








## Epidemiologic characterization of hepatitis B among older adults

Flávio Pasa Brandt<sup>1</sup>   
Valdir Spada Júnior<sup>1</sup>   
Roberto Yamada<sup>1</sup>   
Guilherme Welter Wendt<sup>1</sup>   
Lirane Elize Defante Ferreto<sup>1,2</sup> 

### Abstract

**Objective:** to characterize the epidemiologic profile of Hepatitis B in the population aged 60 years old or more from the southwest region of the state of Paraná, Brazil, between 2007 and 2017. **Method:** an epidemiologic, descriptive, and inferential study was conducted based on notifications obtained from the Notifiable Diseases Information System (or SINAN). **Results:** Hepatitis B was more frequent in men, those with low levels of schooling and among individuals who worked in agriculture. Most of the cases were reported between 2013 and 2017 in subjects who reported having been exposed to biological material. According to logistic regression, hepatitis B infections were associated with non-white ethnicity (OR: 2.89; 95%CI 1.07 – 7.87), a history of blood transfusions (OR: 14.51; 95%CI 5.44 – 38.74), living in municipal regions with 10,000 to 20,000 inhabitants (OR: 4.57; 95%CI 1.59 – 13.12) and also among individuals from municipal regions with 20,000 to 50,000 inhabitants (OR: 4.33; 95%CI 1.61 – 11.56). **Conclusion:** the epidemiological profile reported here represents a risk factor for hepatitis B in this population. The data can support more effective interventions, as well as further studies to guide comprehensive public health policies for older adults.

**Keywords:** Health of the Elderly. Hepatitis B. Epidemiology. Risk Factors.

<sup>1</sup> Universidade Estadual do Oeste do Paraná, Centro de Ciências da Saúde, Curso de Medicina. Francisco Beltrão, PR, Brasil.

<sup>2</sup> Universidade Estadual do Oeste do Paraná, Centro de Ciências da Saúde, Programa de Pós-Graduação em Ciências Aplicadas à Saúde. Francisco Beltrão, PR, Brasil.

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Correspondence  
Lirane Elize Defante Ferreto  
Lirane.ferreto@unioeste.br

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## INTRODUCTION

Hepatitis B is caused by the hepatitis B virus (HBV), a DNA virus belonging to the *Hepadnaviridae* family<sup>1</sup>. Such a virus has high infectivity and can be transmitted directly or indirectly through percutaneous or mucosal exposure to body fluids or blood contaminated with the virus<sup>2</sup>. Negative HBV outcomes are believed to be influenced by factors most commonly found in the older population, including age-related physiological changes and a higher rate of comorbidities<sup>3</sup>.

HBV is therefore a highly significant illness, as the probability of complications resulting from acute and chronic liver disease, as well as the general mortality caused by the virus, also increases with aging. Advanced age also increases the likelihood that an individual has previously undergone a blood transfusion or has had multiple sexual partners, among other risk factors<sup>4,5</sup>. Recent studies have shown that HBV increases the chances of developing a variety of neoplasms, while immunization can reduce the chance of the occurrence and recurrence of cancers<sup>6,7</sup>, which are known to affect a greater proportion of older adults<sup>8</sup>.

Hepatitis B immunization has been part of the vaccination calendar in Brazil since 1998. It is known that, as age increases, so immunogenicity decreases, with only about 75% of vaccinees aged around 60 developing protective antibodies<sup>9</sup>. This is due to changes in the composition of the bone marrow, which reduces the individual's ability to produce and nourish stem cells, atrophying the thymus gland by reducing the production of T cells. In this situation, the response to vaccination is impaired due to functional defects at various levels in the innate and adaptive immune responses<sup>10,11</sup>.

Between 1999 and 2017, Brazil had 218,257 confirmed cases of Hepatitis B, 31.6% of which were concentrated in the southern region of the country. Between 2007 and 2017, the population aged 60 and over underwent an increase in detection rates, from 4.4 to 7.4 cases for every 100,000 inhabitants<sup>12</sup>. In the state of Paraná, between 2007 and 2017, 29,268 cases of Hepatitis B were reported in the

Notifiable Diseases Information System (SINAN), with a downward trend since 2011 and a greater concentration in the west of the state. Of this total, 10.08% of cases were concentrated in the population aged 60 or over<sup>13</sup>. It should be noted that the study area is endemic for hepatitis B<sup>14</sup>.

The epidemiological profile of older individuals involves a high prevalence of chronic diseases, and is associated with higher mortality due to complications and/or the lack of adequate treatment. Considering that around 20% of the population of the state of Paraná will be  $\geq 60$  years old by 2040<sup>15</sup>, together with the consequences of the impact of acute and chronic diseases on health systems, the present study aimed to characterize the profile of and identify the factors associated with Hepatitis B in the population aged 60 or over in the southwest of the state of Paraná, Brazil.

## METHOD

A descriptive and inferential epidemiological study was performed, which quantitatively analyzed secondary data obtained through the Brazilian Notifiable Diseases Information System (or SINAN) between 2007 to 2017<sup>16</sup>. SINAN is one of the main tools available for the collection and processing of disease data, allowing the assessment of the extent and possible impacts of a disease on the general or a specific population, enabling the development of epidemiological hypotheses. The present study was approved by the Human Research Ethics Committee of the Universidade Estadual do Oeste do Paraná (the State University of Western Paraná), under opinion No. 3,359,586 dated May 31, 2019.

Of the total of 589 notifications for Hepatitis B and C in the southwest region of Paraná in the period of the study, 26 cases involved a co-infection (ie, HBV and HCV), and were excluded from the study. The final number of reported cases included in the survey was 563. The inclusion criteria were: individuals aged 60 years or over, residing in one of the 37 municipal regions in the southwest region of Paraná, with a notification of Hepatitis B confirmed from their serological markers for active or past infection (in the case of Hepatitis B, positive for total Anti-HBc, with or without HBsAg reagent).

The outcome analyzed in this study was the presence of hepatitis B (yes /no). The explanatory variables were: sex (male/female), age (grouped according to the classification of the Brazilian Institute of Geography and Statistics)<sup>17</sup>, ethnicity/skin color (white/other), schooling ( $\leq 4$  years and  $>4$  years), population of municipal region of residence (grouped by number of inhabitants: up to 10,000, 10,000 to 20,000, 20,000 to 50,000 and 50,000 to 100,000 inhabitants) and micro-region, notification period (grouped every five years) and professional occupation. Professions were grouped according to the list of the Brazilian Classification of Occupations (or CBO)<sup>18</sup>. In addition, the following variables were included, classified in a dichotomous manner (yes/no): history of sexual contact and contact in the home with people with HBV, history of multiple sexual partners, exposure to injectable drugs/substances, blood transfusions, surgical and dental treatment, hemodialysis and organ transplantation.

The data extracted from the SINAN database were converted into a format compatible with Microsoft Excel for further analysis. The southwest region was considered to be the Microregions of Capanema, Francisco Beltrão and Pato Branco, totaling 37 municipal regions, according to the IBGE classification, which differs from that used by the Instituto Paranaense de Desenvolvimento Econômico e Social (the Paranaense Institute for Economic and Social Development), which includes the Microregion of Palmas, comprising five municipal regions<sup>15</sup>. The initial association analyzes were performed using Pearson's chi-square test ( $\chi^2$ )

and Fisher's exact test. The variables that presented a probability value equal to or less than 0.25 by the  $\chi^2$  test were selected for multivariate analysis, applying a non-conditional logistic regression model. A value of  $p < 0.05$  was adopted as an indication of significance.

## RESULTS

The average age of the sample was 66.05 years ( $\pm 6.09$ ), 65.86 ( $\pm 5.51$ ) of whom were male and 66.28 ( $\pm 6.69$ ) of whom were female. The ages of the participants ranged from 60 to 83 years. Most of the participants (50.6%) performed activities related to agriculture. In the univariate analysis, there was a higher frequency for Hepatitis B among men (53.1%), those aged over 64 years (56.7%), white individuals (93.3%), those with up to four years of schooling (67.1%), those who worked in agriculture (50.6%) and those who resided in municipal regions with up to 10,000 inhabitants (33.9%). In addition, a greater proportion of reported cases occurred between 2013 and 2017 (74.7%), among subjects who had been exposed to injectable drugs/substances (59.4%) and had a history of dental treatment (58.3%).

Table 2 describes the variables that underwent regression analysis. It was observed that those of a non-white ethnicity/skin color (OR: 2.89; 95% CI 1.07-7.87), who had undergone a blood transfusion (OR: 14.51; 95% CI 5.44-38.74), resided in municipal regions with from 20,000 to 50,000 inhabitants (OR: 4.33; 95% CI 1.61 to 11.66) or 10,000 to 20,000 inhabitants (OR: 4.57; 95% CI 1, 59-13,12) were more likely to be infected with HBV.

**Table 1.** Characteristics of older adults with or without Hepatitis B in the southwest region of Paraná, between 2007 and 2017

Variables	Hepatitis B		P value
	Yes (n=522)	No (n=41)	
Sex	N (%)	N (%)	0.714
Male	277 (53.1)	20 (48.8)	
Female	245 (46.9)	21 (51.2)	
Age group (years)			0.949
60 to 64	226 (43.3%)	17 (41.5%)	
> 64	296 (56.7%)	24 (58.5%)	
Ethnicity/skin color:			0.119
White	485 (93.3)	35 (85.4)	
Other	35 (6.7)	6 (14.6)	
Schooling (years)			<b>0.036</b>
Up to 4	322 (67.1)	18 (48.6)	
> 4	158 (32.9)	19 (51.3)	
Occupation			<b>0.006*</b>
Agriculture	118 (50.6)	2 (16.7)	
Retail	15 (6.4)	4 (33.3)	
Construction	11 (4.7)	1 (8.3)	
Drivers	13 (5.6)	0 (0)	
Other	76 (32.6)	5 (41.7)	
Population of municipal region			<b>&lt;0.001</b>
50-100,000	106 (20.3)	22 (53.7)	
20-50,000	85 (16.3)	8 (19.5)	
10-20,000	154 (29.5)	6 (14.6)	
Up to 10,000	177 (33.9)	5 (12.2)	
Microregion			0.131*
Capanema	85 (16.3)	4 (9.7)	
Francisco Beltrão	241 (46.2)	9 (22)	
Pato Branco	196 (37.5)	28 (68.3)	
Notification period			<b>0.016</b>
2007-2012	132 (25.3)	18 (43.9)	
2013-2017	390 (74.7)	23 (56.1)	
Sexual contact with HBV carrier			0.119*
Yes	74 (15.8)	2 (5.9)	
No	394 (84.2)	32 (94.1)	
Contact in the home with HBV carrier			<b>0.002*</b>
Yes	133 (28.1)	1 (3)	
No	340 (71.9)	32 (97)	
Exposure to three or more sexual partners			0.735
Yes	61 (11.8)	6 (15)	
No	454 (88.1)	34 (85)	
Exposure to drugs/injectable substances			0.075
Yes	308 (59.4)	18 (43.9)	
No	210 (40.5)	23 (56.1)	

to be continued

Continuation of Table 2

Variables	Hepatitis B		P value
	Yes (n=522)	No (n=41)	
Blood transfusion			<b>&lt;0.001</b>
Yes	14 (2.7)	11 (27.5)	
No	504 (97.3)	29 (72.5)	
Surgical treatment			0.719
Yes	205 (39.7)	18 (43.9)	
No	311 (60.3)	23 (56.1)	
Dental care			0.582
Yes	302 (58.3)	21 (52.5)	
No	216 (41.7)	19 (47.5)	
Hemodialysis			<b>0.006*</b>
Yes	3 (0.6)	3 (7.3)	
No	516 (99.4)	38 (92.7)	
Organ Transplantation			<b>0.029*</b>
Yes	2 (0.4)	2 (4.9)	
No	516 (99.6)	39 (95.1)	

Source: SINAN. Statistically significant differences are shown in bold; \* Fisher's exact test; HBV: Hepatitis B Virus

**Table 2.** Predictive factors for Hepatitis B in older adults in the southwest region of Paraná, between 2007 and 2017.

Variables	Gross OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Schooling (years)				
Up to 4	1		--	
> 4	2.15 (1.10-4.21)	<b>0.026</b>	--	--
Ethnicity/skin color:				
White	1		1	
Other	2.38 (0.94-6.03)	0.069	2.89 (1.07-7.87)	<b>0.037</b>
Blood transfusion				
No	1		1	
Yes	13.66 (5.70-32.72)	<b>&lt;0.001</b>	14.51 (5.44-38.74)	<b>&lt;0.001</b>
Exposure to drugs/injectable substances				
No	1		--	
Yes	1.87 (0.99-3.56)	0.055	--	--
Population of municipal region				
Up to 10,000	1		1	
50-100,000	2.21 (0.94-5.20)	0.071	1.31 (0.52-3.30)	0.570
20-50,000	4.57 (1.88-11.07)	<b>&lt;0.001</b>	4.33 (1.61-11.66)	<b>0.004</b>
10-20,000	7.35 (2.70-20.00)	<b>&lt;0.001</b>	4.57 (1.59-13.12)	<b>0.005</b>
Notification period				
2007 to 2012	1		--	
2013 to 2018	0.43 (0.23-0.83)	<b>0.016</b>	--	--

Source: SINAN. Statistically significant differences are shown in bold; \* Fisher's exact test; CI: confidence interval; OR: odds ratio.

## DISCUSSION

While sexually transmitted infections are recurrent themes in debates focusing on the younger population, the increase in life expectancy and the change in the behavioral profile of the older population has led to a greater risk of exposure to STIs<sup>19,20</sup>, including HBV infection, among this group<sup>21</sup>. Factors such as a reduced vaccine response, increased susceptibility to diseases and the low efficacy of the immune system<sup>22</sup>, as well as the difficulty in accessing health services in towns in rural areas of Brazil and the lack of or limited knowledge about prevention mechanisms and health status make this population more vulnerable to hepatitis B<sup>23</sup>.

In the present study, older adults living in municipal regions with a population of between 10,000 and 50,000 inhabitants were more likely to be infected with HBV than older adults living in municipal regions with a population of over 50,000 inhabitants. HBV contamination may be associated with the lifestyle of relatively larger cities, with a larger population in vulnerable situations, including those with a greater number of sexual partners and higher rates of drug use. On the other hand, 61.27% of older adults in the present study lived in small towns, with a heavily agricultural economic structure, where the beliefs and taboos related to the sexuality of older adults are more deeply entrenched, and are associated with the reluctance of such adults and health professionals to address the subject<sup>23</sup>. It is understood, therefore, that specific sociodemographic risk factors can make older adults more susceptible to exposure to STIs, both in small and medium-sized cities. In this way, preventive campaigns should focus on such specificities.

The significant number of hepatitis B cases among individuals with a history of blood transfusion presented in this study can be traced back to the 1980s and 1990s, when methods for detecting HBV in the blood of donors and in blood products finally began<sup>24</sup>. In other words, those who underwent this type of procedure before the implementation and improvement of virus detection techniques – most of whom are today older adults – may have been exposed to HBV, explaining the high rate of this source of infection in the population evaluated in

the present study. This indicates the importance of serological testing, through complementary or confirmatory tests, in order to reduce the transmission of viral hepatitis through the transfusion route<sup>25</sup>. In addition, these findings emphasize the importance of comprehensive care for older adults who, even whilst asymptomatic, correspond to one or more of the risk factors associated with HBV infection detected in this study. Furthermore, the importance of epidemiological surveillance related to viral hepatitis is emphasised, in order to encourage policies that expand vaccine coverage in endemic regions, such as that analyzed in the present study.

As biological age increases, society tends to disregard the economic, social and sexual life of aging individuals. Care is directed towards biological health and questions about sexuality are rarely addressed. The use of drugs for erectile dysfunction is a contributing factor to the maintenance of sexual activity among older adults. Allied to this is resistance to the use of condoms, even after their importance has been explained, resulting in unprotected sexual practice – considered a behavior of risk – a further warning of the need to examine for STIs, including hepatitis B<sup>26</sup>. Perhaps for this reason, the sexual and injectable routes are usually the main forms of transmission of HBV<sup>27</sup>.

The highest frequencies of HBV were identified among those older adults who performed agricultural activities. This is most likely because this population is more remote, has greater difficulty in accessing health services and limited knowledge of their own serological status, as well as high rates of illiteracy, among other social and economic needs<sup>28</sup>. Level of schooling was found to be a factor associated with hepatitis B in the population aged 60 or over. Formal education throughout life can be a protective factor in relation to communicable diseases<sup>29</sup>, as level of schooling contributes to increased cognitive aptitude and, consequently, leads to the acquiring of knowledge and skills. When improving the processing and handling of information, education represents a social determinant in the behavior of this population. Thus, the absence of or low levels of schooling can result in reduced understanding of preventive measures, as well as greater exposure to risk factors, although this relationship is not

homogeneous among the population. For example, Henn et al. demonstrated that level of education and risk of infection were not associated<sup>30</sup>.

In relation to the difference in the frequency of notifications between the first and the second halves of the period analyzed, it is likely that the underreporting or underdiagnosis of cases was a determining factor, since, according to the Epidemiological Bulletins of viral hepatitis in Brazil, the incidence of hepatitis has not increased significantly over the years. On the contrary, there was little variation during this period, which suggests that the result presented for this variable may be an indication of improvements in the notification system<sup>31</sup>.

For historical reasons, the entire southern region of Brazil has a predominantly white population<sup>32</sup>, which is related to the greater number of cases of hepatitis among white individuals found in this study. However, a greater chance of occurrence of hepatitis B in the non-white population has been identified, which may be linked to the situations of social vulnerability more commonly found among this group, resulting in greater susceptibility to communicable and non-communicable health problems<sup>33</sup>.

A limiting factor of the present study is its use of secondary data, which are potentially subject to errors in the information registration process, the possibility of case underreporting, and the presence of missing data in the database. Another limitation is the difficulty of establishing temporality and causality<sup>34</sup>. Despite this, the associated factors

identified in this study are important in relation to the predictive model presented. Furthermore, the use of secondary data has the advantage of allowing the identification of relationships between predictor and outcome variables, and has been underused in studies in the context of hepatitis B and population aging. Analysis of secondary data can contribute to the designing of larger studies and provide hypotheses for further investigations.

## CONCLUSION

HBV is relevant for its ability to cause acute hepatitis and chronic infection can result in the development of cirrhosis and hepatocellular carcinoma over time. HBV infection was strongly associated with a non-white ethnicity/skin color, a history of blood transfusion, residing in a municipal region with 10,000 to 20,000 inhabitants or from 20,000 to 50,000 inhabitants. Population aging and the course of infectious diseases, such as hepatitis B, pose a challenge to public health, especially in small towns, where sociodemographic and care characteristics tend to present failings in the provision of specialized listening to patients and screening for HBV. Studies on HBV among the older population allow health professionals to consider a sexually active individual who should be made aware of the risks of contamination and given guidance on treatment, implementing strategies for the monitoring and minimizing of vulnerabilities associated with the stigmas of old age.

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