

Viral hepatitis in Bucharest

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A seroprevalence survey of viral hepatitis was conducted in Bucharest, Romania, between April and July 1990 on a systematic sample of 1355 persons drawn from the general population and groups at higher risk of infection. Sera were tested for hepatitis A, B, and C (HAV, HBV and HCV, resp.) markers using an enzyme-linked immunosorbent assay (ELISA) method.

The prevalences of HAV and HBV markers were high in all groups. A total of 47% of the adults from the general population and 39.8% of the children aged 0–16 years had at least one HBV marker. Of the pregnant women 7.8% were positive for hepatitis B surface antigen. Among infants (0–3 years of age) living in orphanages, the prevalence of at least one HBV marker was 54.6%. The findings also confirmed that HCV was circulating in Romania.

The results are consistent with national surveillance data and confirm that viral hepatitis is a major public health problem in Romania. Preventive measures will have to include HBV immunization of infants, with an appropriately targeted immunization strategy being determined through further epidemiological studies.

Introduction

Viral hepatitis is a major public health problem in all parts of the world. In particular, infections with hepatitis B virus (HBV) are of concern because in some patients the condition can lead to chronic liver disease, cirrhosis of the liver, and hepatocellular carcinoma (1).

Comparative studies of the morbidity rates of HBV and hepatitis A virus (HAV) infections in various European countries indicate that these diseases are highly endemic in Romania (2). According to national surveillance data (3), the reported incidence of all types of viral hepatitis in Romania was 300 per 100 000 in 1989. Viral hepatitis B, which mainly affects young children, was a major public health concern, with an estimated annual incidence of 50 per 100 000.

The number of reported cases of viral hepatitis is a very unreliable measure of the real epidemiological situation, since it covers only a portion of clinically manifested cases. Hepatitis infections having a

non-icteric course are for the most part, not officially reported. For example, in Germany, where the surveillance system is good, the number of unregistered cases of hepatitis infections has been estimated to be twice those that are registered (4). Also, in Romania, data on the etiology of viral hepatitis are scarce; information on its distribution among the various subgroups of the population is also lacking (5–7). Finally, existing data must be examined with caution since laboratory tests for hepatitis virus markers are rarely carried out with the highly sensitive and specific third-generation assays that are now available.

Following the political uprising in Romania in December 1989, the newly appointed Ministry of Health needed to complete epidemiological information to implement appropriate viral hepatitis prevention measures. For this purpose, a prevalence survey was designed and conducted by the National Institute of Virology, the Centre for Preventive Medicine, Bucharest, and Epicentre, Paris. The results are reported in this article.

Materials and methods

A seroprevalence survey of HAV, HBV and hepatitis C virus (HCV) markers was conducted between April and July 1990 on a sample of 1355 persons who were recruited from the population of Bucharest under the supervision of the Centre for Preventive Medicine, Bucharest.

Low-risk sample

The following groups formed the low-risk sample: 201 children aged 0–16 years who had been admitted

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to hospital for the first time in their life and who had a non-infectious diagnosis; 200 healthy adults who were attending premarital or recruitment medical examinations; and 204 pregnant women who were attending antenatal clinics. The city's two largest paediatric hospitals recruited all children who met the inclusion criteria, from the beginning of the study period until the required sample size was obtained. Healthy adults and pregnant women were selected similarly from two specialized clinics and three maternity hospitals, respectively.

High-risk group

The following individuals formed the high-risk group: 214 children under 3 years of age selected at random from the five orphanages in Bucharest; and, on a voluntary basis, 336 medical personnel employed by four different health facilities in the city.

Patients with acute hepatitis

To assess the relative distribution of the viral etiologies involved, we also recruited 100 children and 100 adults from patients who were hospitalized for acute viral hepatitis in two infectious disease clinics.

Risk factors

Although the survey was not designed to study the risk factors for viral hepatitis, a questionnaire was distributed to each of the study subjects. The information collected included their occupation, past history of parenteral treatment, and past history of blood transfusions.

Laboratory tests

Laboratory tests were performed at the National Institute of Virology, Bucharest. Sera were screened for the following: hepatitis B surface antigen (HBsAg); antibody to HBsAg (anti-HBs); antibody to hepatitis B core antigen (anti-HBc), anti-HBc IgM type; antibody to HAV (anti-HAV) and anti-HAV IgM type; and antibody to HCV (anti-HCV) using enzyme-linked immunosorbent assays (ELISA) (Abbott for the HAV and HBV markers; Orthodiagnostic for the HCV markers). HBsAg-positive sera were also tested for hepatitis B envelope antigen (HBeAg) and antibody (anti-HBe).

Data processing and analysis

Data were analysed at Epicentre, Paris, using Epi-Info software.^a The 95% confidence interval (CI)

was chosen as the measure of the precision of the estimates (prevalence \pm 1.96 standard deviations). The relative risk (RR) associated with each of the factors included in the questionnaire was calculated and the statistical significance was assessed using the 95% CI around the RR (Taylor series 95% confidence limits for the RR).

Results

Laboratory tests were performed on all individuals selected for the study ($n = 1355$). The sex ratios differed widely among the different subgroups of the sample (Table 1).

Hepatitis markers

The prevalences of HAV and HBV markers were high in all low-risk groups (Table 2). There were 121 women of childbearing age (15–45 years) in the group of healthy adults and 11 of these women were positive for HBsAg (9.1 \pm 5.1%). This is consistent with the rate of HBsAg positivity for the pregnant women (Table 2). Of HBsAg-positive women who were pregnant or of childbearing age ($n = 27$), five were positive for HBeAg.

A past history of acute hepatitis was reported by 21 (10.5%) of the healthy adults. None of the children in the low-risk sample had lived in orphanages, but five (2.5%) had received a blood transfusion and 135 (67.2%) at least one parenteral treatment. A total of 166 (81.4%) of the pregnant women had received at least one parenteral treatment, while 17 (8.3%) had had a blood transfusion.

The prevalence of anti-HAV markers increased with age (Fig. 1); almost two-thirds of individuals aged <20 years had been infected with HAV. Of the 77 children under 5 years of age, 39 (50.7%) were positive for at least one HBV marker. The preva-

Table 1: Characteristics of the study sample, Bucharest, July 1990

	No.	Age (years)	
		Range	Median
Children	201 (1.0) ^a	0–16 ^b	6
Adults	200 (0.40)	16–82	27
Pregnant women	204 –	14–41	24
Health personnel	336 (0.14)	19–75	40
Orphans	214 (1.20)	0–3	9 months
Children with clinical hepatitis	100 (1.40)	0–16	8
Adults with clinical hepatitis	100 (0.80)	15–72	23

^a Figures in parentheses are the ratio of males to females.

^b 30% of the sample were <3 years of age.

Table 2: Prevalence of viral hepatitis markers in the low-risk sample, Bucharest, July 1990

	No.	% prevalence of:		
		HBsAg	HBV ^a	anti-HAV
Children	201	19.9 (5.5) ^b	39.8 (6.7)	51.7 (6.9)
Adults	200	11.0 (4.3)	47.0 (6.8)	88.0 (4.5)
Pregnant women	204	7.8 (3.6)	45.5 (6.8)	— ^c

^a At least one HBV marker.

^b Figures in parentheses are the 95% confidence intervals.

^c Not determined.

Prevalence of HBV was higher among 0–4-year-olds than among 5–19-year-olds (50.7% versus 34.8%; RR = 1.45, 95% CI: 1.04 – 2.04).

High-risk sample

The prevalences of HAV, HBV, and HCV markers were very high for this sample (Table 3). All the orphans had received parenteral treatments and vaccine injections, but there was no transfusion record in the orphanages. The number of hospital admissions (referrals from the orphanages) ranged from 0 to 9 (median, 1). The risk of being the carrier of an HBV marker increased with the number of hospital admission (χ^2 test for trend = 7.7; $P = 0.005$).

Etiological diagnosis of acute hepatitis

Among individuals hospitalized with acute hepatitis, the viral etiology was assessed by anti-HAV and anti-HBc IgM type (Table 4).

A total of 91% of the children (0–16 years of age) and 70% of the adults had an HAV on HBV eti-

Fig. 1. Age distribution for hepatitis A virus (HAV) and hepatitis B virus (HBV) markers in the low-risk sample (children, adults, and pregnant women, $n = 605$), Bucharest, July 1990.

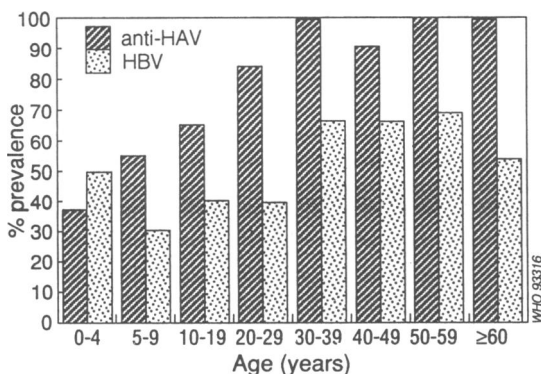


Table 3: Prevalence of hepatitis A virus (HAV) and hepatitis B virus (HBV) markers in the high-risk groups, Bucharest, July 1990

	% prevalence of:		
	HBsAg	HBV ^a	anti-HAV
Orphans	27.1 (5.9) ^b	54.6 (6.6)	45.3 (6.6)
Health personnel	9.2 (3.1)	56 (85.2)	— ^c

^a At least one HBV marker.

^b Figures in parentheses are the 95% confidence intervals.

^c Not determined.

ology; this suggests that about a third of cases of acute hepatitis among adults in Bucharest have a non-A, non-B etiology. The proportions of HBV infection were similar for the adults and children.

Hepatitis C

Anti-HCV was found in all the groups tested, with prevalences that differed markedly from one group to another (Table 5). Institutionalized children appeared, once again, to be the most frequently affected group. As with HBV markers, there were no differences in the anti-HCV prevalences of health personnel and healthy adults (3.9% versus 4.5%; RR = 0.85, 95% CI: 0.37 – 1.96).

Discussion

Sample representativeness

The socioeconomic representativeness of the low-risk sample was ensured by the number of institutions that participated in the study and by their location in various areas of the city. Also, Bucharest is relatively homogeneous in terms of the socioeconomic status of its population.

The children at low risk were hospitalized and hence may not have been representative of the general population. Conditions associated with a higher risk of HBV or HAV infections, such as socioeconomic or ethnic status, might be more prevalent among hospitalized than nonhospitalized children. To minimize potential selection biases, we sampled

Table 4: Prevalence of markers of recent viral hepatitis infection, Bucharest, July 1990

	No.	% prevalence of:		
		anti-HAV IgM	anti-HBc IgM	NA-NB ^a
Children	100	77.0 (8.2) ^b	14.0 (6.8)	9.0 (5.6)
Adults	100	36.0 (9.4)	34.0 (9.2)	30.0 (8.9)

^a NA-NB = no HAV or HBV marker.

^b Figures in parentheses are the 95% confidence intervals.

Table 5: Prevalence of hepatitis C virus (HCV) markers, Bucharest, July 1990

	No.	% prevalence of HCV markers
Low-risk adults	100	4.5 (4.5) ^a
Adults with clinical hepatitis	100	7.0 (5.0)
Children with clinical hepatitis	100	2.0 (2.1)
Health personnel	336	3.9 (2.0)
Orphanages	214	16.9 (4.9)

^a Figures in parentheses are the 95% confidence intervals.

children who had been hospitalized for the first time in their life and for a noninfectious complaint, from two hospitals. None of these children had lived in orphanages. Among this group of children, 0–3-year-olds were overrepresented: 30% of the study sample, versus 17% of the same age group in the general population of Bucharest, according to data from the National Centre for Health Statistics. Since the prevalence of hepatitis markers increases with age, this bias, rather than those associated with the selection of hospitalized children, might have led to an underestimation of the seriousness of the problem among the children.

The overrepresentation of women in the healthy adult group (M/F ratio = 0.25) was probably due to recruitment bias. Since the prevalence of hepatitis markers was similar for males and females, the sex ratio of the sample probably did not affect the estimate of the level of endemicity among the healthy adults.

The health personnel enrolled in the study were volunteers. This might have introduced a selection bias, leading to an overestimate of the real prevalence of viral hepatitis among them, since the professionals most concerned about the problem are usually those who have had the greatest exposure.

Level of endemicity

The main objective of the survey was to establish, using sensitive laboratory methods, the level of endemicity of viral hepatitis in Bucharest, with special regard to hepatitis B. The results are consistent with available surveillance data (3). The prevalence of HBsAg among the general adult population is the most useful marker of hepatitis B endemicity.^b Pre-

vious studies in Romania have reported a similar prevalence, ranging from 5.7% (6) to 10.8% (2). The HBsAg carrier rates for adults and pregnant women were, respectively, $11.0 \pm 4.0\%$ and $7.8 \pm 3.6\%$.

The prevalence of HBsAg in apparently healthy adults varies from 0.1% in parts of Australia, North America, and northern Europe, to 15% in several tropical countries (9). WHO has defined the following broad viral hepatitis B endemicity patterns among adults: low prevalence (<1% positive for HBsAg); moderate (2–7% prevalence of HBsAg); and high (>8% positive for HBsAg) (2). Our results therefore indicate that Romania belongs to the group of countries of high endemicity.

The prevalence of HBV markers was higher among 0–4-year-olds than among 5–19-year-olds (Fig. 1). This uncommon distribution pattern suggests that the risk of hepatitis infection has increased in recent years in Bucharest.

The difference between the prevalence of HBV markers among health personnel ($58.6 \pm 5.3\%$) and healthy adults ($47.0 \pm 6.8\%$) was not statistically significant. The median age of the health personnel sample was 10 years greater than that of the healthy adults and this probably led to an underestimate of the prevalence of HBV among the health personnel. Thus in Bucharest, the risk of HBV infection appeared to be as high among the general population as among those exposed to it professionally.

In our study HCV testing was performed using a first-generation assay that has subsequently proved to be of low specificity. The results obtained therefore have to be interpreted with caution, since they may contain an unknown proportion of false-positives.

Transmission patterns

In addition to confirming the high level of hepatitis B endemicity in Bucharest, the results of the survey highlighted various aspects of the transmission of HBV in the city. The prevalence of HBsAg among women of childbearing age suggested that the mother-to-newborn mode might play a substantial role in transmission. However, the size of our sample did not permit us to assess properly the presence of HBeAg, the main indicator of infectivity, among this population. Further studies therefore need to be carried out to measure the exact risk of this mode of transmission — one of the key factors for establishing an appropriate immunization strategy.

Orphanages

The level of hepatitis infection in the orphanages in Bucharest is of great concern. The prevalence of HBV markers in this population of newborns and

^b Beasley, R. Immunization strategies against hepatitis B. Unpublished document WHO/EPI/GEN/88.5.

infants (under-3-year-olds) is associated with a poor prognosis. The risk of becoming a chronic HBV carrier, and thus of developing long-term complications, such as cirrhosis of the liver or primary hepatocellular carcinoma, is directly related to an individual's age at infection; the risk that a 1–4-year-old child who is infected with HBV will become a chronic carrier has been estimated to be 20–30% (10, 11) and 60–80% for under-1-year-olds (11).

An epidemic of acquired immunodeficiency syndrome (AIDS) in orphanages in Romania was described at the beginning of 1990, with prevalences reaching 50% in some of the country's institutions (12). For both human immunodeficiency virus (HIV) and HBV infections, the iatrogenic route was suspected to be the main mode of transmission. Although the information to make a proper epidemiological assessment is not available, the lack of disposable needles and medical supplies, together with the policy of regularly transfusing small quantities of untested blood for the management of growth retardation and malnutrition, are probably responsible for the extensive spread of blood-borne diseases in Romanian orphanages (12, 13). The high prevalence of HCV markers that we found among the study children further supports this hypothesis.

Conclusions

Our findings together with available surveillance data indicate that prevention and control of HBV infection are major health priorities in Romania. Since January 1990 various measures have been taken by the Ministry of Health to reduce iatrogenic transmission of HBV, including vaccination campaigns in orphanages and paediatric facilities. Moreover, several blood banks are carrying out HBsAg screening using sensitive tests. There is now enough epidemiological evidence to recommend hepatitis B immunization, not only for identified risk groups, but also for the general population. However, further studies are needed to elaborate an appropriate strategy for integrating this procedure into the current childhood immunization programme.

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Résumé

Hépatite virale à Bucarest

Entre avril et juillet 1990, une enquête sur la séro-prévalence de l'hépatite virale a été effectuée à Bucarest (Roumanie) sur un échantillon systématique de 1315 personnes choisies dans la population générale et parmi des groupes à risque. On a recherché dans le sérum de ces sujets les marqueurs des virus de l'hépatite A, B et C (HAV, HBV, HCV), au moyen d'épreuves immuno-enzymatiques (ELISA).

Dans tous les groupes étudiés, la prévalence des marqueurs du HAV et du HBV était élevée. Au total, 47% des adultes de la population générale et 39,8% des enfants de 0 à 16 ans étaient porteurs d'au moins un marqueur du HBV. Parmi les femmes enceintes, 7,8% étaient positives pour l'antigène de surface de l'hépatite B. Chez les enfants de 0 à 3 ans vivant en orphelinat, la prévalence d'au moins un marqueur du HBV était de 54,6%. L'enquête a confirmé la circulation du HCV en Roumanie.

Ces résultats concordent avec les données de la surveillance nationale et confirment que l'hépatite virale est un problème majeur de santé publique en Roumanie. Les mesures préventives devront comprendre une vaccination des nourrissons contre l'hépatite B, selon une stratégie vaccinale convenablement ciblée d'après les résultats d'études épidémiologiques à venir.

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