



RESEARCH ARTICLE

OPEN ACCESS

EPIDEMIOLOGICAL PROFILE OF VIRAL HEPATITIS IN THE STATE OF MARANHÃO BETWEEN 2008 AND 2017

¹Aline Brito Damasceno,²Roseane Mara Cardoso Lima Verde,¹Jéssica Larissa Sousa Vaz,¹Amália Roberta de Moraes Barbosa, ¹Ana Karoline Matos da Silva, ¹Karina Aparecida da Silva Souza, ¹Soliane Cristina Rodrigues Costa, ¹Mateus Flóro da S. Costa, ¹Lucas Pereira L. Da Cruz,¹Sarah Daisy Mota Feitosa, ³Francisco das Chagas Araújo Sousa and ⁴*Evaldo Hipólito de Oliveira

¹Graduation in Pharmacy, Universidade Federal do Piauí - UFPI, Teresina, Brazil

²PhD student, Biomedical Engineering Postgraduate Program - PPGEB, Universidade Brasil, São Paulo, Brazil

³PhD Faculty of Medical Sciences, State University of Piauí – UESPI, Teresina, Brazil

⁴PhD Pharmacy Course, Universidade Federal do Piauí - UFPI, Teresina, Brazil

ARTICLE INFO

Article History:

Received 20th June, 2019

Received in revised form

13th July, 2019

Accepted 17th August, 2019

Published online 30th September, 2019

Key Words:

Viral Hepatitis; Epidemiology;
Public Health.

ABSTRACT

Introduction: Hepatitis is an important public health problem in Brazil, with different regional distributions. **Objective:** This study analyzed the epidemiological profile of viral hepatitis in the State of Maranhão between 2008 and 2017. **Method:** An observational, quantitative, longitudinal and retrospective study of the cases reported in SINAN was performed. 6,876 confirmed cases were registered, predominantly in the urban area and in the capital city of São Luís. **Results and Discussion:** Hepatitis A was the most prevalent during this period, frequent in children from 5 to 9 years, especially in the acute form and by means of contaminated food and water. As of 2014, the number of cases of hepatitis A sharply decreased, with hepatitis B and C predominating in the following years in individuals aged 20 to 59 years, most of whom contracted the virus sexually. Concerning the level of education, 32.15% of the cases refer to individuals with incomplete primary education. A total of 695 cases of hepatitis were reported in pregnant women, which is pertinent, since there is a possibility of vertical transmission.

Copyright © 2019, Aline Brito Damasceno et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Citation: Aline Brito Damasceno, Roseane Mara Cardoso Lima Verde, Jéssica Larissa Sousa Vaz et al. 2019. "Epidemiological profile of viral hepatitis in the state of Maranhão between 2008 and 2017", *International Journal of Development Research*, 09, (09), 29849-29854.

INTRODUCTION

Viral hepatitis is a common infectious condition, sometimes severe, that leads to liver inflammation and necrosis. Infections have distinct clinical and laboratory characteristics, which may evolve asymptotically or symptomatically, with acute, chronic or fulminant hepatitis, depending on the viral agent involved and the immunogenic factors of the patient (GOMES *et al*, 2012; BRASIL, 2017a; NUNES *et al*, 2017). Despite having a universal distribution, viral hepatitis exhibits important differences according to the etiology and geographic regions affected. This disease is commonly caused by five agents: Fecal-Oral transmitted hepatitis A and E viruses and the parenterally transmitted hepatitis B, hepatitis C and hepatitis D viruses.

*Corresponding author: Evaldo Hipólito de Oliveira,
PhD Pharmacy Course, University Federal of Piauí - UFPI, Teresina, Brazil

However, on a smaller scale, other pathogens may be implicated, including hepatitis G virus (HBV-C/VHG), transfusion transmitted virus (TTV), Epstein-Barr virus, cytomegalovirus and yellow fever virus (PORTUGAL, 2017; GOMES *et al*, 2012). In 1998, in view of the myriad of individuals affected and/or with possibilities of contracting this disease, the national epidemiological surveillance system established the compulsory notification of hepatitis, to monitor the behavior of these diseases, their conditioning and determining factors, recommend prevention and control measures and evaluate their impacts (BRASIL, 2016). Based on this, according to the Epidemiological Bulletin of Viral Hepatitis of the Ministry of Health (2017b), more than 500,000 confirmed cases of viral hepatitis were reported in the Information System for Aggravated Notification (SINAN) in Brazil from 1999 to 2015. Given the above and considering the relative scarcity of regional studies on the subject, the

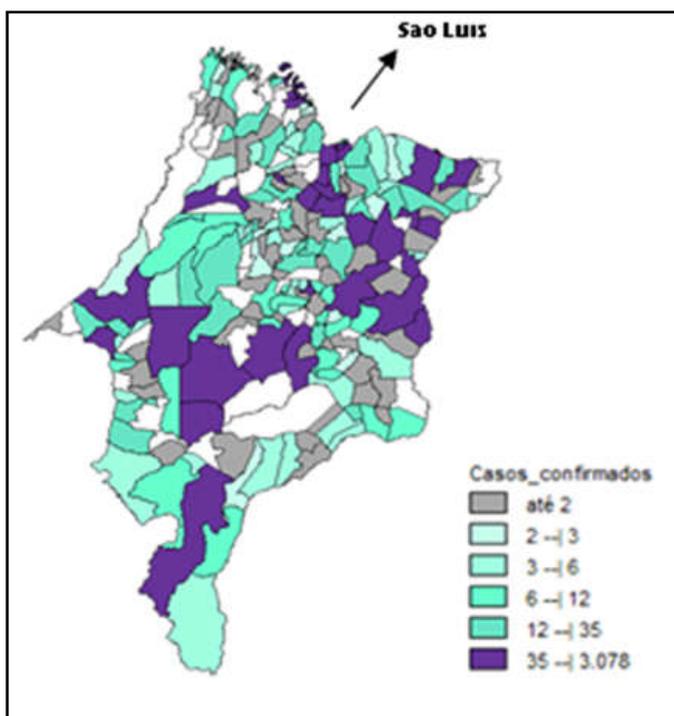
objective of this study was to analyze the epidemiological profile of hepatitis triggered by viral agents in the state of Maranhão in the period between 2008 and 2017.

METHODOLOGY

This is an observational, quantitative, longitudinal and retrospective study of cases of viral hepatitis reported in the state of Maranhão from 2008 to 2017. The data were obtained through SINAN, a tool provided by the Department of Informatics of the Brazilian Unified Health System - DATASUS, outlining the epidemiological and serological profile of this state. The variables analyzed were: year of occurrence, notification municipality, place of residence, etiologic classification, final classification, age, source of infection mechanism, gender, level of education, and pregnant women. For exploratory analysis of the data, absolute frequencies and percentages were calculated and the results were organized in tables and graphs using Microsoft Excel® software. The relationship between the municipalities and the number of reported hepatitis cases was made using the program Tab for Windows - TabWin, version 4.14, developed by DATASUS.

RESULTS AND DISCUSSION

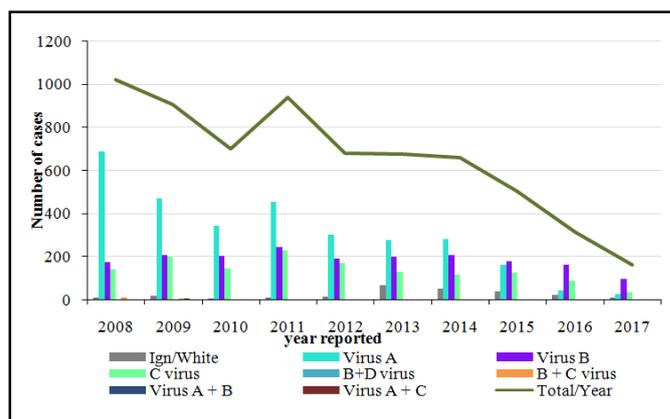
From 2008 to 2017, 6,876 confirmed cases of viral hepatitis in the state of Maranhão were registered in SINAN, making it the third state with the highest number of notifications in the northeastern region and the 15th in Brazil during the study period. Out of a total of 217 municipalities, 180 registered cases of hepatitis. There is a large variation in the distribution of confirmed cases between municipalities, as can be seen in Map 1. São Luís, the state capital, concentrates the largest proportion of infections, 3,078 occurrences, corresponding to 44.76% of the total.



Source: Ministry of Health /SVS - Notifiable Diseases Information System- Sinan Net, 2018.

Figure 1. Confirmed cases of viral hepatitis in the state of Maranhão registered from the year 2008 to 2017

Regarding the place of residence, it was found that 70.19% of the reported cases from 2008 to 2017 occurred in urban area, in which there was a similar prevalence of hepatitis A, B and C viruses. The annual number of occurrences in the rural area was always lower than in urban zone, however, there is a predominance of only one etiologic agent, the hepatitis A virus (70.22%). It should be noted that, despite the varied distribution during the years, there is a downward trend in the total number of reported cases (Chart 1). The highest number of cases was reported in 2008, in which the incidence rate of viral hepatitis was 16.19 cases per 100,000 inhabitants. A total of 1,021 cases were reported, with a majority of 686 (67.18%) caused by hepatitis A virus, followed by 172 (16.84%) hepatitis B cases, 141 (13.80%) hepatitis C cases and 14 (1.37%) coinfections/superinfections of the hepatitis virus.



Source: Ministry of Health /SVS - Notifiable Diseases Information System- Sinan Net, 2018.

Graph 1. Confirmed cases of viral hepatitis according to etiologic class in the State of Maranhão reported between 2008 to 2017

In 2017, there was a significant drop in the number of notifications, leading to 160 occurrences, equivalent to an incidence of only 2.28 cases per 100,000 inhabitants. However, unlike in 2008, there was a higher prevalence of hepatitis B virus, 94 cases (58.75%), followed by hepatitis C virus, 23 occurrences (14.37%), hepatitis A virus, 33 cases (20.62%) and finally 2 cases of coinfections/superinfections of the hepatitis virus (1.25%) which was the lowest incidence. Virus A predominated as the main etiologic agent of viral hepatitis until 2014 and in the following years there was a higher prevalence of hepatitis B. Of the total number of cases, the highest incidence rates of hepatitis C were recorded in 2011 (3.77/100,000 inhab.) and 2012 (3.73/100,000 inhabitants), frequently affecting males over 20 years age. Coinfections/superinfections are low prevalence conditions, corresponding to only 74 reported cases, 1.07% of all reported cases during the study period. In these cases, the patient will tend to develop an acute disease, more severe, increasing its risk of evolving into fulminant forms (BRASIL, 2010a). The 67th World Health Assembly requested in 2014 the technical support needed to enable Member States to develop robust national strategies for the prevention, diagnosis and treatment of viral hepatitis with temporal goals. In response to this Resolution, the World Health Organization initiated the activities of the global health sector strategy for viral hepatitis from the year 2016 to 2021, which includes measures to eliminate viral hepatitis B and C which are a threat to public health by 2030, thereby meeting up with the United Nations 2030 Agenda for Sustainable Development (TELES, 2017).

Table 1. Confirmed cases of viral hepatitis in the state of Maranhão regarding infection mechanism, reported between 2008 and 2017

Mechan. Infection	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total
Ign/White	314	279	252	332	197	244	204	179	87	49	2340
Sexual	72	63	62	72	101	79	93	80	91	47	799
Transfusional	24	21	26	17	18	10	14	21	12	8	198
Use of Injectable Drugs	7	9	5	3	3	6	7	4	3	-	50
Vertical	5	4	2	2	2	4	9	7	3	-	42
Work/Accident	4	2	3	3	4	8	4	-	2	-	37
Hemodialysis	2	3	1	5	6	3	5	2	-	1	34
Home	116	55	32	51	28	54	82	37	22	17	503
Surgical Treatment	22	35	8	9	20	13	7	11	25	5	186
Dental Treatment	22	27	16	53	15	15	10	15	14	11	214
Person person	14	23	5	7	17	19	15	5	5	4	118
Food/Water	380	338	236	320	230	215	213	132	25	13	2117
Others	39	49	51	64	45	32	17	25	25	8	389
Total	1021	908	699	938	686	702	680	518	314	163	7027

Image Caption: Mechan. (Mechanism); Ign. (Ignored).

Source: Ministry of Health /SVS - Notifiable Diseases Information System- Sinan Net, 2018.

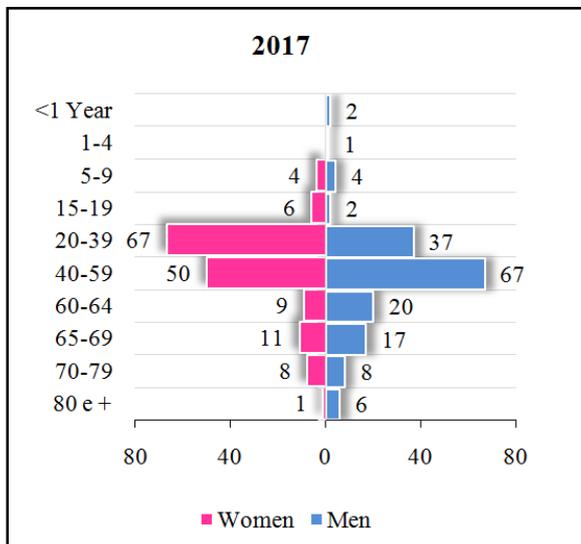
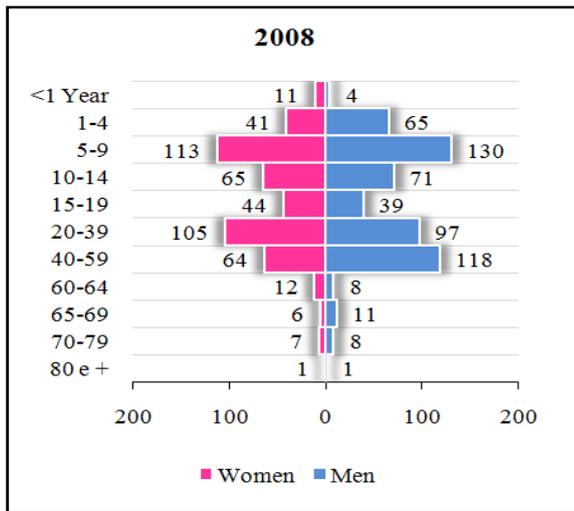
The mode of transmission most reported during the study period was by food/water, 2,117 cases (31.19%), which predominated in the first eight years analyzed (Table 1). Among these cases, 2,040 (96.36%) are associated with virus A, since its main transmission route is fecal/oral. The high prevalence may be related to unfavorable sanitary and socioeconomic conditions, with infections occurring mainly in young children (GOMES *et al*, 2011). Ximenes *et al* (2010) identified a direct association between age and seropositivity for antibodies against the virus A (anti-HAV) and an inverse association between seropositivity for anti-HAV and the socioeconomic conditions of individuals, in a study that included 26 capitals of five macro-regions in Brazil and the Federal District, conducted between 2004 and 2009. Moura, Landau and Luz (2014) found that, in 2010, 63.16% of the population had only rudimentary facilities, such as a cesspool, a ditch, discharge into rivers, lakes or the sea, and that in the state of Maranhão, about 57.84% of the population had a rudimentary sanitary facility. Silva *et al* (2017) classified the sewage situation in the state of Maranhão as severe, demonstrating that few municipalities have a reasonable number of sanitary facilities and only the capital São Luís has more sanitary facilities and more households with water supply. They identified in year 2000 that of the 217 counties, nine had between 10,000 and 20,000 sanitary facilities and 200 had less than 10,000 sanitary facilities. In 2010, 189 counties were found with less than 10,000 sanitary facilities.

From 2014 there was a decrease in the number of cases diagnosed annually with hepatitis A, reflecting progressively better results inherent to prevention policies. Improvements in the living conditions of the population, through access to treated water and basic sanitation which have reduced the prevalence of hepatitis A and contributed to reducing the burden of this infection in developing countries, such as Brazil (TELES, 2017). However, sewage treatment is not, by itself, sufficient to control the disease, since the inactive sewage treatment of 20 to 80% of infectious particles, allows a significant portion of viruses to reach the water bodies, contaminating them. When individuals lack treated water services, the use of boiled or chlorinated water is recommended (PRADO, MIAGOSTOVICH, 2014; BRAGA, 2008). Silva *et al* (2007) warn that, even though water and food are considered safe, biologically they can be sources of risk of outbreak events due to the stability of the hepatitis A virus, which may exhibit resistance to chlorine treatment. These aspects make it easy to disseminate, even in places with adequate sanitary circumstances.

In 2014, a major step was taken towards disease control following the introduction of hepatitis A vaccine in the National Immunization Program (NIP) on a single-dose regimen for children aged 12 months to 2 incomplete years. The Brazilian strategy aims to reduce the incidence of HAV by immunizing children, who represent the main reservoir of the virus (BANDEIRA, 2017). From the second half of 2015 onwards, sexually transmitted infections prevailed (Table 1), which was responsible for 25.28% of cases in 2016 and 29.06% of cases in 2017. Over the 10 years studied, the sexual route was mainly related to infections caused by the B virus, 592 cases (74.37%) and with infections caused by the C virus, 156 cases (19.59%). Infections with the B virus, as well as with the C virus, are caused by contact with blood or other body secretions. In this way, infections may occur by sexual intercourse, transfusion of blood and/or blood derivatives, use of illicit injectable drugs, especially by shared syringes and needles, mother-to-child transmission (during pregnancy and/or in the passage through the birth canal and breastfeeding), prolonged interpersonal contact and accidents with sharp material, to which health professionals are greatly exposed, besides invasive aesthetic procedures, such as the habit of extracting cuticles, piercings and tattoos. (SILVA *et al*, 2012; GAZE *et al*, 2013).

Fortunately, since the introduction of mandatory screening in blood banks (1978 for hepatitis B and 1993 for hepatitis C), transmission via transfusion of blood and blood derivatives are relatively rare (BRAZIL, 2005). It has been found that 84% of hepatitis cases between 2008 and 2017 due to use of injecting drug are related to the C virus. Currently, injecting drug users represent the group at greatest risk of contracting the hepatitis C virus and they are potential sources of transmission to the general population. Despite the lack of hepatitis C vaccine, new antivirals are available that can eliminate the virus, but access to treatment is still limited in many parts of the world (TELES, 2017). In Brazil, immunization actions against Hepatitis B Virus (HBV) started in 1989. The implementation of hepatitis B vaccine for minors and one year old children throughout the country took place in the year 1998/1999. Over the years, there has been a gradual increase in the supply of the vaccine to most of the population, and at the beginning of 2016, it was extended to all ages, regardless of the conditions of social and behavioral vulnerability (SANTOS, SANTOS, OLIVEIRA, 2017). The distribution of viral hepatitis cases according to age group and sex (Figure 3) shows that, in 2008, the cases mainly concentrated among individuals of up to 59 years of age. Infections caused by the virus A are the

most common, corresponding to 82.92% of cases in individuals up to 39 years old (mainly between 5 and 9 years old), regardless of sex,

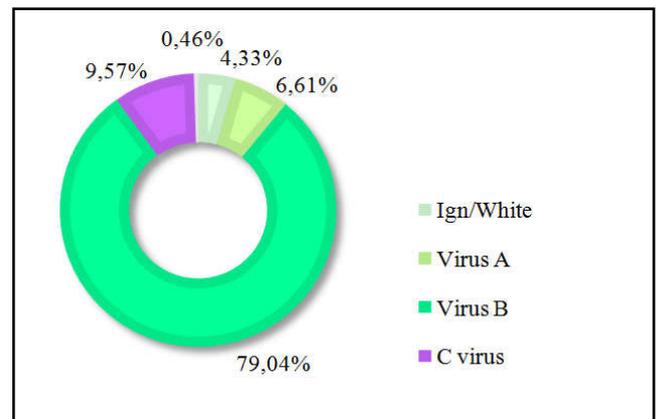


Source: Ministry of Health /SVS - Notifiable Diseases Information System-Sinan Net, 2018.

Graph 3. Distribution of cases of viral hepatitis in the State of Maranhão, by age group and sex, in 2008 and 2017

However, the C virus is the etiologic agent responsible for most of the cases (51.64%) in the 40 to 59-year-old age group with its highest prevalence among men. In the following years, the incidence of hepatitis among patients of up to 19 years of age showed a decreasing tendency. Similarly, the 2015 Epidemiological Bulletin on Viral Hepatitis (2015a) states that, between 2005 and 2014, there was a decrease in the number of annually diagnosed occurrences of hepatitis A, the largest number of cases was observed in the 5 to 6 year old age group, and that the North and Northeast Regions had the highest concentration of cases. In 2017, notifications concentrated among individuals aged 20 to 59 years, as seen by the narrowing of the top of the pyramid, whereby transmission mechanism is mainly through sexual relations, corresponding to 34.38% of reported cases and the main causative agent of infections is the B virus, responsible for 68.77% of notifications. These data suggest that this age group is the most exposed to hepatitis B transmission mechanisms. In addition, it should be considered that this period corresponds to the sexually active population and reproductive age. In the 20-39

age group, women are the most affected by infection, while in the 40-59 age group, hepatitis is prevalent in men. In relation to education level, the majority, 32.15%, of the cases of hepatitis refer to individuals with incomplete elementary education, whose prevalent age group is from 20 to 59 years of age. In this study this category includes those with incomplete 1st to 4th grades, complete 1st to 4th grades and incomplete 5th to 8th grades. Subsequently, 14.99% of the notifications involves people with incomplete secondary education, 5.07% refer to those with complete or incomplete higher education and 2.64% include illiterate individuals. It should be noted that, this information was ignored in 18.62% of notifications. Among the cases of hepatitis, pregnant women deserve special attention due to the possibility of vertical transmission and a possible use of effective measures for the prevention of infection of the newborn. According to SINAN records, 695 cases of pregnant women with hepatitis were reported, equivalent to 9.89% of the total number of occurrences between 2008 and 2017, whose distribution according to etiological class can be seen in Graph 4. The number of cases of hepatitis in pregnant women increased significantly between the first four years of the study period, from 53 reported cases in 2008 to 104 in 2011, but decreased over the following years, with 28 reported cases in 2017. In pregnant women, the prevalence of hepatitis B varies according to the endemicity of the infection in the geographical region and population studied; however, there are few studies to screen this disease during pregnancy (SOUZA, PINHO, SANTOS, 2012).



Source: Ministry of Health /SVS - Notifiable Diseases Information System-Sinan Net, 2018.

Graph 4. Etiological classification of confirmed cases of pregnant women with viral Hepatitis, from 2008 to 2017, in the State of Maranhão

Merrill and Hunter (2011) point out that, in relation to the probability of infection, children are the most affected by the B virus, because they still have a weak antiviral immune response, and, consequently, higher probability of becoming chronic carriers of the disease and efficient transmitters of this virus. The Clinical Protocol and Therapeutic Guidelines for the prevention of mother-to-child transmission of HIV, Syphilis and Viral Hepatitis (2015b) states that the investigation of Hepatitis B virus (HBV) infection in pregnant women should be conducted with HBsAg research in all pregnant women during the first trimester of pregnancy or when prenatal care is initiated. Reagent HBsAg research in pregnant women should be referred to obstetric units that ensure the administration of vaccine and immunoglobulin specific for hepatitis B virus (HBsAg) to the newborn. Pregnant women who were not evaluated during prenatal care for this infection should conduct HBsAg screening at the time of hospital admission for delivery.

Table 2. Confirmed cases of viral hepatitis regarding clinical form and etiological class from 2008 to 2017, in the State of Maranhão

Class. Etiological	Ign/White	AcuteHepatitis	Chronic/Hepatitis / Carrier	FulminantHepatitis	Inconclusive	Total
Ign/White	90	77	29	3	39	238
Virus A	66	2928	25	7	33	3059
Virus B	33	489	1428	4	66	2020
C virus	18	117	1372	1	40	1548
B+D virus	-	4	5	-	-	9
B + C virus	2	15	27	1	1	46
Virus A + B	1	19	1	-	-	21
Virus A + C	-	2	3	-	-	5
Notapplicable	3	53	12	1	12	81
Total	213	3704	2902	17	191	7027

Subtitles: Class. (Classification); Ing (Ignored).

Source: Ministry of Health /SVS - Notifiable Diseases Information System- Sinan Net, 2018.

However, the great importance of hepatitis is not limited to the enormous number of people infected; it also extends to the complications of acute and chronic forms. Hepatitis-causing viruses determine a wide variety of clinical presentations, from asymptomatic carrier or acute or chronic hepatitis to cirrhosis and hepatocellular carcinoma (FERREIRA, SILVEIRA, 2004). Regarding the clinical form, from 2008 to 2014, there was a higher occurrence of cases of acute viral hepatitis, of which 79.04% were related to infections caused by virus A and 27.72% affected children from 5 to 9 years of age (Table 2). Most cases of symptomatic acute hepatitis are due to viruses A and B. The C virus usually has an acute oligo/symptomatic phase, as a result it accounts for only a small part of symptomatic acute hepatitis (BRAZIL, 2010b). Thus, in this study, it was found that the C virus is responsible for only 3.15% of notifications of acute infection. In the Health Surveillance Guide (2017a), the Ministry of Health explains the characteristics of the different hepatitis conditions. The clinical and virological aspects of the acute phase (acute hepatitis) are limited to the first six months of the infection and the persistence of the virus after this period characterizes the chronification of the infection.

The hepatitis B, C and D viruses are those that usually cause chronic disease (persistence of the virus after 6 months), and this can occur in an oligo-/asymptomatic or symptomatic way. In these cases, individuals display histological signs of liver damage and serological or virological markers of viral replication. Thus, Table 2 shows that 96.48% of chronic infections are caused by B and C viruses. Individuals with chronic infection, who do not exhibit clinical manifestations, with low or no viral replication, and who do not show evidence of serious changes in liver histology, are considered asymptomatic carriers (evolution tends to be benign), capable of transmitting hepatitis and are epidemiologically important in the spread of endemic disease. The most severe clinical expression of hepatitis is the fulminant stage, reported in 17 cases during the study period. Finally, the guide published by the Ministry of Health clarifies that fulminant hepatitis is characterized by acute impairment of hepatocellular function, which manifests itself by a decrease in coagulation factors and presence of hepatic 8 weeks after the onset of jaundice. It also reports that fulminant hepatitis is a rare and potentially fatal condition, with high lethality (40 to 80% of cases). Brazil (2015b) clarifies that non-fulminant HBV infection does not interfere in the evolution of pregnancy, nor does pregnancy worsen the evolution of hepatitis B. In this study, 66.76% of pregnant women had chronic hepatitis, 24.89% had acute hepatitis and 0.43% had the fulminant form of infection. In the state of Maranhão, the incidence of hepatitis has decreased considerably over the years, following the trend of what occurs

throughout Brazil. In Brazil and around the world, the situation of viral hepatitis has undergone major changes in recent years. The improvement of hygiene and basic sanitation conditions in the population, vaccination against hepatitis B and new molecular techniques to diagnose the hepatitis C virus are important factors that are linked to changes in the profile of these diseases (BRAZIL, 2017a). However, the greatest burden of these infections is in impoverished populations, and/or those that demonstrate greater social and individual vulnerability such as users of illicit drugs, sex professionals, homosexuals, among others. In these social subgroups, access to public health services and diagnostic and treatment technologies is generally limited (TELES, 2017; PEREIRA, XIMENES, MOREIRA, 2010). The information contained in the notification records is also an important aspect in defining the epidemiological profile of the disease. The use of the item "not applicable" corresponds to situations in which there is an impossibility of a certain concept being applied or of a certain fact or event in relation to a certain person or situation, and "ignored" corresponds to situations in which the information is unknown (GONÇALVES, 2012). The notification of cases of viral hepatitis became mandatory in 1998, but despite the improvement in the quality of records and notification platforms, there is still a large amount of incomplete and ignored data, making it difficult to develop effective strategies for controlling this infection. This highlights the need to improve epidemiological information at the municipal level. The cases ignored in relation to the etiological classification, for example, may omit the occurrence of other types of hepatitis, such as those caused by the E virus. Regarding the transmission mechanism of the reported cases, it was found that in 33.30% of the cases this information was recorded as "ignored" or "blank", impairing a better evaluation of the real prevalent sources of transmission and consequent preventive actions. Thus, despite the progress in reducing cases, this infection still finds favorable habitat in the municipalities and population of the state of Maranhão, which points to a greater demand for public health interventions in this state.

Final considerations

In this study it was possible to visualize the change in the epidemiological scenario of hepatitis in the state of Maranhão, reaffirming the effectiveness of immunization initiatives for hepatitis A and B and how they were able to reduce the incidence of infections, outbreaks, mortality and hospitalizations. In addition, regardless of the discrete improvement in the state's sanitary and socioeconomic conditions, this study highlights the need for efficient public prevention policies, as well as improved access to the health network, to reduce the incidence not only of this disease, but

also of other recurring infectious and parasitic diseases in the region. Despite the deficiencies in the notification records, the information made available by this system enables the identification of the situation of hepatitis, providing subsidies for the improvement of actions to control and prevent this infection. However, training and guidance programs on the importance of reporting cases of viral hepatitis, aimed at health professionals and other levels of public management, would contribute to improving epidemiological control.

REFERÊNCIAS

- BANDEIRA, D. M. Etiologias de casos de hepatites agudas e perfil epidemiológico dos casos de hepatite A atendidos no ambulatório de hepatites virais da Fiocruz, Rio de Janeiro, 1997 a 2015. Dissertação (Mestre em Medicina Tropical). Instituto Oswaldo Cruz, 2017.
- BRASIL. Ministério da Saúde. Secretaria de Vigilância em Saúde. Coordenação-Geral de Desenvolvimento da Epidemiologia em Serviços. Guia de Vigilância em Saúde. 2ª ed. Brasília: Ministério da Saúde, 2017a.
- _____. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de DST, Aids e Hepatites Virais. Boletim Epidemiológico de Hepatites Virais, v. 4, n. 1, 95 p., 2015a.
- _____. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de DST Aids e Hepatites Virais. Protocolo clínico e diretrizes terapêuticas para o tratamento da hepatite viral crônica B e coinfeções. Brasília: Ministério da Saúde, 2010a.
- _____. Ministério da Saúde. Secretaria de Vigilância em Saúde Departamento de DST, Aids e Hepatites Virais. Protocolo Clínico e Diretrizes Terapêuticas para prevenção da transmissão vertical de HIV, Sífilis e Hepatites Virais. 2015b.
- _____. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância, Prevenção e Controle das IST, do HIV/Aids e das Hepatites Virais. Boletim Epidemiológico - Hepatites Virais. Brasília: Ministério da Saúde, 2016.
- _____. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância, Prevenção e Controle das IST, do HIV/Aids e das Hepatites Virais. Boletim Epidemiológico - Hepatites Virais 2017. Brasília: Ministério da Saúde, v. 48, n. 24, 2017b.
- _____. Ministério da Saúde. Secretaria de Vigilância em Saúde. Doenças infecciosas e parasitárias: guia de bolso. 8. ed. Brasília, 2010b.
- _____. Secretaria de Vigilância em Saúde. Guia de Vigilância Epidemiológica. 6. ed. Brasília, DF: Ministério da Saúde, 2005.
- BRAGA, R. C. C.; *et al.* Estimativa de áreas de risco para hepatite A. Cad. Saúde Pública, v. 24, n. 8, p.1743-52, 2008.
- FERREIRA, C. T.; SILVEIRA, T. R. da. Hepatites virais: aspectos da epidemiologia e prevenção. Revista Brasileira de Epidemiologia. v. 7, n. 4, p. 473-48, 2004.
- GAZE, R.; *et al.* Das hepatopatias e icterícias às hepatites virais: configuração de um caleidoscópio. Revista de Saúde Pública, v. 47, n. 1, p.116-22, 2013.
- GONÇALVES, K. R.; Análise espacial dos acntes de trabalho assentados no sistema de informação de agravos de notificação (SINAN) em uma capital brasileira. Dissertação de mestrado: Universidade Federal de Minas Gerais. Belo Horizonte, 2012.
- GOMES, A. P.; *et al.* Hepatites virais: abordagem clínica com ênfase nos vírus A e E. Revista da Sociedade Brasileira de Clínica Médica. São Paulo, v. 10, n. 2, p. 139-146, 2012.
- GOMES, M. A. C; *etal.*Hepatite A: soroprevalência e fatores associados em escolares de São Luís (MA), Brasil. Revista Brasileira de Epidemiologia, v. 14, n. 4, p. 548-555, 2011.
- MERRILL, R. M.; HUNTER, B. D. Seroprevalence of markers for hepatitis B viral infection. International Journal of Infectious Diseases, v. 15, n. 2, p. 78-121, 2011.
- MOURA, L.; LANDAU, E.C.; LUZ, W.V. Esgotamento sanitário nas áreas de maior concentração da agricultura familiar: situação da região nordeste. Anais do Simpósio Regional de Geoprocessamento e Sensoriamento Remoto – GEONORDESTE, Aracaju, Brasil, 2014.
- NUNES, H. M.; *et al.* As hepatites virais: aspectos epidemiológicos, clínicos e de prevenção em municípios da Microrregião de Parauapebas, sudeste do estado do Pará, Brasil. Revista Pan-Amazônica de Saúde, v. 8, n.2, p. 31-37, 2017.
- PEREIRA, L. M. M. B.; XIMENES, R. A. A.; MOREIRA, R. C. Estudo de prevalência de base populacional das infecções pelos vírus das hepatites A, B e C nas capitais do Brasil. Recife: Universidade Federal de Pernambuco; 2010. 295 p.
- PORTUGAL. Ministério da Saúde. Direção-Geral da Saúde. Programa Nacional para as Hepatites Virais 2017. Lisboa: Direção-Geral da Saúde, 2017.
- PRADO, T.; MIAGOSTOVICH, M. P. Environmental virology and sanitation in Brazil: a narrative review. Cad. Saúde Pública, v. 30, n. 7, p.1367-78, 2014.
- SANTOS, J. M. J.; SANTOS, L. A.; OLIVEIRA, F. M. Exposição aos fatores de risco e vacinação contra hepatite B em estudantes do ensino médio da rede pública. Revista Brasileira em Promoção da Saúde, v. 30, n. 2, p. 195-204, 2017.
- SILVA, A. L. de; *et al.* Hepatites virais: B, C e D: atualização. Revista Brasileira de Clínica Médica, v. 10, n. 3, p. 206-218, 2012.
- SILVA, P. C.; *et al.* Hepatite A no município do Rio de Janeiro, Brasil: padrão epidemiológico e associação das variáveis socioambientais. Vinculando dados do SINAN aos do Censo Demográfico. Cad. Saúde Pública. v. 23, n. 7, p. 1553-64, 2007.
- SILVA, R. A.; *et al.* Sanitary facilities in the state of Maranhão, Brazil. Journal of Geospatial Modelling, v. 2, n. 2, p. 9-15, 2017.
- SOUZA, M. T.; PINHO, T. L. R. DE; SANTOS, M. D. C.; *et al.* Prevalence of hepatitis B among pregnant women assisted at the public maternity hospitals of São Luís, Maranhão, Brazil. The Brazilian Journal of Infectious Diseases, v. 16, n. 6, p. 517-20, 2012.
- TELES, S. A. Hepatites Virais: um desafio para enfermagem. Revista Brasileira de Enfermagem, v. 70, n. 2, p. 243-244, 2017.
- XIMENES, R. A. A.; *et al.* Methodology of a nationwide cross-sectional survey of prevalence and epidemiological patterns of hepatitis A, B and C infection in Brazil. Cad. Saúde Pública, v. 26, n. 9, p. 1693-1704, Rio de Janeiro: 2010.