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Outbreak Investigation of Unusual Deaths in Cases of Acute Hepatitis Syndrome, in Makronia Municipal Area of Sagar Disitrict of Madhya Pradesh

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ABSTRACT

Introduction: Eleven (11) cases of sudden deaths were reported in patients suffering from jaundice in Sagar district of Madhya Pradesh during March-July 2018. All the cases were HBsAg positive and died due to hepatic encephalopathy and or hepatorenal failure.

Methods: outbreak investigation was done using semi-structured profarma. The clinical history, investigation reports, death certificates and other available documents were analysed and findings recorded. House to house survey and health camps were also organised to find other cases with similar illnesses. The blood samples family members and suspected cases with jaundice were sent to ICMR NIRTH Jabalpur for viral isolations.

Results: All the cases of deaths were localised within an area of about 10 Kms. About 72% cases recorded died within 3 days of illness. Jaundice, abdominal pain and vomiting were the common symptoms. All cases were Hepatitis b surface antigen (HBSAg) test +ve, SGPT raised in 90.90 % cases, SGOT raised in 81.82 cases.

Conclusion: In ICMR NIRTH Jabalpur, reports leptospira positivity was found in 05 cases. There was no other underlying cause except Leptospira co-infection/super-infection which was responsible for such a high fatality in cases with acute Hepatitis.

Key words: Hepatitis B, leptospirosis, co-infection, super infection Hepatorenal Syndrome.

INTRODUCTION

In the municipal area of Makronia under district Sagar outbreak of jaundice caused 11 cases of deaths. The patients died within a period of 01 week from onset of jaundice in spite of treatment at recognised tertiary care hospitals in Sagar and Bhopal (M.P.). Acute hepatitis is generally caused by Hepatitis A and E viruses but mortality is not so high and rapid (Hepatitis A has case fatality rate of less than 0.1 per cent). Hepatitis E generally causes community-level outbreaks, and may rarely cause fulminant hepatitis (acute liver failure) and death. [1]

Acute Hepatitis B Virus Infection: Hepatitis B presents with serum sickness-like syndrome during prodromal period, followed by constitutional symptoms. The jaundice generally disappears after 1-3 months. [2] Liver failure characterized by severe deterioration in liver functions, hepatic encephalopathy, severe jaundice, coagulopathy, and hepatorenal syndrome (HRS) is unusual, occurs in approximately 0.1-0.5% of patients. Fulminant hepatitis B with liver failure is believed to be due to massive immune-mediated lysis of infected hepatocytes. [3-4] In hepatitis B also the sudden acute mortal-

ity is rare. The 5-year survival rates are 97% , 86% and 55% for chronic persistent, chronic active hepatitis ,and chronic active hepatitis with cirrhosis rspectively. The usual cause of death was liver failure and its sequelae.[5]A western European study revealed 5 year survival rate of 71% in HBsAg-positive liver cirrhosis cases.[6]

Co-infections

Coinfection of HCV and HBV, or acute HCV on pre-existing chronic HBV have been reported to increase the risk of severe hepatitis and fulminant hepatic failure.[7-8] HDV superinfection of a chronic HBsAg carrier may present as a severe acute hepatitis.[2] Hepatitis E infection in a cirrhotic patients is associated with rapid de-compensation and deaths.[9] Human Parvo virus (HPV) B-19 also causes acute hepatitis and fulminent hepatitis specially in immunocopromised cases.[10-11] Co infection with leptospira and acute hepatitis caused by Leptospira infection may also cause fulminant hepatitis with jaundice, renal failure, and bleeding manifestations (Weil's disease) . Mortality in severe forms remains high even when optimal treatment is provided . [12-14] The objective of the study was to identify the cause of jaundice with such rapid de-compensation and death and suggest control measures to health department for limiting the spread of outbreak.

METHODS: OUTBREAK INVESTIGATION

Makronia is an urban area located in Sagar district of Madhya Pradesh. It is almost 5 kms away from the district head quarter. Details of the death cases were obtained from the district health officials. A survey form to review death cases was designed by departmental research committee. The survey form included the details of deceased person like name, age, sex, occupation, date of disease onset, common signs and symptoms, name of consulted physician/ place of treatment (hospital), referral details and cause of referral, lab investigation reports for malaria, widal, serum bilirubin, liver function test reports, immunological investigation reports (HbsAg), date and place of death , cause of death as mentioned in death certificate and remarks and additional findings. The survey also included details of history of similar illness in the past, other family members suffering from similar illness, any death in the past six month and cause of death, history of travel, alcohol and drug abuse and other details.

House-to-house survey was done in the identified areas of Makronia i.e. shankargarh, Durganagar, Abhinandan nagar, Ratanganj, Rajakhedi and Village jinda of Makronia. active search of cases was done to identify symptomatic cases , unreported deaths caused by similar illness (acute hepatitis). The details of water supply, sanitation and water testing report for any microbiological contamination and residual chlorine was taken from public health engendering department.

Health camps were organised with the help of health department for screening of patients suffering from jaundice and any other undiagnosed illnesses. The contacts of all the deceased were also screened for HBsAg and other common illnesses malaria, typhoid.

The first reported case of acute hepatitis, from rajakhedi area of Makronia Sagar was admitted in Gandhi Medical college Bhopal for treatment of severe jaundice where he died on the 6th march 2018. He was found widal and HBsAg positive as per medical records. Another case of acute hepatitis died on 16th March In Sagar Sri Hospital of Sagar due to Hepatic Encephalopathy with septicaemia with septic shock with respiratory failure and was HBsAg positive as mentioned in medical records. Similarly other 09 cases of acute hepatitis, HBsAg positive died one after another at different tertiary care hospitals of Sagar and Bhopal within 2 months. Surprisingly in all 11 cases of deaths, HBsAg was positive and all died in short duration of illness due to hepatic failure /encephalopathy. However it was on 22 may 2018, health department after getting reports from media and local news got alert and asked Community medicine department of medical college sagar for investigation of the cause of deaths in patients suffering from jaundice.

House to house survey was initiated on 23rd May 2018 and continued for next 15 days by investigation team of community medicine in Makronia urban area of Sagar and all the available information was collected.

RESULT

The areas where death cases occurred were residential areas of Makronia municipality of district Sagar. The areas have good road connectivity and drainage channels.

The pipeline for supply of water was along common drainage line. So the team has suspicion of water borne viral hepatitis, Hepatitis A or E. All these cases were found to be positive for hepatitis B (HBsAg). The survey found total deaths due to jaundice related illness was 11 and 01 live case of jaundice.

Table 1: Cases and their HBsAg status

HbsAg positivity	Death cases	Live cases	Total
Positive	11	1	12
Negative	0	0	0

Table 2: Distribution of death cases according to their Locality

Name of Locality	Death Cases	Percentage
Shankargarh	03	27.27
Durganagar Rajakhedi	04	36.36
Abhinandan nagar	01	9.09
Ratanganj	01	9.09
Gournagar	01	9.09
Village jinda	01	9.09
Total	**11**	**100**

Table 3: Age and sex distribution of death cases

Age group	Male	Female	Total	Percentage
<20	2	1	03	27.27
20-40	5	1	06	54.54
>40	Nil	2	02	18.18
Total	07 (63%)	04 (37%)	11	100%

Table 4: total duration of illness before death

Cases	Date of onset of disease	Date of death	Total duration of illness
1	03.03.18	06.03.18	03 days
2	14.03.18	16.03.18	02days
3	17.04.18	24.04.18	07 days
4	24.04.18	26.04.18	02days
5	03.05.18	10.05.18	07 days
6	09.05.18	12.05.18	03 days
7	13.05.18	16.05.18	03days
8	25.04.18	27.04.18	02 days
9	18.05.18	20.05.18	02 days
10	03.06.18	04-06-2018	01 days
11	01-06-2018	05-06-2018	07 days

Table 5: Common symptoms recorded in death cases

Common symptom	Cases	Percentage
Fever	06	54.54
Vomiting	11	100
Jaundice	11	100
Headache	02	18.18
Abdominal pain	11	100

Table 6: Lab finding of the deceased cases (as available in the medical records)

Name of test	Cases	Percentage
HBsAg	11	100
SGPT (raised)	10	90.90
SGOT (raised)	09	81.81
Malaria Positive	01	9.09
Widal Positive	02	18.18
Serum Bilirubin (Raised)	10	90.90

Table 7: Serological test results for samples collected by ICMR NIRTH Jabalpur

Total samples collected	53
Positive samples for one or other etiology	13
Hepatitis A virus	0
Hepatitis E virus	2
HBsAg	1
Hepatitis C virus	0
Chikengunia virus IgM	2
Leptospira IgM	5

The first case of death held on 06/03/2018 of Rahul Sahu aged 20 years of Rajakhedi, Makronia, Sagar. Last case of death till now was on 05/06/2018 of Suman Ahirwar aged 38 years of Village Jinda, Makronia, Sagar. The symptomatic live case was found in the family of a deceased (mother of the deceased) and was on treatment in Medical College Sagar, in stable condition. (Table 1)

All the cases of deaths held in a perimeter of 10 kms in the Makronia municipality area of Sagar. The cases were mostly dispersed in geographical area except for clustering of 3 cases in Shankargarh and 04 cases in Durganagar Rajakhedi (Table 2) Approx 55% of death cases were from Shankargarh and Durganagar locality. Among the identified death cases 63% were males and 55% were in the adult age group of 20-40 years. The youngest was 9 year male and the oldest was 56 year female (**Table 3).** Among the cases the 3 persons (aged <20 years) were school going students. The 03 females were housewives and 01 female was working in ICDS as Aganwadi sahayika. Rest of the five cases (05) was working in hardware shops/steel welding shops. None of them was a hospital employee, or working in the jobs with higher risk of getting hepatitis B infection. None of the cases were injecting drug users as per history. There was also no history of getting injected with reused syringes. 10 out of 11 cases seek medical care from registered medical practitioner (MBBS/BAMS) and only 01 case (village-Jinda) has history of medical care from quacks. No history of Blood transfusion and surgeries in the last 6 months. All of the deaths have occurred within 7 days of illness in which 72.72% in within 3 days of illness whereas 27.27% were from 3-7 days of illness (Mean duration of illness was 3.54 days, std dev. 2.2 days)**.** (Table 4) All the cases have few common symptoms like jaundice and abdominal pain and vomiting (Table 5). All the deceased cases had been treated at tertiary care hospitals; they have undergone various pathological tests. The test reports revealed Hepatitis b surface antigen (HBsAg) test +ve in 100% of cases ,SGPT raised in 90.90 % cases, SGOT raised in 81.82 cases. 9.09% cases were malaria positive, 18.18% cases were WIDAL positive and in 90.90% cases serum bilrubin was raised. (Table 6)

The camps organised with the help of health department areas where deceased cases were reported from mid May to mid June 2018. A total of 2395 individuals were examined. Of this 141 persons were screened for HBsAg and only one was found positive. 163 individuals were examined for malaria and none was found malaria positive.

Due to unavailability of lab infrastructure for isolation of HAV/HEV and serological investigations,

ICMR NIRTH Jabalpur was requested to carry out investigation for confirmatory findings.

Further investigation was done by a joint team with members from ICMR NIRTH Jabalpur, IDSP and members from Community Medicine department of BMC Sagar. This joint team collected 53 samples of blood from close family contacts of the deceased (death cases) and individuals suffering from fever and jaundice like illnesses. The results of the sample testing revealed 13 positive samples for different serological tests. Among all the serological test positivity the highest (05 cases positive and 03 equivocal) were for Leptospira IgM. (Table 7)

DISCUSSION

The HBsAg positivity was one of the major findings of outbreak investigation. Though the team suspected hepatitis A/ hepatitis E infection initially as in India, most of the outbreaks of viral hepatitis are due to faeco-orally transmitted hepatitis. But hepatitis B surface antigen positive results in all the cases (death cases) was a crucial unexpected finding .[15-17] A similar unusual clustering of cases of viral hepatitis B was recently observed in rural areas of Mehasana district, Gujarat State, India. As in the present study there was no history of hospital admission, blood transfusion, intravenous injections, tattooing, or dental treatment in last 6 months. But there was significant history of unsafe injections by local practitioners which in not found in this study.[18] Another outbreak of Hepatitis B was also reported from Gujrat`s Modasa town of Sabarkantha district in 1995.[19] The cause of Hepatitis B positivity remain unidentified in this study due to lack of sexual history / personal habits (75% cases were adults), also the ICMR Nirth Lab findings found only 01 positive case among 53 samples from contacts, family members and suspects. Also the HbsAg is only a screening test for Heptitis B and may have HBV-DNA negativity rates more than 50%.[20]

The case fatality rate of 91.67 was very high compared to 46.7% in Mehsana outbreak .[17] So Co-infection with hepatitis B and D viruses (IgM-HBc positive) as well as super infections (IgMHBc negative) have been reported to cause both Viral hepatitis B outbreak in India fulminent hepatitis and high mortality rates, but ICMT NIRTH findings were negative for Hepatitis C and D viruses.[21-22] The leptospira IgM positivity in about 40% samples suggested the possible cause of high mortality rate, but this was a diagnostic challenge in limited laboratory support as in this study.[23]

CONCLUSION

The above observation and result support that all the deaths were due to acute hepatic injury leading to hepatic encephalopathy and its sequels. It is also evident that all the cases were HBsAg positive hence hepatitis B role in hepatic injury is almost certain. But such a high fatality in acute period of a week or less is not documented in hepatitis B infection. So there might be co infection with other infectious agents (most probable hepatitis A, D or E) which resulted in acute hepatic failure and death. We were not able to confirm the exact cause of deaths in these HBsAg positive cases, so the report with suitable recommendations was submitted to health department along with need for further investigation.

To come out with definite result a joint team with members from ICMR NIRTH, IDSP and members from Community Medicine department carried out investigation again and came with findings (Table 7) and Leptospira co-infection/super-infection found to be responsible for such a high fatality in cases with acute Hepatitis.

Recommendations:

As per the results of primary investigation by community medicine department of BMC Sagar, healths camps were organised for screening HBsAg positive cases in the community and surveillance for finding cases with acute jaundice. Hepatitis B vaccination was also started in these camps and 1505 individuals were vaccinated with hepatitis B vaccine. All the preventive steps like IEC on safe injection practices and safe drinking water were recommended to healh department.

The major recommendation is for investigators/ epidemiologists. Epidemiologists investigating the hepatitis B outbreaks with sudden and increased mortality in short duration of illnesses should investigate all the aetiologies like hepatitis A, C and E and never miss the leptospira investigation. Though Leptospirosis co-infection & superinfection with hepatitis B is not documented much in the text, but a high index of suspicion should be maintained in patient presenting with acute hepatitis, especially in individuals with HBsAg positive. Early diagnosis and application of preventive measures to control leptospira is imperative to stop the casualties by this potentially dangerous disease.

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