural water courses and can then be transmitted to humans by fecal-oral routes . Therefore, detection of HEV in sewage would provide an important overview of its spread in an entire population, revealing the appearance of asymptomatic infections, and of its circulation between the environment and the human population in a given area.[31,32]

There are also proven evidences available in literature that chlorination specifically in winters require more contact time for proper disinfection, which was not followed as usual practice at Asthwini khad WTP Shimla.[33] Winter epidemics have also been reported in other countries located in different climate zones.

The drinking water is provided to all 25 wards under SMC by Irrigation and Public Health Department (IPH). The supply to the affected areas is through piped water and is from Ashwani Khad treatment plant. The water lifted from Ashwani Khadis treated at the source itself using rapid sand filters and chlorination is done before transmission to the reservoir for further supply and distribution. Ashwani Khad pumps/lifts water to Kwalag reservoir (about 450 meters above) and then Kwalag reservoir pumps water to Kasumpati reservoir (about 750 meters above) and then water is further pumped to Mansfield reservoir (about 710 meters above) in the Chotta Shimla. The water supplied from Kasumpati and Mansfield reservoir caters to 4 most affected municipal wards viz. Chota Shimla (ward No 22), Kasumpati (ward No 21), Patiyog (ward No 23) and Khalini (ward No 24).All the areas in the above 4 wards are connected with pipeline supply of water at household level by SMC. In this report, families who received their water exclusively from the Ashwini khad pumping station had the highest attack rates.

The SMC area is divided into sewer zones eachzone is having a sewerage treatment plant (STP) for treating the waste water. The waste water under goes several processes of treatment and effluents are disposed in to the adjoining Nallas. Further, the areas without a proper sewerage systemhave installed septic tanks in their dwellings and the effluent from these is discharged in to open drains. Moreover, open disposal of sewerage is also practiced in AswiniKhud area, Kasumpati,Chota Shimla, Pateyog and Kahlini wards. The open defecation is more rampant in areas habituated by large number of construction workers viz. Ashwini Khud, Pateyog and in areas near STP in Malyana and Dhalli.

The factors found responsible for outbreak were, poorly functional sewerage treatment plant from where improperly filtered sewage released directly into the Ashwani Khud rivulet, inadequate contact period for chlorination at Ashwani Khud WTP and poor water surveillance system of city. This is supported by the lack of required residual chlorine and the high coliform counts.

Conclusion

In a resource-limited setting, particularly when urban areas grow rapidly, provision for sewage and protected water supply is often neglected, with serious consequences for public health. These findings suggested that better

engineering of sewage canals and drinking water distribution systems and a continued process of maintenance and chlorination are needed.

Recommendation

At Ashwini Khud water treatment plant, IPH Department must ensure the following:-

a) Adequate quantity of alum should added and properly mixed in the pre-treatment water tank based on quantity of water.
b) Proper chlorination of filtered water at supply level from Ashwini Khud and also at end user level must be focused upon.
c) Immediate repair/replacement of the leaked water pipes at Ashwini Khud,

At STP located in Malyana &Dhalli, IPH Department must ensure the following:-

a) STPs must be made to function properly as untreated sewage increases the load of treatment at Ashwini Khud and thereby raising chances of water contamination.
b) Strict action must be initiated against agency responsible for treating sewerage at STPs.
c) Improve sanitation standards and general cleanliness including open defecation, particularly in areas having construction activity viz. around Ashwini Khud treatment plant, Pateyog and in areas near STP in Malyana and Dhalli.
d) All these activities must be supervised by pollution control board along with a joint team of health functionaries from Shimla Municipal Corporation, state surveillance unit and IPH Department.

At community level district administration must ensure the following:-

a) Raise the community awareness about good hygiene practices particularly hand washing and boiling of water.
b) As during discussion few people revealed that due to contaminated water supply they have started drinking water from baweris, despite written warnings not to drink water from baweris. This aspect needs attention with special emphasis on regular IEC activities in rural and far flung areas.
c) Proper media briefing should be done to dispel the myths about Hepatitis, availability of treatment/testing facilities, maintenance of hygiene & boiling of water so as to restore confidence in the community about the measures being initiated by the Government.

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