

# Epidemiology of endemic viral hepatitis in an urban area of India: a retrospective community study in Alwar\*

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*In a community study during a reference period of 1 year, 192 cases of jaundice were detected in an urban population of 69440 in Alwar, Rajasthan. Detected by paramedics and confirmed by physicians, these cases gave an annual incidence of 2.76 (95% CI: 2.37–3.15) per 1000 population. At least one of these patients died, giving a case fatality ratio of 0.6%.*

*The jaundice cases occurred in all areas investigated, and affected all socioeconomic strata. About 94% of the affected families had only single cases. Although cases occurred throughout the year, more than 59% occurred during June–September, which are the summer and monsoon months. The incidence was highest (5.23 per 1000) among under-5-year-olds and declined progressively and significantly thereafter. Males had a higher incidence than females at all ages; the differences were not significant.*

*Blood samples from 56 cases who had jaundice in the last 3 months of the reference period were tested for markers of viral hepatitis. Of these, 18 (32.1%), 1 (1.8%), 0, 2 (3.6%), and 4 (7.1%) were found to have hepatitis A, B, C, D and E, respectively. The etiology of the remaining 31 cases (55%) could not be established; previously, they would have been included in the NANB (non-A, non-B) category, inflating its proportion. Hepatitis A (HA) was the predominant type; being comparatively mild, it is perhaps under-represented in hospital-based data. Many HA cases were in adults, which may be the beginning of an age shift of HA to the right owing to improvements in living standards of the study population. Five cases were carriers of hepatitis B virus (HBV), indicating the importance of HBV infection in India as well. Finally, the study found the annual incidence of laboratory-supported cases of viral hepatitis to be 1.24 (95% CI: 0.98–1.5) per 1000 population, which suggests that it is a major public health problem in India.*

## Introduction

Viral hepatitis is an important public health problem in India. Many workers have studied its etiology and established that most of the epidemic cases and more than half of the acute, sporadic cases were due to non-A, non-B (NANB) hepatitis viruses (1–4). Their conclusions, however, regarding sporadic cases were drawn from highly selective institutional data, and their diagnosis of NANB viral hepatitis was estab-

lished by excluding hepatitis A (HA) and hepatitis B (HB). Epidemiological and clinical studies further indicated that, unlike the situation in Western countries, in India NANB was predominantly enterically transmitted (1, 3) and, therefore, the majority of NANB cases were considered to be caused by hepatitis E virus (HEV). Commercial kits have now been made available for antibodies against HCV (hepatitis C virus) and HEV, which can make the diagnosis of NANB hepatitis more precise.

Against this background, we carried out a study in September 1994 in the urban population of Alwar in Rajasthan to understand the epidemiology of endemic viral hepatitis in this community. There was no report of any outbreak of viral hepatitis or acute diarrhoeal disease in this area. We are not aware of any other study of a similar nature on viral hepatitis in India.

## Materials and methods

Alwar, a district headquarter in Rajasthan State in north India, has a population of 205086 (1991

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census) which is distributed in 40 wards. Fourteen of these wards were randomly selected and the whole population was surveyed through house-to-house visits in September 1994 by trained paramedics who inquired about any case of jaundice that had occurred in the previous year. These cases were further examined by a medical epidemiologist (RSG) for epidemiological and clinical data. Blood samples were drawn from all cases who had had jaundice in the previous 3 months; the serum was separated in the local laboratories of the National Institute of Communicable Diseases (NICD), and then transported in a cold chain to the main laboratories of NICD in Delhi. The sera were stored at  $-20^{\circ}\text{C}$  till tested for immunological markers of viral hepatitis.

The sera were tested by macro enzyme-linked immunosorbent assay (ELISA) (bead ELISA), using kits (Abbott Laboratories, Abbott Park, IL, USA) for IgM anti-HAV, IgM anti-HBc, HBsAg, anti-HCV, anti-HDV, and anti-HEV. The samples were also tested for IgM anti-HEV using ELISA kits (Genelabs Diagnostics, Singapore). HA, HB and hepatitis E (HE) were confirmed by the presence of IgM anti-HAV, IgM anti-HBc and IgM anti-HEV, respectively. HBsAg carriers who were found to be positive for anti-HDV were taken as cases of viral hepatitis D (HD). Cases of jaundice who were nega-

tive for IgM anti-HAV, IgM anti-HBc, HBsAg and IgM anti-HEV but were positive for anti-HCV were considered to be suffering from viral hepatitis C (HC).

## Results

A total of 192 cases of jaundice were detected during the reference period (1 year) in the 69440 population. The annual incidence of jaundice was therefore 2.76 (95% CI: 2.37–3.15) per 1000 population. As shown in Table 1, the cases were almost uniformly distributed in all the 14 wards surveyed during the study. Only six affected families had two cases each — the rest had only single cases. Although cases occurred throughout the year, more than 59% occurred during June–September, which are the summer and monsoon months in this part of the country (Fig. 1).

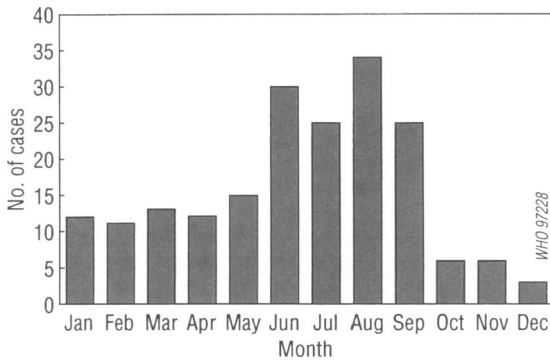
The age- and sex-specific incidences of jaundice cases are shown in Table 2. The incidence was highest (5.23 per 1000) among under-5-year-olds. Thereafter, it declined progressively and significantly with increase in age; the incidence in adults was 2.21 per 1000 persons. Although males had higher rates than females at all ages, the differences were not significant.

Table 1: Distribution of jaundice/viral hepatitis A (HA) cases in 14 wards of Alwar in September 1994

Ward number	No. surveyed	No. of jaundice cases	Incidence/1000 population	No. of samples tested in laboratory	No. of HA cases
1	3 434	9	2.62	6	2
10	4 531	12	2.65	3	2
19	9 145	23	2.52	7	3
20	6 282	24	3.82	4	—
21	1 933	3	1.55	1	—
26	5 605	7	1.25 <sup>a</sup>	3	1
28	5 112	22	4.30	7	4
29	4 894	9	1.84	2	—
30	4 433	2	0.45 <sup>a</sup>	0	—
31	9 167	46	5.02 <sup>a</sup>	13	4
34	5 545	15	2.71	5	—
36	1 517	2	1.32	0	—
37	4 529	12	2.65	4	1
38	3 313	6	1.81	1	1
Total	69 440	192	2.76	56	18

<sup>a</sup> The incidences of jaundice in ward 26 and 30 were significantly less, and in ward 31 significantly more than the overall incidence of 2.76 per 1000 population.

Fig. 1. Seasonality of jaundice cases in a retrospective community study in Alwar town, from September 1994.



The education level and occupation of patients and the parents of under-15-year-olds with jaundice are given in Table 3 and Table 4, respectively. Cases came from all socioeconomic strata. About 82%

Table 2: Age and sex distribution of jaundice cases in Alwar

Age group (years)	No. of cases		Total
	Males	Females	
0-4	23 (541) <sup>a</sup>	18 (502)	41 (523) <sup>b</sup>
5-14	31 (320)	24 (281)	55 (302)
≥15	52 (222)	44 (220)	96 (221) <sup>b</sup>
All ages	106 (284)	86 (268)	192 (276)

<sup>a</sup> Figures in parentheses show the incidence per 100 000 persons.

<sup>b</sup> The difference in rates between these age groups is statistically significant.

Table 3: Education level of patients and mothers of under-15-year-olds who had jaundice

Education level	No. of cases	No. of mothers of under-15-year-olds
Pre-school	55 (28.6) <sup>a</sup>	—
Illiterate or just literate	25 (13.0)	27 (28.1)
Formal schooling	92 (47.9)	52 (54.2)
Graduate	20 (10.4)	17 (17.7)
All	192 (100.0)	96 (100.0)

<sup>a</sup> Figures in parentheses are percentages.

Table 4: Occupations of patients and fathers of under-15-year-olds who had jaundice

Occupation	No. of cases	No. of fathers of under-15-year-olds
Dependent	120 (62.5) <sup>a</sup>	0 (0)
Housewife	25 (13.0)	—
Landowner	0 (0)	2 (2.1)
Business	16 (8.3)	44 (45.8)
Regularly employed	24 (12.5)	42 (43.8)
Retired	3 (1.6)	1 (1.0)
Labourer	4 (2.1)	7 (7.3)
All	192 (100.0)	96 (100.0)

<sup>a</sup> Figures in parentheses are percentages.

of them had access to a sanitary latrine, and 79% and 17%, respectively, used soap and earth to wash their hands after defecation. More than 83% used tap water for drinking purposes. About 92% of the affected families stored drinking-water in wide-mouthed containers; 44% of cases were in the habit of drawing water from them by other than using a tap or ladle. The education status, occupations and hygienic practices were similar among the laboratory-confirmed viral hepatitis cases and the other cases of jaundice.

Among the 192 cases of jaundice, 26 (14%) had one or more risk factors for parenterally transmitted viral hepatitis within 6 months of the onset of jaundice. All 26 cases had received multiple injections and some had been admitted to hospital ( $n = 8$ ) or been operated on ( $n = 4$ ). One of the 6 cases with confirmed HBV infection (acute or chronic) had all these risk factors. None of the jaundice cases provided any history of blood donation or transfusion, tattooing, or dental treatment. We did not inquire into extramarital sexual contacts.

Blood samples were collected from 56 cases whose jaundice had appeared in the previous 3 months (IgM antibodies persist for 3 months), and were tested for markers of viral hepatitis (Table 5). Of these cases, 18 (32.1%), 1 (1.8%), 0, 2 (3.6%), and 4 (7.1%) respectively, had HA, HB, HC, HD and HE. The etiology of the remaining 31 cases (55%) could not be established. Five patients were carriers of HBsAg, which include two cases of HD. The age distribution of these 56 cases is shown in Table 6; many adult patients had HA.

We revisited 181 of these patients in January 1995. Of them, 1 had died, while 3 still had jaundice.

Table 5: Incidence of jaundice/viral hepatitis in urban Alwar, September 1994

Population surveyed	No. of jaundice cases in last 1 year	Incidence of jaundice per 1000 population	No. of jaundice cases in last 3 months (n)	No. of viral hepatitis cases					Incidence of viral hepatitis per 1000 population	
				A	B	C	D	E		Others
69 440	192	2.76	56	18 <sup>a</sup> (32.1) <sup>b</sup>	1 (1.8)	0 (0)	2 (3.6)	4 (7.1)	31 <sup>c</sup> (55.4)	1.24

<sup>a</sup> Includes two patients who were HBsAg carriers.

<sup>b</sup> Figures in parentheses indicate percentages with *n* as denominator.

<sup>c</sup> Includes one patient who was an HBsAg carrier and 6 patients who were anti-HEV positive.

Table 6: Distribution of 56 cases who were tested for viral hepatitis markers, by age group

Age group (years)	No. surveyed	HA cases	HB cases	HD cases	HE cases	Negative	Total
0-4	7 839	2	0	0	1	11	14
5-14	18 221	4 <sup>a</sup>	1	2	2	3	12
≥15	43 380	12 <sup>a</sup>	0	0	1	17 <sup>a</sup>	30
Total	69 440	18	1	2	4	31	56

<sup>a</sup> Includes one patient who was a carrier of HBsAg.

## Discussion

Our results seem to be at variance with the published literature that HB and NANB, respectively, account for about one-third and over half of the acute sporadic cases of viral hepatitis in India (1-3). Similar findings have previously been reported from Alwar, where 16% and 57% of acute sporadic viral hepatitis cases had been diagnosed as HA and NANB, respectively (4). These conclusions were drawn from cases treated in health institutions (1-4). In contrast, the present study used the community approach and found that enterically transmitted HA and HE together were responsible for 88% of the laboratory-diagnosed endemic viral hepatitis cases. HA alone accounted for 72% of the diagnosed cases; as it is mild compared with other infections, it is under-represented in hospital-based data.

There is another factor which has inflated the proportion of hepatitis E (NANB) in India. Since the immunological markers of viral hepatitis C, E, and the recently discovered viral hepatitis F and G (5) are not easily available and affordable, the diagnosis of NANB is made by exclusion of HA and HB. Had we used this criterion to diagnose NANB viral hepatitis, a large number of our undiagnosed cases of jaundice would have been included in the NANB category, increasing its proportion. Although some of these undiagnosed cases could be due to causes other than viral hepatitis, for example, drug toxicity,

others may have been due to the recently discovered agents (F, G) of viral hepatitis. One could argue that some of these cases may not have been cases of jaundice because only 19 patients had jaundice during the survey; the rest were identified on the basis of a positive history of jaundice. The laboratory results for these 19 cases, however, do not support these arguments; 6 of them were confirmed as HA, 2 as HE, and the remaining 11 were negative for all the acute markers, despite having raised serum bilirubin levels. Furthermore, the majority of the cases who cleared their jaundice before our survey had been examined by their physicians and treated as viral hepatitis (see below). The results suggest that in India many illnesses that are compatible with viral hepatitis occur, caused by agents which cannot be identified by currently available laboratory tests.

Viral HB is a serious health problem due to the sequelae associated with chronic persistent infection, which include chronic active hepatitis, cirrhosis, and liver carcinoma. Although the present study was not designed to study the HBV chronic carrier rate in the community, the presence of 5 chronic carriers among 56 cases of jaundice (including 2 HD cases) indicates the importance of HBV infection in the study area. None of our samples tested positive for anti-HCV, but it is difficult to comment upon HCV prevalence because of the limitations of our data. The results, however, suggest that in the study area HCV is far less prevalent than HBV.

Table 7: Cases of viral hepatitis treated in the General Hospital, Alwar, 1989–94, with case fatality rates (CFR)

Year	No. treated as outpatients	No. admitted to hospital	No. who died in hospital	Overall CFR (%)
1989	44	25	3	6.8
1990	107	45	12	11.2
1991	55	35	5	9.1
1992	85	59	13	15.3
1993	80	58	17	21.3
1994	105	75	23	21.9
Total	476	297	73	15.3

Overall, 25 out of 56 (44.6%) jaundice cases were confirmed as viral hepatitis by the laboratory. Assuming the same proportion of viral hepatitis in all the jaundice cases, we estimate the annual incidence of viral hepatitis in the study area to be 1.24 (95% CI: 0.98–1.5) per 1000 population.

The laboratory results (Table 5) and the occurrence of the majority of jaundice cases in the summer and monsoon months (Fig. 1) indicate a predominantly faeco-oral transmission of viral hepatitis in Alwar town. Owing to poor hygiene and environmental sanitation, a large number of persons are exposed to faeco-orally transmitted viruses early in life (6). The age-specific incidences of jaundice (higher in children than adults), shown in Table 2, are consistent with such a situation. Nevertheless, the occurrence of many HA cases in adults may be the beginning of an age shift of HA towards the right because of improvements in the living standard of the study population, as is happening in Thailand (7). It may be mentioned that there was no evidence of an HA epidemic in Alwar in 1994; the laboratory-confirmed HA cases were widely scattered in the study area without any epidemiological linkages (Table 1).

Widespread distribution of jaundice cases in the study area (Table 1), the occurrence of disease in all socioeconomic strata (Table 3 and 4), and the data on viral hepatitis from the General Hospital (Table 7) suggest that viral hepatitis is endemic in Alwar. On an average, 80 cases of viral hepatitis were treated annually in the General Hospital, Alwar, during 1989–94 with a case fatality ratio of about 15% (CFR was 25% for the hospital-admitted cases). Conversely, the CFR was less than 1% in our community survey; clearly, only serious and complicated cases are admitted to hospital. Nevertheless, 78% (149/192) of the jaundice cases found in the community survey during 1994 had received treatment from qualified allopathic doctors, mostly private physicians.

Finally, a similar exercise in an urban population of a tribal district in Madhya Pradesh State confirms most of the findings of the present study (J. Singh et al., unpublished data, 1994). Studies carried out in a limited geographical area cannot be representative of the entire country. There is therefore a need for more community studies to generate data on viral hepatitis, which are essential for an understanding of the natural history of the disease.

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### Résumé

#### Epidémiologie de l'hépatite virale endémique dans une zone urbaine en Inde: étude rétrospective en communauté à Alwar

Lors d'une étude en communauté portant sur une période de référence d'un an, 192 cas d'ictère ont été observés dans une population urbaine de 69 440 habitants à Alwar, au Rajasthan. L'incidence annuelle de ces cas, dépistés par le personnel paramédical et confirmés par un médecin, était de 2,76 pour 1000 habitants (IC 95% : 2,37–3,15). Un au moins des malades est décédé, ce qui donne un taux de létalité de 0,6%.

Les cas d'ictère ont été trouvés dans tous les secteurs étudiés et dans toutes les couches socio-économiques. Environ 94% des familles touchées ne comptaient qu'un seul cas. Bien que des cas aient été observés toute l'année, plus de 59%

d'entre eux sont survenus pendant les mois de juin à septembre, qui sont les mois d'été et de la mousson dans cette partie du pays. L'incidence était maximale (5,23 pour 1000) chez les enfants de moins de cinq ans puis diminuait sensiblement, de façon progressive. Quel que soit l'âge, l'incidence était plus forte dans le sexe masculin, mais cette différence n'était pas significative.

Des prélèvements sanguins réalisés au cours des 3 derniers mois de la période de référence chez 56 patients atteints d'ictère ont été soumis à une recherche des marqueurs de l'hépatite virale. On a trouvé 18 cas (32,1%) d'hépatite A, 1 cas (1,8%) d'hépatite B, 2 cas (3,6%) d'hépatite D, et 4 cas (7,1%) d'hépatite E. Aucun cas d'hépatite C n'a été trouvé. L'étiologie des 31 cas restants (55%) n'a pu être établie; dans le passé, ils auraient été classés comme non A-non B, ce qui aurait augmenté la proportion de cas entrant dans cette catégorie. Le type prédominant était l'hépatite A; relativement bénigne, elle est peut-être sous-représentée dans les données hospitalières. De nombreux cas d'hépatite A concernaient des adultes, ce qui pourrait être le début d'un glissement vers la partie droite de la distribution par âges, dû à l'amélioration des conditions de vie dans la population étudiée. Cinq cas étaient porteurs du virus de l'hépatite B, ce qui montre que l'Inde n'est pas épargnée par cette infection. Enfin, l'étude a révélé une incidence

annuelle des cas d'hépatite virale confirmés au laboratoire de 1,24 pour 1000 (IC 95% : 0,98–1.5); il pourrait donc s'agir d'un grave problème de santé publique dans le pays.

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