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A severe and explosive outbreak of hepatitis B in a rural population in Sirsa district, Haryana, India: unnecessary therapeutic injections were a major risk factor

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SUMMARY

Most outbreaks of viral hepatitis in India are caused by hepatitis E. This report describes an outbreak of hepatitis B in a rural population in Haryana state in 1997. At least 54 cases of jaundice occurred in Dhottar village (population 3096) during a period of 8 months; 18 (33·3%) of them died. Virtually all fatal cases were adults and tested positive for HBsAg (other markers not done). About 88% (21/24) of surviving cases had acute or persistent HBV/HCV infections; 54% (13/24) had acute hepatitis B. Many other villages reported sporadic cases and deaths. Data were pooled from these villages for analysis of risk factors. Acute hepatitis B cases had received injections before illness more frequently (11/19) than those found negative for acute or persistent HBV/HCV infections (3/17) ($P = 0{\cdot}01$). Although a few cases had other risk factors, these were equally prevalent in two groups. The results linked the outbreak to the use of unnecessary therapeutic injections.

INTRODUCTION

Epidemics of parenterally transmitted viral hepatitis are not easily recognized in India [1]. Faeco-orally transmitted hepatitis E virus (HEV) has been considered responsible for virtually all the outbreaks of viral hepatitis reported in the country [2–4]. However, recently, we investigated an outbreak of hepatitis B in a rural community in Gujarat state which occurred due to the use of unsafe injections [1]. After a few weeks, we came across another unusual clustering of viral hepatitis cases in Haryana state where most cases were found positive for hepatitis B surface antigen and many for hepatitis C markers. We describe this episode in this paper.

Health authorities in Sirsa district, Haryana, discovered in February 1997 that cases of jaundice had been occurring in Dhottar village (under Rania Administrative Block) since December 1996 and some of them had died. All the health institutions in the district were asked to search actively for jaundice cases and report them to the health authorities. By the second week of April 1997, 8 cases were reported to have died in Dhottar village (population: 3096) and one each in 5 other villages. Since all the fatal cases were HBsAg positive and were reported to have been administered injections by the local medical practitioners before they developed jaundice, the outbreak was investigated systematically.

METHODS

Epidemiological investigations

We began investigations in the second week of April 1997. Five villages in the Rania block which contributed most of the cases and deaths and 3 villages in other blocks which had also reported fatal cases by that time were visited. Some distantly located villages

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in the district which had reported only single/sporadic cases were not investigated.

Age, sex, education, occupation, place of work, date of onset of illness, signs and symptoms, and results of laboratory investigations were obtained for all the cases of jaundice. They (and/or their family members) were also interviewed for the presence of any risk factors of viral hepatitis within 6 months but 15 days prior to the onset of illness. The following risk factors of hepatitis B were considered: injections, blood transfusion, dental treatment, surgical operation, hospital admission due to any cause, drug addiction, tattooing, extramarital sexual contact and contact with a case of jaundice within or outside family. The interviewers were not aware of the HBsAg status of the cases at the time of interview.

A house to house survey was carried out in Dhottar village, the main focus of outbreak, in the second week of April 1997. Health workers went from house to house to inquire about any episode of jaundice since *Diwali* (festival of lights: 10 November 1996). The cases of jaundice detected during the survey were examined/interviewed by senior physicians for epidemiological information and risk factors of viral hepatitis. Similar surveys were not undertaken in other villages. Instead, community leaders, health workers and local private practitioners were contacted to get information on cases that had jaundice in the last 5 months. Cases and deaths due to jaundice continued to occur up to July 1997.

Laboratory investigations

The investigators collected 44 blood samples in the affected villages during the study (in the second week of April 1997). Of these, 38 were from cases (having jaundice currently or in the recent past) and 6 were from apparently healthy persons. Serum samples were separated in the laboratories of the Government Civil Hospital, Sirsa and then transported to the laboratories of the National Institute of Communicable Diseases (NICD), Delhi for testing for viral hepatitis markers by enzyme-linked immunosorbent assay (ELISA) (bead ELISA) (Abbott Laboratories, North Chicago, IL, USA). These serum samples from cases were tested for anti-HAV IgM, anti-HBc IgM, HBsAg, anti-HCV, and anti-HEV. All samples found positive for HBsAg were also tested for anti-HDV. Viral hepatitis A, and B were confirmed by the presence of anti-HAV IgM and anti-HBc IgM respectively. Cases who were positive for anti-HCV were considered to be suffering from acute or chronic HCV. Cases positive for HBsAg and anti-HDV but negative for anti-HBc IgM were taken as cases of viral hepatitis D.

RESULTS

A total of 25 cases were reported to have died due to jaundice in Sirsa district between the middle of December 1996 and the middle of July 1997; most of them (19/25) died during February–May 1997. Virtually all of them (24/25) were adults and two-thirds (16/25) were males. Table 1 describes the epidemiological characteristics of 13 cases of jaundice who had died by the second week of April 1997. All of them were found to be positive for HBsAg in the government or private laboratories, but were not tested for other markers of viral hepatitis; samples were not available for subsequent analysis. Most of them died within a week of onset of illness due to fulminant hepatitis. Such data are not available for 12 other deaths which occurred later on.

Eighteen of 25 (72%) deaths due to jaundice occurred in one village (Dhottar: population 3096) which indicated that it was the focus of outbreak. The mortality rate of jaundice in the village was found to be 5·81 per 1000 population. Other villages reported only sporadic deaths due to jaundice.

A house to house survey carried out by the paramedical workers in Dhottar village in the second week of April 1997 revealed that 48 cases of jaundice (including 8 deaths) had occurred since *Diwali* (total population surveyed 3007). This gave an attack rate of 16 per 1000 population. The age- and sex-specific attack rates of jaundice calculated from these data are shown in Table 2. The attack rates were significantly higher in adults ($\geqslant$ 15 years) than in children ($P = 0{\cdot}0000008$); and significantly higher in males than in females ($P = 0{\cdot}049$). No child below 11 years of age was reported having jaundice in this village.

Published reports of the Haryana state later revealed that cases and deaths continued to occur up to July 1997. A total of 85 cases of jaundice (including 25 deaths) occurred in 30 villages of Sirsa district. Out of them, 54 cases (including 18 deaths; case fatality rate 33·3%) occurred in Dhottar village giving an attack rate of 17·4 per 1000 population.

Blood samples from 38 cases of jaundice and 6 apparently healthy persons were tested for markers of

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Table 1. *Deaths due to hepatitis B in Sirsa district between December 1996 and 11 April 1997*

Age	Sex	Village	Date of onset of symptoms	Date of death	Serum bilirubin levels (mg %)
21*	M	Dhottar	13.12.1996	18.12.1996	NA‡
35	M	Dhottar	16.12.1996	19.12.1996	NA
25	F	Dhottar	27.12.1996	03.01.1997	NA
58*	M	Dhottar	15.02.1997	19.02.1997	5·6
30†	M	Dhottar	18.02.1997	20.02.1997	12·3
35	M	Dhottar	15.02.1997	25.02.1997	29·0
19	M	Dhottar	20.02.1997	25.02.1997	9·1
40†	M	Dhottar	04.04.1997	09.04.1997	19·5
25	M	Rania	03.02.1997	07.02.1997	6·4
46	M	Beharwala	07.02.1997	14.02.1997	9·0
22	F	Gidranwali	22.02.1997	27.02.1997	7·5
60	F	Natar	22.01.1997	17.03.1997	34·8
40	M	Sultanpuria	15.12.1996	31.12.1996	19·7

* Uncle and nephew; † Brothers.
‡ NA = Data not available.
Note: All cases were positive for HBsAg; the samples were not tested for other markers of viral hepatitis.

Table 2. *Age- and sex-specific attack rates of jaundice in Dhottar village* (*November 1996–11 April 1997*)

Age group (years)	Male Number surveyed	Number with jaundice	Attack rate per 1000	Female Number surveyed	Number with jaundice	Attack rate per 1000	Total Number surveyed	Number with jaundice	Attack rate per 1000
0–4	199	0	0	168	0	0	358	0	0
5–9	186	0	0	188	0	0	374	0	0
10–14	237	1	4·2	190	1	5·3	427	2	4·7
15–44	727	26	35·8*	669	12	17·9*	1396	38	27·2
45+	241	5	20·7	211	3	14·2	452	8	17·7
Total	1581	32	20·2†	1426	16	11·2†	3007	48	16·0

* Difference is significant, $P = 0{\cdot}04$.
† Difference is significant, $P = 0{\cdot}049$.
Note: Overall attack rates are significantly higher in adults ($\geqslant$ 15 years) than in children ($P = 0{\cdot}0000008$).

viral hepatitis in the NICD laboratories. The results are shown in Table 3. Overall 50 % (19/38) cases had acute hepatitis B infection (positive for anti-HBc IgM: group 1), 57·9 % (22/38) had acute or chronic hepatitis B infection (positive for anti-HBc IgM and/or HBsAg: group 2), and 71·1 % (27/38) had acute or chronic hepatitis B and/or hepatitis C infections (positive for anti-HBc IgM, HBsAg or anti-HCV: group 3). The comparative figures in Dhottar village were 54·2 % (13/24), 66·7 % (16/24) and 87·5 % (21/24) respectively. Most of the cases found negative for all the markers of viral hepatitis had resolved their jaundice 2–3 months previously. All the six samples from non-cases were negative for markers of hepatitis A to E.

While collecting blood samples, cases (as well as non-cases) were interviewed to identify risk factors for viral hepatitis B within 6 months but 15 days prior to onset of jaundice. Once the laboratory results became available, cases having acute hepatitis B infection (group 1), acute or chronic hepatitis B infection (group 2) and acute or chronic hepatitis B/hepatitis C infection (group 3) were compared with those (cases as well as non-cases) who were negative for acute and chronic HBV/HCV infections (negative for anti-HBc IgM, HBsAg and anti-HCV: group 4). The results are shown in Table 4. History of therapeutic injections was significantly higher ($P \leqslant 0{\cdot}01$) in group 1 (11/19; 57·9 %) or group 2 (14/22; 63·6 %) or group 3 (15/27; 55·6 %) than in group 4 (3/17; 17·6 %). Other potential risk factors for hepatitis B were equally prevalent in all the four groups.

The local health authorities collected a large number of blood samples from the apparently healthy

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Table 3. *Seropositivity of viral hepatitis markers in cases of jaundice*

Village	Number of samples tested	Number (%) anti-HAV IgM positive	Number (%) anti-HBc IgM positive	Number (%) HBsAg positive	Number (%) anti-HCV positive	Number (%) anti-HEV positive	Number (%) negative for all these markers
Dhottar	24	0	13 (54)*†	3*‡	8*†‡	3*	3 (13)
Sultanpuria	5	0	3§	0	0	2§	1
Abuthgarh	2	0	2	0	0	0	0
Rania	3	1	1	0	0	1	0
Gidranwali	1	0	0	0	0	1	0
Beharwala	3	0	0	0	0	1	2
Total	38	1	19 (50)	3 (8)	8 (21)	8 (21)	6 (16)

* One positive for anti-HEV also.
† Two cases positive for anti-HBc IgM were also positive for anti-HCV.
‡ One HBsAg carrier was positive for anti-HCV.
§ One case positive for anti-HBc IgM was positive for anti-HEV.
Note: All cases positive for hepatitis B markers were negative for anti-HDV.
Six additional samples from non-cases (not having jaundice) were negative for anti-HAV IgM, anti-HBc IgM, HBsAg, Anti-HCV and anti-HEV.

Table 4. *Prevalence of potential risk factors of hepatitis B in different groups within 6 months but 15 days prior to onset of jaundice*

Risk factor	Acute hepatitis B infection (group 1) $n = 19$ (%)	Acute or chronic HBV infection (group 2) $n = 22$ (%)	Acute or chronic HBV/HCV infection (group 3) $n = 27$ (%)	Negative for acute or chronic HBV/HCV infection (group 4) $n = 17$ (%)
Hospital admission	2 (10·5)	3 (13·6)	3 (11·1)	1 (5·9)
Therapeutic injections	11 (57·9)*	14 (63·6)†	15 (55·6)‡	3 (17·6)§
Blood transfusion	0	0	0	1 (5·9)
Surgical operation	0	0	0	0
Dental work	3 (15·8)	3 (13·6)	3 (11·1)	0
Tattooing	0	0	0	0
Drug addiction	2 (10·5)	2 (9·1)	2 (7·4)	0
Extramarital sexual contact	2 (10·5)	2 (9·1)	2 (7·4)	0
Contact with a case of jaundice in family	1 (5·3)	2 (9·1)	2 (7·4)	0
Contact with a case of jaundice outside family	1 (5·3)	1 (4·5)	1 (3·7)	1 (5·9)
Any of risk factors	12 (63·2)¶	15 (68·2)††	16 (59·3)‡‡	4 (23·5)**

When compared with §: *OR = 6·42, $P = 0·01$; †OR = 8·17, $P = 0·004$; ‡OR = 5·83, $P = 0·01$.
When compared with **: ¶OR = 5·57, $P = 0·02$; ††OR = 6·96, $P = 0·006$; ‡‡OR = 4·73, $P = 0·02$.

persons in the affected villages and tested them for HBsAg by latex agglutination. The results of 1001 samples were available for analysis. As shown in Table 5, 2·1% (21/1001) were HBsAg positive. Virtually all HBsAg positive persons were in 15–44 years age group. Interestingly, only 0·6% (96/16004) of the blood donors tested in the Government Civil Hospital, Sirsa during 1993–7 were HBsAg positive;

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Table 5. *Prevalence of HBsAg in apparently healthy persons in the affected villages*

Age group (years)	Number tested*	Number positive	% positive
0–4	14	0	0
5–14	41	0	0
15–44	774	20	2·6
45+	172	1	0·6
Total	1001	21	2·1

* Tested by latex agglutination.

the rates were not different in different years. It is worth mentioning that only highly educated and motivated male persons donate blood in Sirsa district.

Only 54 and 35 cases of viral hepatitis were reported from the Sirsa district in 1995 and 1996 respectively. The data for the previous years were not available with the district health authorities.

DISCUSSION

At least 54 cases of jaundice occurred in Dhottar village during an 8 month period; 18 (33·3%) of them died. This gave a 17·4 per 1000 population attack rate of jaundice and a mortality rate of 5·81 per 1000 population. All the fatal cases were HBsAg positive (not tested for other markers). While 88% (21/24) of surviving cases had acute or persistent HBV/HCV infections, 54% (13/24) had acute hepatitis B (Tables 1, 3). These results clearly showed that Dhottar village had an explosive outbreak of hepatitis B in 1997. Many other villages reported only sporadic cases and deaths which perhaps reflects the endemicity of disease in the study area.

For analysis of risk factors, data were pooled from Dhottar as well as other villages which reported deaths due to viral hepatitis B. Table 4 compares the prevalence of potential risk factors of viral hepatitis B in cases having acute hepatitis B infection (group 1) to those found negative for acute or persistent hepatitis B/hepatitis C infections (group 4). Acute hepatitis B cases had received injections more frequently (11/19; 57·9%) than those found negative for acute or persistent HBV/HCV infections (3/17; 17·6%) before the onset of jaundice. The difference between the two groups was significant (odds ratio = 6·42, $P = 0{\cdot}01$). The results remained significant in spite of a small number of subjects in both the groups. Although a few cases had other risk factors of hepatitis B, these were equally prevalent in two groups. These results indicate that injections probably played a major role in the transmission of hepatitis B during the outbreak.

In addition to the high prevalence of hepatitis B infection in Dhottar village, 33% (8/24) of cases were also positive for anti-HCV which is high. Studies indicate that the risk of sexual, intrafamilial and perinatal transmission of HCV is low [5]. Since none of our patients ever had blood transfusion or surgical operations, most of the HCV transmission was perhaps through unsafe injections. In fact, it has been recently hypothesized that unsafe injections may be a major source of hepatitis C transmission in the developing world where blood transfusions are not widely available [6]. These observations also suggest that inadequately sterilized needles and syringes were the major factors in the transmission of hepatitis B in this outbreak.

Most of the affected villages including Dhottar had only unqualified medical practitioners who were consulted for treatment of common ailments. Although we could not interview the medical practitioners in Dhottar village because of their non-availability, we had the opportunity to examine the sterilization practices of unqualified practitioners in three other villages where cases had died due to hepatitis B. These medical practitioners did not have any recognized medical qualification which allows them to prescribe and administer medicines and injections. All of them were found using disposable single use needles and syringes many times. None was aware that blood-borne pathogens can be transmitted by these practices. Arrangement for sterilization were inadequate in their clinics. They administered injections to the majority of patients for all types of ailments because they were paid more money for giving injections than for giving oral medicines. They said that many patients also demanded injections, which were never denied. Such settings are not uncommon in the country, especially in the rural areas [7]. Since the risk of blood-borne infections from a contaminated needle is very high, 20–40% for hepatitis B, 6% for hepatitis C, and 0·3% for HIV [6], we feel that unnecessary and unsafe injections may be responsible for a substantial proportion of HBV and HCV transmission in India. In fact, epidemiological studies have already provided some evidence for such an occurrence [1, 8, 9]. Although more data would be necessary to determine the exact contribution of unnecessary and unsafe injections in the spread of blood-borne infection in India, there is an urgent need

to initiate efforts to make the injections safe and only given when medically indicated.

Occurrence of virtually all clinical cases and deaths in adults confirms that the severity of hepatitis B increases with the increase in age [5]. However, why so many people died during this outbreak is not entirely clear. HDV co-infection was blamed for the high fatality rates in the Gujarat outbreak [1], but evidence of HDV infection was absent in the present outbreak. In contrast, a high proportion of surviving cases had laboratory evidence of HCV (8/38) or HEV (8/38) infections (Table 3). Although fulminant hepatitis is not common in acute primary HCV or HEV infection, simultaneous infections with HBV and HCV, or HBV and HEV might have been responsible for increased risk of fulminant hepatitis and death in the present outbreak. In addition, drinking alcohol was common in the affected areas, although not many cases admitted it for themselves because the Haryana state was dry (prohibition was legally implemented) at the time of outbreak. Alcoholism may magnify the effect of HBV or HCV on liver disease [10–13].

It is worth noting that the outbreak was first reported in the newspapers. But for the high mortality rates, the outbreak would have never been recognized. Although community studies indicate that viral hepatitis has been a major public health problem in India [14, 15], only a small number of cases (less than 50 in a year) were reported in the district (population: more than one million) through the routine surveillance system. This also indicated the poor efficiency of the surveillance system. Ineffective surveillance probably explains the absence of many reports of community outbreaks of hepatitis B in the Indian literature despite widespread use of unsafe injections in the country, especially in the rural areas, by the unqualified medical practitioners.

Overall, 2·1% (21/1001) of the population in Dhottar and other affected villages were found to be HBsAg positive. This is an underestimate because samples were tested by the local health authorities by latex agglutination technique which has a low sensitivity. Nevertheless, the data indicated that HBV was circulating in the community and that the HBsAg positivity rate in the affected area was not much different from the national rate which has been estimated to be around 3–5% [16]. Although none of the children below 15 years of age was found positive for HBsAg, there were too few examined to draw any useful inference.

Finally, 21% of blood samples were also found positive for anti-HEV. Since these samples were not tested for anti-HEV IgM, it is difficult to say when they had acquired hepatitis E infection. Nevertheless, there was a high potential for transmission of faeco-orally transmitted agents in Dhottar village and other villages. Most of the population used open fields for defecation, a large number of residents used raw canal water for drinking purpose while working in the field and there were many leaks in the piped water line in Dhottar village which were detected and repaired after the occurrence of outbreak. Almost one-third of water samples from different sources were found unfit for human consumption by the state health authorities. It was therefore, not surprising that many cases were positive for markers of the faeco-orally transmitted viral hepatitis E.

In conclusion, unnecessary and unsafe injections seem to be responsible for this outbreak of viral hepatitis which was marked by high prevalence of HBV and HCV infection. The study emphasized the need to educate medical practitioners, especially working in rural areas, as well as the general community for taking all preventive measures to avoid unnecessary and unsafe injections.

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