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Epidemiological profile of viral hepatitis in Rio Grande do Sul and its health macro-regions

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ABSTRACT

Introduction: Viral hepatitis comprises a group of viruses characterized by high global prevalence and hepatic tropism. Its epidemiology is extremely variable throughout the world, and South America is an endemic place. A better understanding of the regional reality is fundamental for proposing new public health measures.

Methods: We conducted an aggregate temporal study of the Viral Hepatitis Database of the Ministry of Health of the state of Rio Grande do Sul (RS), with an epidemiological profile of the reactive results of HBsAg and Anti-HCV tests, together with data on mortality from acute Hepatitis B and chronic viral hepatitis from the respective Health Macro-Regions from 2007 to 2015.

Results: The incidence of new cases of hepatitis B in RS during the analyzed period was 11 (95% CI, 9.7-12.1) cases per 100,000 inhabitants. Meanwhile, the Northern region of the state, represented by the municipality of Passo Fundo, had 32.7 (95% CI, 28.3-37) and 22.8 (95% CI, 19.5-26) new cases of hepatitis B per 100,000 inhabitants for men and women, respectively. The incidence of new cases of hepatitis C in the State of Rio Grande do Sul was 29.2 (95% CI, 24.5-34.9 in 100,000 inhabitants).

Conclusion: Viral hepatitis remains an important pathology in the context of Rio Grande do Sul and its Macro-Regions.

Keywords: *Hepatitis; epidemiology; mortality*

Viral hepatitis is a set of viruses with primary capacity to infect the liver parenchyma leading to physiological dysfunctions and/or inducing an inflammatory process, with the possibility of clinical repercussions. Existing subtypes include hepatitis A, B, C, D, and E, which currently account for 90 percent of all infections. However, the main subtypes in the Brazilian context are hepatitis A, B and C[1-3].

Each virus has its peculiarities, such as etiological agent and form of transmission. While viruses A and E are transmitted by the fecal-oral route, subtypes B, C and D are spread parenterally. However, the major common point of these viral infections is liver involvement through hepatotropism[2,4-6].

These viruses are of a great importance in public health, and are associated with several conditions of morbidity and mortality, such as acute inflammatory conditions of the liver or chronic processes. Chronic infection can lead to the development of cirrhosis, ascites, esophageal varices and metabolic changes that can culminate in encephalopathy. The development of hepatocarcinomas, a condition closely related to chronic lesions in the liver, is associated with high mortality in this population due to late diagnosis and low physiological reserve of these patients[4,5,7,8].

The main representatives of chronic viral hepatitis are hepatitis B and C, of which hepatitis C infection is one of the most common chronic liver diseases, accounting for most organ transplants in the United States. Approximately 5 to 30% develop cirrhosis over a period of about 25 years among those who suffer from HCV infection[3,9,10].

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Hepatitis A is the most common cause of acute hepatitis in the world. Considered as benign pathology, there are cases of acute and severe manifestations that culminate in acute liver failure or fulminant hepatitis[2,11-13].

Hepatitis B can lead to acute and chronic clinical features. The clinical course of a patient on first contact with B virus depends largely on their age. Vertical transmission is associated with high chronification rates, close to 95%, while newly infected adult patients have a low chronification rate, associated with only 5%. Viral markers in a hepatitis B infection are HBsAg, Anti-HBc and the presence of viral DNA[8,14].

When analyzing the epidemiology, it is noticeable that the pattern is endemic in certain regions of the world[15]. Brazil represents an intermediate prevalence site for both hepatitis B and C. However, it is worth mentioning that the diagnostic rates are extremely high in the South region, being three times higher than the national average[1,16,17].

Epidemiological studies are important because they allow the understanding of how the pattern of the diseases affects the population, enabling the development of actions of control and cure. It is from the data obtained through this type of research that better allocations of resources can be made, such as public policies aimed at reducing the transmission of viruses or aimed at early diagnosis, for example. In this sense, the present study aimed to analyze data from the state of Rio Grande do Sul regarding the epidemiology of hepatitis in its Health Macro-Regions. An individual study of each of these regions makes it possible to know more about the regional setting, providing theoretical information for specific actions in each region.

METHODS

The present analysis was a descriptive and temporal aggregate epidemiological study related to the period between 2007 and 2015, with information from the Brazilian Ministry of Health. The data was obtained from the Information System of Notifiable Diseases (SINAN) and the Mortality Information System (SIM) databases. SINAN is a system in which the information about compulsory notification diseases are released and includes every state of Brazil and its subdivisions. Similarly, SIM is a system that collects data on the mortality of various diseases around the country. Both systems can be accessed on the Department of computer science of the Sistema Brazilian public Unified Health System[18] de Saúde website (DATASUS) and contains information on public and private health systems. The demographic data was collected from the Brazilian Institute of Geography and Statistics[19] (IBGE).

The study population consisted on all population of Rio Grande do Sul with positive results from HBsAg and Anti-HCV reagents and cases of acute hepatitis B and chronic viral hepatitis mortalities that were diagnosed and recorded, represented by the SINAN and SIM systems. Data were analyzed and separated according to the age range (0-19, 20-39, 40-59, 60-79 and 80 years or more), sex (female and male), health macro-regions of the State of Rio Grande do Sul (North, Mountainous region, Missionary, Metropolitan, South, Midwest and Valleys) and absolute population of each subcategory.

The statistical study was done with the program GraphPad Prism version 6 and Microsoft Office Excel 2016 (United States). Statistical comparisons between the years and populations were made by Student's *t* test for the parametric variables and Mann- Whitney for the non-parametric variables. The data was also treated in descriptive ways. The results were presented through graphs and tables for better interpretation and exposure of the results. The significant p-values of each analysis were defined as being less than or equal to 0.05 and the confidence interval adopted for the study was 95% (95% CI).

RESULTS

During the years 2007 to 2015, there were 10,876 and 29,056 new cases of reagent exams for HBsAg and Anti-HCV in the state, respectively. In the evaluation of crude mortality the amount of deaths were 2,755 from chronic viral hepatitis and 152 from acute hepatitis B.

Diagnostic rates of viral hepatitis B (table 1) in Rio Grande do Sul were 12 (95% CI,10.8-14) cases for men and 9.5 (95% CI, 8.6-10.4) for women in every 100,000 population people over the assessed period. The Northern region, whose largest city and regulatory center is Passo Fundo, had 32.7 (95% CI, 28.3-37) and 22.8 (95% CI 19.5-26) new cases of hepatitis B per 100,000 inhabitants for men and women, respectively. On the other hand, the region that presented the lowest incidence was the Southern region, represented by Pelotas, with 3.13 (95% CI, 2.24 - 4.02) for males and 1.58 (95% CI, 1, 13-2.02) for women, as described in Figure 1.

When the diagnostic rates for viral hepatitis C (table 2) were analyzed, the values found were 33 (95% CI, 26.5-39) cases for males and 26 (95% CI, 20.6-31) for females in every 100,000 populationinhabitants. While the Missionary Macro-Region, represented by Ijuí, presented an average of 8.6 (95% CI, 5.4-11.8) for men and 6.2 (95% CI, 4-8.3) for women, the Metropolitan

Macro-Region had rates of 51.1 (95% CI, 39-63.2) for males and 42.3 (95% CI, 32.5-52) for females (Figure 2).

The incidence of hepatitis B among women and men was significantly different between these groups, in which the incidence in men represented 56 percent of all cases in the analyzed period (p <0.007). This difference was not found in hepatitis C (p> 0.1).

The mortality rates of hepatitis B during the years 2007 to 2015 showed a significant fall of almost 68 percent, with the rate being between 0.1-0.2 deaths per 100,000 inhabitants (p <0.036). The mortality rate, on the other hand, from chronic viral hepatitis was 3.27 (95% CI, 3.1-3.5) for men and 2.27 (95% CI, 2.1-2.47) for women, and these differences obtained *p* <0.0001. However, the mortality

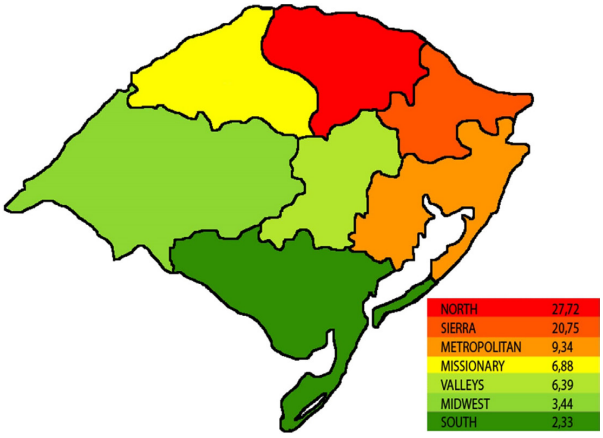

Figure 1: Incidence of positive HBsAg tests per 100,000 inhabitants by Health Macro-Region in the State of Rio Grande do Sul. Source: DataSUS.

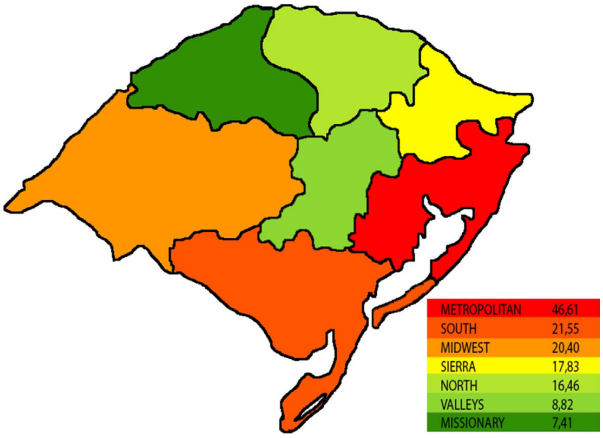

Figure 2: Incidence of positive Anti-HCV tests per 100,000 inhabitants by Health Macro-Region in the State of Rio Grande do Sul. Source: DataSUS.

Table 1: Incidence of Hepatitis B in RS and in its Macro-Regions per 100,000 inhabitants.

Region	Men	Women
Rio Grande do Sul	12.4 (CI 95%, 10.8 - 13.98)	9.52 (CI 95%, 8.63 - 10.4)
Midwest	4.13 (CI 95%, 2.97 - 5.28)	2.8 (CI 95%, 1.99 - 3.59)
Metropolitan	10.41 (CI 95%, 8.65 - 12.17)	8.33 (CI 95%, 7.11 - 9.54)
Missionary	6.72 (CI 95%, 5.39 - 8.05)	7.05 (CI 95%, 6.01 - 8.1)
North	32.7 (CI 95%, 28.3 - 37.1)	22.8 (CI 95%, 19.5 - 26.1)
Saw	22.46 (CI 95%, 19.7 - 25.2)	19.1 (CI 95%, 16.8 - 21.3)
South	3.13 (CI 95%, 2.24 - 4.02)	1.58 (CI 95%, 1.13 - 2.02)
Vouchers	5.63 (CI 95%, 4.23 - 7.03)	5.5 (CI 95%, 4.17 - 6.94)

Table 2: Incidence of hepatitis C in RS and in its Macro-Regions per 100,000 inhabitants.

Region	Men	Women
Rio Grande do Sul	32.6 (CI 95%, 26.5 - 39.1)	25.7 (CI 95%, 20.5 - 31)
Midwest	25 (CI 95%, 17 - 32)	16.5 (CI 95%, 10.9 - 22)
Metropolitan	51 (CI 95%, 39 - 63.2)	42.3 (CI 95%, 32.5 - 52)
Missionary	8.6 (CI 95%, 5.4 - 11.8)	6.2 (CI 95%, 4 - 8.3)
North	18.5 (CI 95%, 17 - 20)	14.4 (CI 95%, 12.7 - 16.2)
Saw	21.6 (CI 95%, 17.9 - 25.2)	14.1 (CI 95%, 11.8 - 16.4)
South	26.6 (CI 95%, 19.9 - 33.3)	16.7 (CI 95%, 12.2 -21.1)
Vouchers	10.7 (CI 95%, 8.8 - 12.7)	6.9 (CI 95%, 5.3 - 8.5)

of chronic viral hepatitis did not show a significant reduction during the analyzed years.

DISCUSSION

Viral hepatitis is currently a source of great morbidity and mortality in society and the ninth leading cause of death in the world, accounting for 1.4 million deaths a year. Its epidemiology is extremely variable across the world and regions like South America and Asia are endemic for hepatitis B, while the United States and Europe have a prevalence of less than 0.5 percent[1,16].

In this context, Brazil presents intermediate prevalence for both viral B and C hepatitis. However, regional projections have demonstrated a heterogeneous profile of B virus distribution in the five regions, in which the state of Rio Grande do Sul presented a two-fold higher incidence of hepatitis B compared to the national average and much higher than the North region[8,16,17,20].

It is also worth mentioning the economic impact that these viruses cause. A study in the United States in 2001 evaluated that the impact of the C virus in the year 1997 was close to 5.5 billion dollars for its economy, mainly due to chronic liver disease and hepatocellular carcinoma. However, the present study did not analyze the impact of pain and the family cost in the treatment of the disease. This suggests that the economic and social impact that this disease causes should be higher than the present study indicates[9,21].

Based on the analyzed information, it was possible to identify that the regional profile of viral hepatitis is also very heterogeneous. Some of these differences are alarming when analyzed individually, but neutralized when examined in a joint investigation. As an example, the Northern Macro-Region, represented by Passo Fundo, presented a statistically significant difference almost three times higher than the RS incidence of hepatitis B. And it was ten times higher than the result found for other regions, such as Pelotas. However, the data shows a decrease in the acute hepatitis B mortality rate[1].

In contrast, the Metropolitan region, represented by Porto Alegre, presented the highest incidence of new cases of hepatitis during the analyzed period. This higher incidence could possibly be due to higher rates of injecting drug use - whose use is a risk factor[9,10,21,22].

The mortality rate of chronic viral hepatitis remains a challenge, and the complications - cirrhosis and death - caused by chronicity of viral hepatitis tend to increase in subsequent years. Despite presenting a fall in their incidence rate, we reiterate this assertion since they did not have significant change during the analyzed period[23].

Another important point indicated by the research is the high percentage of involvement among the age groups of young adults, with the most affected groups being those of 20-39 and 40-59 years for hepatitis B and among 40-59 and 60-79 years for hepatitis C. Government actions should be structured in vaccination campaigns against hepatitis B aiming greater coverage, because access is already available to the entire population regardless of age, according to Ordinance n. 1,533 of August 18, 2016[23].

According to a paper released by the Government of Rio Grande do Sul about a research made between the years 1999 and 2009, the rates of viral hepatitis B and C in 2009 were 9.66 and 22.44 for each 100,000 inhabitants, respectively. The most common age of impairment was from 30 to 59 yeas of age in hepatitis B and 40 to 69 in hepatitis C[24]. This shows that the incidence rate is growing through the years for both viruses and, fortunately, the age of diagnosis for the B virus is decreasing. Probably, this decrease in the age of diagnosis occurred because of better health policies, which encourage early diagnosis. In addition, for both the incidence of hepatitis B and C, women had a diagnosis earlier than men. This fact can be explained by prenatal screening programs[6,14,25].

However, a difficulty imposed for this research refers to underreporting data for the Ministry of Health's Viral Hepatitis database. Therefore, the data presented in this study tends to be even greater, which makes these diseases even more relevant to the regional context[1].

The wide variation of results obtained within the state of Rio Grande do Sul is noteworthy. This diversity is due to several social aspects, risk factors, and notification. Nonetheless, more regionalized epidemiological studies are fundamental, since they analyze smaller contexts showing patterns of incidence that are hidden when only the state average is analyzed.

Conflicts of Interest

The authors declare no conflicts of interest.

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