

Seroprevalence of hepatitis B virus infection in patients with mental problems

Soroprevalência da infecção pelo vírus da hepatite B em portadores de doença mental

Márcia Maria de Souza^a, Maria Alves Barbosa^a, Ana Maria Tavares Borges^b, Roberto Ruhman Daher^b, Regina Maria Bringel Martins^b and Divina das Dôres de Paula Cardoso^b

^aNursing School, Federal University of Goiás. Goiânia, GO, Brazil. ^bInstitute of Tropical Pathology and Public Health, Federal University of Goiás. Goiânia, GO, Brazil

Abstract **Objectives:** Hepatitis B virus (HBV) infection is an important worldwide public health problem and it has been cause of elevated morbidity and mortality rates. This study aimed to determine the HBV infection seroprevalence in psychiatric institutions and in individuals with Down's syndrome, to detect viral DNA in HBsAg and anti-HBc total positive serum samples and to determine the HBsAg subtypes circulating these groups. **Methods:** The study assessed 433 subjects, with 408 being mentally disordered inpatients (71 had also chemical dependence), and 25 were Down's syndrome outpatients. Blood samples were collected and tested for HBV markers: HBsAg, anti-HBs and anti-HBc total by enzyme-linked immunoabsorbent assay (ELISA). HBsAg positive samples were also tested for anti-HBc IgM, HBeAg, anti-HBe, and subtyped by radial immunodiffusion. HBV-DNA was investigated in HBsAg and/or anti-HBc total positive samples by PCR methodology. **Results:** A global HBV positivity of 22.4% was detected. HBsAg was found in 1.6% of the samples. Among them, five were subtyped as *adw*₂, *adw*₄ and *ayw*₃. Viral DNA was found in 3 HBsAg samples and in 11 HBsAg and in anti-HBc total/anti-HBs positive samples, respectively. Risk factor analysis showed that multiple hospital admission was significantly associated with HBV markers. **Conclusion:** These results show high HBV seroprevalence in the investigated groups and reinforce the importance of HBV-specific preventive measures to reduce the risk of hepatitis B in individuals with mental disturbances and retardation.

Keywords Hepatitis B. HBV. Seroprevalence. Subtypes. Mental disorders. Mental retardation. Chemical dependence. Down's syndrome.

Resumo **Objetivos:** O vírus da hepatite B representa um importante problema de saúde pública mundial e é responsável por altos índices de morbidade e de mortalidade. Este estudo objetivou a determinação da soroprevalência da infecção pelo vírus da hepatite B (VHB) em pacientes internados em instituições psiquiátricas e em indivíduos com síndrome de Down, a detecção do DNA viral nas amostras positivas para HBsAg e anti-HBc total, e a caracterização dos subtipos do HBsAg. **Métodos:** O estudo avaliou 433 indivíduos, sendo que 408 eram portadores de doença mental e internos em instituições psiquiátricas (71 deles tinham também dependência química) e 25 eram indivíduos com síndrome de Down, não institucionalizados. Amostras sanguíneas de todos os participantes foram testadas para os marcadores do VHB: HBsAg, anti-HBs e anti-HBc total pelo ensaio imunoenzimático (ELISA). Soro positivos ao HBsAg foram testados também para o anti-HBc IgM, HBeAg, anti-HBe, e subtipadas pela técnica de imunodifusão radial. A detecção do DNA-VHB foi realizada em amostras reagentes ao HBsAg e/ou anti-HBc total, utilizando-se a metodologia da Reação em Cadeia pela Polimerase (PCR). **Resultados:** Foi observado um índice global de soropositividade para o VHB de 22,4% sendo que 1,6% dos indivíduos foram positivos para HBsAg. Dentre as amostras HBsAg positivas, 5 foram subtipáveis pela metodologia de imunodifusão radial, tendo sido observados os subtipos *adw*₂, *adw*₄ e *ayw*₃. O DNA viral foi detectado, pela metodologia da PCR, em três amostras positivas para o HBsAg e em 11 amostras positivas para anti-HBc total/anti-HBs. No grupo de indivíduos com problema mental, com ou sem dependência química

(N=408), a admissão hospitalar múltipla (reinternação) foi considerada fator de risco para infecção pelo VHB. **Conclusão:** Estes resultados indicam alta prevalência do VHB nesta população e reforçam a necessidade de medidas profiláticas específicas para reduzir o risco de infecção entre indivíduos com distúrbio mental e retardo mental.

Descritores Hepatite B. VHB. Soroprevalência. Subtipos. Instituições psiquiátricas. Retardo mental. Síndrome de Down.

Introduction

Hepatitis B virus (HBV) is responsible for high morbidity and mortality rates in the human population.¹ Patients with mental problems and mental retardation are predisposed to viral infection due to their special behavior and the duration of their stay at institutions.²

Subjects with Down's syndrome are a risk group for HBV infection due to different factors such as immunological impairment, individual and institutional bad hygiene condition, aggressive attitudes or even aggressive manifestation of affection as well as long periods of stay at open or closed institutions.³⁻⁴

Studies performed in different parts of the world show high rates of seroprevalence of HBV infection in inpatients with mental problems, associated or not with chemical dependence,⁵⁻⁶ and it has been observed that the duration of stay in the institution has an influence in catching the disease with longer periods of institutionalization increasing the chances for viral transmission.^{2,7}

In Brazil there is few information regarding HBV infection among patients with mental retardation, associated or not with chemical dependence, and in subjects with Down's syndrome, and, as far as we know, this is the first study in the country's Center-West region on the seroprevalence of this infection in this kind of population. This information is needed for the public health system to implement preventing and controlling measures against this disease.

This study shows the seroprevalence of hepatitis B virus (HBV) infection among inpatients in psychiatric institutions and among subjects with Down's syndrome, the detection of viral DNA in positive samples for HBsAg (hepatitis B surface antigen) and antibody against the core antigen (anti-HBc total), besides the characterization of HBsAg subtypes.

Methods

Population

This was a cross-sectional study, performed from November 1999 up to May 2001, in six out of ten psychiatric institutions in the city of Goiania-GO and in the only institution in the city of Anapolis-GO (all institutions were invited to participate in the study and seven accepted). The sample (N=433) included 408 subjects with mental disorders hospitalized in

Goiania or Anapolis (representing 70% of hospitalized patients in the mentioned cities) and 25 non-hospitalized subjects with Down's syndrome. Among hospitalized patients, 71 had chemical dependence.

For this study, blood samples were obtained by means of authorization and consent from patients and directors of the mentioned institutions. A questionnaire about personal data, hepatitis antecedents and risk factors associated to HBV infection was applied. For patients who could not be interviewed we obtained information consulting medical charts, employees and the patients' family members.

Data from interviews and the results of serological and molecular tests were entered in a PC and analyzed by the software Epi Info 6 version 6.04, developed by the Centers for Disease Control and Prevention (CDC), US. Chi-square test (χ^2) was used to analyze categorical variables with 95% confidence intervals. There was no sample loss during the process of collecting and analyzing clinical specimens. Of hospitalized patients, in the period of data collection, 30% had not allowed the collection of specimens and had not participated in the study.

Detection of serological markers

For the analysis of seroprevalence of HBV infection it was investigated the presence of HBsAg and its corresponding antibody (anti-HBs), as well as of anti-HBc total in all 433 blood samples. HbsAg-positive clinical specimens were also tested for the anti-HBc IgM, 'e' antigen (HBeAg) and antibody for 'e' antigen e (anti-HBe). For the procedure it was used the immunoenzyme trial employing commercial kits (Hepanostika-Organon Teknica), according to the manufacturer's instructions.

Subtyping

HbsAg-positive samples were submitted to subtyping by radial immunodiffusion according to the description.⁸

Detection of viral DNA

HBsAg and/or anti-HBc total positive samples were submitted to analysis to detect viral DNA using polymerase chain reaction (PCR). The procedure to extract viral DNA and the PCR was performed as described elsewhere.⁹ Amplified products were submitted to electrophoresis in 2% agarosis gel, dyed with ethidium bromid and visualized in ultraviolet transluminator.

Table 1 – Percentage distribution of serological markers for hepatitis B virus (HBV) infection regarding the studied population type.

Markers	MP ¹		MP/CD ²		DS ³		Total		X ² ; fd*; p
	N	%	N	%	N	%	N	%	
HBsAg/anti-HBc total/anti HBe	5	1.5	0	0	0	0	5	1.1	X ² = 1.44; fd=2; p=0.48
HBsAg/anti-HBc total/HBeAg	2	.6	0	0	0	0	2	.5	X ² = 0.57; fd=2; p=0.75
Anti-HBc total/anti-HBs	52	15.4	10	14.1	1	4.0	63	14.5	X ² = 2.51; fd=2; p=0.28
Anti-HBc total	16	4.7	2	2.8	1	4.0	19	4.4	X ² = 0.53; fd=2; p=0.76
Anti-HBs	7	2.1	0	0	1	0	8	1.6	X ² = 2.07; fd=2; p=0.39
Total	82	24.3	12	16.9	3	12.0	97	22.4	X ² = 3.51; fd=2; p=0.172

¹Mental problems without chemical dependence (N=337);

²Mental problems with chemical dependence (N=71);

³Down's syndrome (N=25).

X² = p>0.05

*freedom degrees

Results

Seroprevalence

The seroprevalences for HBV infection in patients with mental problems without chemical dependence (N=337), those with mental problems associated with chemical dependence (N=71) and in subjects with Down's syndrome (N=25) are shown in Table 1. Of the studied 433 subjects, 22.4% were seropositive for the virus. The analysis, considering the type of the studied population, showed prevalence rates of 24.3%, 16.9% and 12.0% for patients with mental problems without chemical dependence, mental problems associated with chemical dependence and in subjects with Down's syndrome, respectively.

Out of 97 seropositive samples, 7 were positive for HBsAg, 82, for anti-HBc total/anti-HBs and 8, only for anti-HBs, (p>0.05).

Prevalence analysis of HBV infection regarding the age range showed that there was positivity for the virus in all age ranges considering the anti-HBc total/anti-HBs markers.

The analysis of risk factors in the group of subjects with mental problems, with or without chemical dependence (N=408), showed a statistically significant association between rehospitalization (multiple hospital admission) and HBV infection (p<0.05) (Table 2).

Subtyping

Out of the seven HbsAg-positive samples that were analyzed to determine their viral subtype, five were possible to be subtyped, being three *adw*₂, one *adw*₄ and the other *ayw*₃.

Detection of viral DNA

It was observed that of the 7 HbsAg-positive samples, 3 were positive for viral DNA and from 82 anti-HBc total/anti-HBs positive samples, 11 were positive for viral DNA. All DNA-HBV-positive samples were detected by the first amplification reaction.

Discussion

This study was performed with a population composed by patients who had mental problems, associated or not with chemical dependence, hospitalized in psychiatric institutions and in non-institutionalized subjects with Down's syndrome.

The 22.4% global seroprevalence for HBV infection detected in this study agrees with studies performed in different regions

of the world which show 4.0% to 46.9% prevalence for the same population groups.^{1,6}

The seropositivity percentages detected in this study for the groups of patients with mental problems with and without chemical dependence (24.3% and 16.9%, respectively) agree with other studies which showed variable positivity rates, from 3.1% to 25%.^{7,10} Regarding subjects with Down's syndrome, it was detected a 12% prevalence, what agrees with other studies which showed rates of seropositivity to the virus which varied from 10% to 32.6%.¹¹

The analysis of the global seropositivity of HBV infection

Table 2 – Seroprevalence for hepatitis B virus (HBV) infection regarding associated risk factors, in subjects with mental problems associated or not with chemical dependence (N=408).

Risk factors	Pos./total	%	X ² c	P value
Schooling				
Illiterate	24 / 83	28.9	3.66	>.05
Some elementary school	49 / 255	19.2		
Some high school	14 / 63	22.2		
College	2 / 7	28.5		
Hospitalization				
Rehospitalization	61 / 242	25.2	4.01*	>.05
First hospitalization	28 / 166	16.9		
Acupuncture				
Yes	2 / 10	20.0	.02	>.05
No	81 / 369	21.9		
Does not know - 29*				
Tattoo				
Yes	10 / 41	24.4	.17	>.05
No	78 / 362	21.5		
Does not know - 5*				
Blood transfusion				
Yes	12 / 51	23.5	.06	>.05
No	71 / 322	22.0		
Does not know - 35*				
Dental treatment ^a				
Yes	22 / 101	21.8	.0	>.05
No	61 / 282	21.6		
Does not know - 25*				
Injectable drug				
Yes	7 / 30	23.3	.05	>.05
No	78 / 360	21.6		
Does not know - 18*				
Sexual promiscuity ^b				
Yes	19 / 104	18.2	.61	>.05
No	62 / 283	21.9		
Does not know - 21*				
Sexual activity				
Heterosexual	75 / 363	20.7	2.14	>.05
Homo/Bisexual	8 / 24	33.3		
Does not know - 21*				

^aIn the last six months

^bMore than three sexual relationships in less than six months

*Does not know answers were not considered in the analysis

regarding the age range showed positivity in all age ranges, although the HBsAg was detected only above 21 years of age. This result agrees with some studies,^{4,12} although others show higher seropositivity rates for this serological marker in lower age ranges.¹³

It was observed that 8 subjects were positive only for anti-HBs and for none of them there was confirmation of previous vaccination against HBV. This result can be understood considering that these subjects might have been contaminated by a clinical specimen containing only HBsAg, therefore functioning as a virus immunizing agent for the receiving subject.

In the group of subjects with mental problems, with or without chemical dependence (N=408), multiple hospital admissions (rehospitalization) were considered as a risk factor for HBV infection, agreeing with previous studies.^{3,7,14}

The greater detection of the subtype *adv*₂ among the five samples able to be subtyped reinforces the information that this is the main viral subtype circulating in Brazil.¹⁵ Besides, other studies performed in Goiania-GO showed a predominance

of this subtype in hemodialysed patients¹⁶ and in subjects with clinical suspicion of hepatitis.¹⁷

Viral DNA was detected in 3 HbsAg-positive samples and in 11 anti-HBc total/anti-HBs-positive samples. The detection of seropositivity for viral DNA in samples with positive anti-HBc total/anti-HBs has been also observed in other studies as well as in samples without any serological marker for the virus.^{17,18} In this sense, this study reinforces the fact that although HBsAg was not detected by serological technique, what would mean the absence of the virus in the body, viral DNA was detected by *PCR*. This reaffirms the credibility of this technique as having high sensitivity and as an important instrument for the monitoring of HBV infection.

The results of this study corroborate the need of adopting routine preventive measures in the hospital environment, besides implementing vaccination of patients and health professional and also of subjects with Down's syndrome, as only a common and constant effort may interrupt the circulation of this virus in these specific populations.

References

1. Kao JH, Chen DS. Global control of hepatitis B virus infection. *Lancet Infect Dis* 2002;2(7):395-403.
2. Asencio F, et al. Prevalence of hepatitis B infection in long-stay mentally handicapped adults. *Eur J Epidemiol* 2000;16(8):725-9.
3. Fernandez JA, et al. Prevalencia de infección por el virus de la hepatitis B en instituciones de deficientes mentales. Características epidemiológicas en la provincia de Vizcaya. *Med Clin Barc* 1989;92:323-7.
4. Chang T, Lin H, Yen YS, Wu HL. Hepatitis B and hepatitis C among institutionalized psychiatric patients in Taiwan. *J Med Virol* 1993;40:170-773.
5. Lunding S, et al. Occurrence of hepatitis B and C among mentally retarded. *Ugeskr Laeger* 1999;161(31):4393-6.
6. Eveillard M, Daroukh A, Desjardins P, Legrand S, Odzo-Gakala M, Bourlioux P. Séroprévalence des virus des hépatites B et C en Milieu institutionnel psychiatrique. *Path Biol* 1999;47:543-8.
7. Vellinga A, Van Damme P, Meheus A. Hepatitis B and C in institutions for individuals with intellectual disability. *J Intellectual Disab Res* 1999;43:445-53.
8. Le Bouvier GL. The heterogeneity of Australia antigen. *J Infect Dis* 1971;123:671-5.
9. Gomes SA, Yoshida CFT, Niel C. Detection of hepatitis B virus DNA in hepatitis B surface antigen-negative serum by polymerase chain reaction: evaluation of different primer pairs and conditions. *Acta Virologica* 1996;40:133-8.
10. Vermeltfoort JA. Re-vaccination against hepatitis B of non-and hyporesponders in a group of mentally handicapped persons. *Nederlands Tijdschrift Voor Geneskunde* 1991;135:217-35.
11. Van Damme, Vellinga A. Immunogenicity of a recombinant DNA hepatitis B vaccine in institutionalized patients with Down's syndrome. *Vaccine* 1998;23:53-6.
12. Gust ID, Dimitrakakis M, Sharma DLB. The prevalence of HbeAg and anti-Hbe in institution for the mentally retarded. *Aust NZ J Med* 1978;8:471-3.
13. Hollinger FB, Goyal RK, Hersh T, Powell HC, Schulman RJ, Melnick JL. Immune response to hepatitis virus type B in Down's syndrome and other mentally retarded patients. *Am J Epidemiol* 1972;95:356-561.
14. Devuyst O, Maessen-Collard Y. Hepatitis B in a Belgian institution for mentally retarded patients: epidemiological study. *Acta Gastroenterologica Belgica* 1991;54:12-8.
15. Gaspar AMC, Yoshida CFT. Geographic distribution of HBsAg subtypes in Brazil. *Mem Inst Oswaldo Cruz* 1987;82:253-8.
16. Teles AS, Martins RMB, Vanderborcht B, Stuyver L, Gaspar AMC, Yoshida CFT. Hepatitis B virus: genotypes and subtypes in Brazilian hemodialysis patients. *Artificial Organs* 1999;23:1076-8.
17. Silva CO. Soroprevalência para a infecção pelo vírus da hepatite B em indivíduos com suspeita clínica de hepatite em Goiânia-Goiás, detecção do DNA viral e determinação dos subtipos [dissertação de mestrado]. Goiânia: Universidade Federal de Goiás; 2000.
18. Saito T, Shinzawa H, Uchida T. Quantitative DNA analysis of low-level hepatitis B viremia in the patients with serologically negative chronic hepatitis B. *J Med Virol* 1999;58:325-30.

Correspondence:

Márcia Maria de Souza
Faculdade de Enfermagem – UFG
Rua das Quaresmeiras Qd. 24 Lt. 10
74680-210 Goiânia, GO, Brazil
E-mail: marciamms.enf@bol.com.br
