



## Article/Artigo

# Hepatitis B marker seroprevalence and vaccination coverage in adolescents in the City of Itajaí, State of Santa Catarina, Southern Brazil, in 2008

Soroprevalência de marcadores da hepatite B e cobertura de vacinação em adolescentes no município de Itajaí, Estado de Santa Catarina Sul do Brasil, em 2008

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### ABSTRACT

**Introduction:** Hepatitis B infection constitutes an important cause of morbidity and mortality worldwide. In Brazil, however, the current epidemiological situation is not clear. Considering the importance of establishing this prevalence, the aim of this study was to determine the prevalence of HBV markers in voluntary adolescents, junior high (secondary school) students, in the City of Itajaí, State of Santa Catarina, Brazil. **Methods:** A seroepidemiological, transverse study was conducted with 353 randomly chosen adolescents from elementary school in 2008. Blood samples were analyzed for HBsAg, anti-HBc and anti-HBs. All analyses were conducted by automated microparticle enzyme immunoassay (Abbott®, AxSYM system, Deerfield, IL, USA), according to the manufacturer's instructions. **Results:** The prevalence of HBsAg was 0.6% (CI 95% 0.1 - 2.0), that of anti-HBc was 1.1% (CI 95% 0.3 - 2.9) and that of detectable anti-HBs was 83.6% (CI 95% 79.3 - 87.3). Hepatitis B vaccination coverage was 97.5% (CI 95% 95.2 - 98.8). **Conclusions:** These results demonstrate the success of the vaccination program against hepatitis B in the region studied and indicate that prevention strategies must be maintained and, if possible, expanded to contribute to the establishment of positive prevalence rates in all age groups.

**Keywords:** Hepatitis B. Prevalence. Vaccination.

### RESUMO

**Introdução:** A hepatite B constitui uma causa relevante de morbidade e mortalidade em todo o mundo. No Brasil, entretanto, a situação epidemiológica atual não é claramente conhecida. Considerando-se a importância do estabelecimento de tal prevalência, o objetivo deste estudo foi determinar a prevalência dos marcadores de HBV em adolescentes voluntários, estudantes do ensino fundamental na Cidade de Itajaí, Santa Catarina, Brasil. **Métodos:** Trata-se de um estudo soroprevalência, transversal, conduzido com 353 adolescentes do ensino fundamental, randomicamente selecionados, em 2008. As amostras de sangue foram analisadas quanto à presença dos marcadores HBsAg, anti-HBc e anti-HBs. Todas as análises foram conduzidas em ensaio imunoenzimático de micropartículas automatizado (Abbott®, AxSYM system, Deerfield, IL, EUA), de acordo com as instruções do fabricante. **Resultados:** A prevalência do HBsAg foi de 0,6% (CI 95% 0,1 - 2,0), do anti-HBc foi de 1,1% (CI 95% 0,3 - 2,9) e de títulos detectáveis de anti-HBs foi de 83,6% (CI 95% 79,3 - 87,3). A cobertura vacinal nos adolescentes estudados foi de 97,5% (CI 95% 95,2 - 98,8). **Conclusões:** Estes resultados demonstram o sucesso do programa de vacinação contra a hepatite B na região estudada e indicam que as estratégias de prevenção devem ser mantidas e, se possível, expandidas para que contribuam no estabelecimento de taxas de prevalência positivas em todas as faixas etárias.

**Palavras-chaves:** Hepatite B. Prevalência. Vacinação.

### INTRODUCTION

Infections with hepatitis B virus (HBV) represent a significant cause of morbidity and mortality worldwide and constitute a problem of global public health importance<sup>1</sup>.

The World Health Organization (WHO) estimates that, currently, more than two billion individuals among the global population have been infected with HBV and of these, approximately 360 million are chronically infected<sup>2</sup>.

In Brazil, the prevalence of HBV is variable, increasing from South to North. Previous studies have indicated a low prevalence rate in southern Brazil, a medium prevalence rate in the Northeast and Southeast, and a high prevalence rate in the Amazon region, State of Espírito Santo, and in the west of the State of Santa Catarina<sup>3</sup>.

However, due to territorial extension, cultural and economic differences in Brazil and since few studies have been conducted among the general population, the current epidemiological situation is not clear.

The elimination of HBV transmission is achievable through vaccination, clearly the most effective strategy for preventing hepatitis B and hepatocellular carcinoma. The HBV vaccine is now one of the most widely used vaccines in the world<sup>4</sup>. The official immunization schedule in Brazil includes the HBV vaccine for newborns, children and young adults up to 19 years of age, pregnant women after the first trimester and individuals at risk of HBV infection<sup>5-7</sup>. Conversely, only minimal data is available concerning the risk factors for HBV infection in Latin American countries, including Brazil<sup>8</sup>, since most studies regarding HBV prevalence in the country are performed in specific groups, such as blood donors<sup>9-12</sup> or HIV-seropositive patients<sup>13,14</sup>.

It is known that establishing the prevalence of HBV in the general population is crucial to anticipating its future impact on the health system

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and also to ensuring an adequate allocation of financial resources<sup>15</sup>. Thus, the aim of this study was to determine the prevalence of HBV markers and assess hepatitis B vaccination coverage in voluntary adolescents, junior high (secondary school) students, in the City of Itajaí, State of Santa Catarina, Brazil.

## METHODS

Itajaí is located in the northern coast of the State of Santa Catarina, Southern Brazil and houses the main port in the state.

This cross-sectional study included junior high (secondary school) student volunteers, adolescents aged between 10 and 15 years-old, residents of the City of Itajaí, from April to September 2008.

A random sampling plan was conducted for the selection of volunteers, so that it would reproduce the distribution of the adolescent population in junior high (secondary school) (Brazilian grade 5 to 8) in the City of Itajaí, including the administrative category of school attendance (public or private) and their dimensions and geographic locations within the city.

The minimum number of samples was calculated to be statistically representative of the target population and capable of determining HBV prevalences up to 30%, with an admissible error of 5% and a confidence interval of 95%<sup>16</sup>. Although the prevalence of these markers in the population studied was unknown, according to the Ministry of Health it is expected to be less than 2%<sup>17</sup>. Thus, our group overestimated that for this specific group, the prevalence could be up to 30%, to ensure that sample size would not interfere in the results.

Using such criteria the minimum sample number was defined as 322 and by the end of the process, 353 students were enrolled to participate in the study.

A 10mL blood sample was collected of each volunteer by venous puncture. Serology comprised HBsAg, anti-HBc and anti-HBs. Samples which tested positive for anti-HBc total were also tested for anti-HBc IgM. Every test was performed using automated microparticle enzyme immunosorbent assay (Abbott®, AxSYM System, Deerfield, IL, USA), in accordance with the manufacturer's instructions.

The vaccination coverage assessment was performed by vaccination cards checks in 100% of the volunteers.

HBsAg and anti-HBc results were categorized as 'reactive' or 'nonreactive', strictly in accordance with the manufacturer's instructions. The state of HBV infection was defined as reagent anti-HBc in the volunteer, according to the Brazilian Ministry of Health<sup>18</sup>.

Anti-HBs titers were categorized as: undetectable (anti-HBs = 0mIU/mL), detectable (0mIU/mL < anti-HBs < 10mIU/mL), and reactive (anti-HBs ≥ 10mIU/mL).

Statistical analysis consisted of inferential analysis of data for different proportions. The prevalence of each antibody was defined as the percentage of reagent samples and the 95% confidence interval (95%CI) was calculated for each prevalence rate. All data were tabulated and analyzed in the Statistical Package for Social Sciences (SPSS Inc., version 11.0, Chicago, USA).

### Ethical considerations

The study was approved by the Research Ethics Committee of the Federal University of Santa Catarina (Project 284/07). Free, informed consent was obtained from a parent or guardian of each volunteer.

## RESULTS

The age of the participants varied from 10 to 15 years-old, with a mean age of 13.3 years-old and standard deviation of 1.2 years. The distribution of adolescents according to sex and age is shown in **Table 1**.

**Table 2** shows the distribution of HBV serological markers in the sample studied.

HBV vaccine coverage was determined as 97.5% (CI 95% 95.2 - 98.8), with 92.1% (CI 95% 88.7 - 94.7) receiving the complete vaccination scheme of three doses of the HBV vaccine. **Table 3** shows the distribution of the number of vaccine doses received by the adolescents.

**TABLE 1 - Distribution of voluntary adolescents from Southern Brazil according to gender and age, 2008.**

	Number	Percentage
<b>Gender</b>		
male	129	36.5
female	224	63.5
<b>Total</b>	<b>353</b>	<b>100.0</b>
<b>Age</b>		
10-11	24	6.8
12-13	157	44.5
14-15	172	48.7
<b>Total</b>	<b>353</b>	<b>100.0</b>

**TABLE 2 - Seroprevalence of HBV markers in voluntary adolescents from Southern Brazil, 2008.**

HBV markers	Number	Percentage	CI 95%
HBsAg alone	2	0.6	0.1 - 2.0
Anti-HBc alone	4	1.1	0.3 - 2.9
HBsAg/Anti-HBc	2	0.6	0.1 - 2.0
Anti-HBc/Anti-HBs	2	0.6	0.1 - 2.0
Anti-HBs ≥ 10IU/L alone	183	51.8	46.5 - 57.2
0IU/L < anti-HBs < 10IU/L alone	112	31.7	26.9 - 36.9
Absence of HBV markers	52	14.7	11.2 - 18.9

HBV: hepatitis B virus, HBsAg: hepatitis B surface antigen, anti-HBc: hepatitis B core antibody, anti-HBs: hepatitis B surface antibody.

**TABLE 3 - Vaccination coverage in voluntary adolescents from Southern Brazil, 2008.**

Doses of vaccine	Number	Percentage
None	9	2.5
One	8	2.3
Two	11	3.1
Three or more	325	92.1
<b>Total</b>	<b>353</b>	<b>100.0</b>

## DISCUSSION

In this study, a low prevalence of HBV infection of 1.1% was verified, similar to that of adolescents and young adults from developed countries, where hepatitis B vaccination programs are fully implemented, such as Italy (0.9%)<sup>19</sup>, Spain (0.9%)<sup>20</sup> and the United

States (1%)<sup>21</sup>, and that verified in a nationwide study in northeastern and central-western Brazil (1.3%)<sup>22</sup> and by our group in the metropolitan area of Florianópolis, Santa Catarina, Brazil (0.5%)<sup>23</sup>. In contrast, this prevalence is lower than that of Greece (2.5%)<sup>24</sup> and of developing regions, where HBV vaccination programs are only partially implemented or not implemented at all, such as Mexico (5%)<sup>25</sup>, Bolivia (6.9%)<sup>26</sup> and central Brazil (5.9%)<sup>27</sup>.

The low prevalence of HBV infection determined in this study indicates a significant reduction in the residual risk of HBV transmission and can be explained by the low rate of vertical and intrafamilial transmission, but can also be attributed to the impact of AIDS campaigns in indirectly decreasing the prevalence of HBV. Moreover, this age group is expected to be less exposed to risk factors of transmission, such as intravenous drug use, blood transfusions and occupational infection<sup>20</sup>.

Additionally, such a low prevalence can also be attributed to recent efforts to vaccinate children against hepatitis in this region. This is justified, at least in part, by the fact that the greater part (92.1%) of the volunteers received three or more doses of hepatitis B vaccine. Thus, considering that almost half of those who participated in this study were born in the same year as hepatitis B vaccine implementation in the state (1993) or on the following year and considering that although implemented in 1993, it might have taken some time to be fully functional, this rate is very favorable. Additionally, the hepatitis B vaccine coverage verified in this study (97.5%) is higher than that expected by the Ministry of Health (95%) for adolescents and recently achieved for infants under one year old (95%) in the State of Santa Catarina<sup>5,28</sup>, or at least very similar (considering only those who received the complete vaccination scheme).

In addition to past cured infections, immunity against HBV infection is achieved through vaccination and anti-HBs are responsible for this immunity. Primary vaccination with a three-dose series of hepatitis B vaccine results in seroprotection: defined as the development of anti-HBs at a concentration greater than 10 mIU/mL in > 95% of vaccinated infants and children<sup>29</sup>. However, following completion of the primary series, anti-HBs concentrations decline and can fall below 10mIU/mL after several years<sup>30-33</sup>.

Several studies discuss the necessity of booster doses of the vaccine for those with detectable anti-HBs titers below 10mIU/mL. Moreover, certain authors argue that strong immunological memory persists for up to 22 years, once the complete vaccination scheme has been administered properly and therefore, an anamnestic anti-HBs response capable of preventing against chronic or symptomatic infections is achieved after HBV contact, even if anti-HBs titers are not higher than 10mIU/mL<sup>34-38</sup>. Therefore, considering that the students were vaccinated up to 15 years ago, we opted to consider as immunized, all individuals previously vaccinated with a three-dose series of hepatitis B vaccine and with detectable anti-HBs titers (anti-HBs > 0mIU/mL). Consequently, it can be affirmed that at least 83.6% of the volunteers in this study are successfully immunized against HBV.

Although this rate is lower than that of volunteers who have received the primary vaccination with a three-dose series of hepatitis B vaccine (92.1%), consideration must be made that the expected gradual decrease in anti-HBs titers over the years may have made them undetectable and that not all the volunteers received the vaccine in the first few years after being born (data not shown) and thus, up

to 10% of those vaccinated may not have developed proper antibody titers, since it has been well established that the rate of seroconversion is approximately 90% when adolescents and adults are considered<sup>39-42</sup>.

Although the reality described here cannot be extrapolated to older age groups in the region studied, the observations made reveal that a successful vaccination strategy will result in a population of adults protected against HBV, within a few years, with prevalence rates in this age group that are also similar to that of developed countries. This high vaccine coverage will also have an impact on lowering future hepatic cancer rates in this population, thus allowing public health economic resources to be spent in less preventable illnesses.

In conclusion, the results obtained showed a low prevalence of HBV markers of infection in adolescents from Itajaí, State of Santa Catarina, with great vaccination coverage and high prevalence of anti-HBs. These results demonstrate the success of the vaccination program against hepatitis B initiated in 1993 and indicate that this prevention strategy must be maintained and, wherever possible, expanded, while other prevention forms should be developed to prevent HBV transmission and contribute to the establishment of positive prevalence rates in all age groups.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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