

INCIDENCE OF ACUTE HEPATITIS C IN BRAZIL: TEMPORAL TREND OF CASES NOTIFIED BETWEEN 2007 AND 2018

INCIDÊNCIA DE HEPATITE C AGUDA NO BRASIL: TENDÊNCIA TEMPORAL DOS CASOS NOTIFICADOS ENTRE 2007–2018

Karolyne Hellen Braga Nunes¹ , Luiz Henrique Bizinoto Sales¹ , Olavo Silva Valente¹ , Francisco José Dutra Souto^{1,2} 

ABSTRACT

Introduction: With the improvement of biosafety and quality of blood products, hepatitis C virus (HCV) transmission decreased in Brazil. Analyzing temporal trends in the incidence of acute cases may indicate how current HCV circulation is. **Objective:** To analyze the temporal trend of acute hepatitis C cases from 2007 to 2018. **Methods:** Analysis of reported cases of acute hepatitis C, using data from the National System of Notifiable Diseases (*Sistema Nacional de Agravos de Notificação* – SINAN) and the Health Surveillance Department, Ministry of Health. The non-parametric Cusick test was applied to analyze temporal trend. **Results:** 6,199 cases of acute HCV were reported between 2007 and 2018. The annual incidence rate ranged from 0.17 cases per 100,000 inhabitants in 2007 to 0.28 (2018) ($p=0.005$). Regarding the age group, the trend of increased notifications was significant in individuals <5 years ($p=0.025$) and >40 years ($p=0.008$) of age. **Conclusion:** Despite the few acute cases reported annually, there has been an increase in recent years, especially in age extremes. Cases in >40 years may mean that some of them are not new, but chronic infections, or because of the growing importance of sexual transmission as a consequence of relaxation in safe sex. Despite possible inconsistencies and weaknesses in the notification systems, these numbers are of concern, justifying efforts to review cases for better classification and clarification of contagion routes.

Keywords: hepatitis C; epidemiology; public health.

RESUMO

Introdução: Com a melhoria da biossegurança e qualidade dos hemoderivados, houve queda da transmissão do vírus da hepatite C (HCV) no Brasil. Analisar tendência temporal da incidência de casos agudos pode indicar como está a circulação do HCV atualmente. **Objetivo:** Analisar a tendência temporal dos casos de hepatite C aguda entre 2007 e 2018 no país. **Métodos:** Análise de casos notificados de hepatite C aguda, utilizando dados do Sistema Nacional de Agravos de Notificação e da Secretaria de Vigilância em Saúde, do Ministério da Saúde. Teste não paramétrico de Cusick foi aplicado para analisar tendência temporal. **Resultados:** Foram notificados 6.199 casos de hepatite C aguda entre 2007 e 2018. A taxa de incidência anual variou de 0,17 casos por 100 mil habitantes em 2007 a 0,28 (2018) ($p=0,005$). Quanto à faixa etária, tendência de aumento de notificações mostrou-se significativa em indivíduos <5 anos ($p=0,025$) e >40 anos ($p=0,008$). **Conclusão:** Apesar dos poucos casos agudos notificados anualmente, houve aumento em anos recentes, especialmente nos extremos etários. Os casos em >40 anos podem significar que alguns deles não sejam infecções novas, mas crônicas ou por crescente importância da transmissão sexual, como consequência de relaxamento quanto à prática de sexo seguro. Em que se pesem as possíveis inconsistências e fragilidades nos sistemas de notificação, esses números trazem preocupação, justificando esforços para revisão dos casos para melhor classificação e esclarecimentos das rotas de contágio.

Palavras-chave: hepatite C; epidemiologia; saúde pública.

INTRODUCTION

Infection with the hepatitis C virus (HCV) is a public health problem that affects millions of people worldwide, causing disability and death. It presents a great tendency to chronification, a form of the disease that is responsible for almost all the morbidity and mortality generated by the disease. The World Health Organization (WHO) estimates that there are 71 million HCV carriers worldwide⁽¹⁾. Approximately 1 million people die each year (~2.7% of all deaths) from causes related to chronic viral hepatitis, such as cirrhosis and hepatocellular carcinoma. It is estimated that 57% of liver cirrhosis cases and 78% of hepatocellular carcinoma cases are the result of chronic hepatotropic virus infection⁽²⁾.

According to Kershenobich et al.⁽³⁾, the prevalence of HCV in Latin American countries, such as Brazil, Mexico, Argentina, and Puerto Rico, varies from 1.0 to 2.3%. It is usually higher among patients

living with the human immunodeficiency virus (HIV)⁽⁴⁾. The number of patients diagnosed and treated is less than necessary, as the disease remains asymptomatic and not noticed for a long time, often making liver cirrhosis or hepatocellular carcinoma the first clinical manifestations of the infection.

Hepatitis C is a notifiable disease to the National System of Notifiable Diseases (*Sistema Nacional de Agravos de Notificação* – SINAN). Until 2014, confirmed cases were characterized by individuals with two blood markers: anti-HCV antibodies and HCV ribonucleic acid. As of 2015, the system started to consider the confirmed presence of one of the two markers. Thus, there is a tendency toward an increased detection rate in all Brazilian regions from 2015, producing an artificial increase in notifications when comparing the rates to those of previous years⁽⁵⁾.

Despite the improvement in biosafety in health units and in the quality of blood products transfused in the country, high detection of HCV chronic infection cases is expected in the coming years in Brazil. This is due to infections occurred between 25 and 50 years ago, before the development of effective diagnostic methods to prevent transmission. The notifications of cases to the SINAN do not demonstrate the intensity of the current circulation of HCV, in fact representing what happened decades ago.

¹Faculdade de Ciências Biomédicas de Cacoal – Cacoal (RO), Brazil.

²Faculdade de Medicina, Universidade Federal de Mato Grosso – Cuiabá (MT), Brazil.

OBJECTIVE

To evaluate notifications classified as acute infections, whose contamination would have occurred weeks or a few months before detection, in order to better understand the current levels of viral circulation.

METHODS

This is a descriptive study on secondary data, having as main source the National System of Notifiable Diseases (*Sistema Nacional de Agravos de Notificação* – SINAN) (www.tabnet.datasus.gov.br) and data from the Health Surveillance Secretariat, of the Ministry of Health, available at indicatorshepatites.aids.gov.br, which were analyzed as a historical series of cases and stratified by age group. The period studied was from 2007 to 2018.

The reported cases were computed as: final classification – laboratory confirmation; clinical form – acute hepatitis; etiological diagnosis – hepatitis C. Co-infections with hepatitis A or B were defined as exclusion criteria to increase specificity. Incidence rates were calculated using the Brazilian Institute of Geography and Statistics estimates for the Brazilian population by age group year by year.

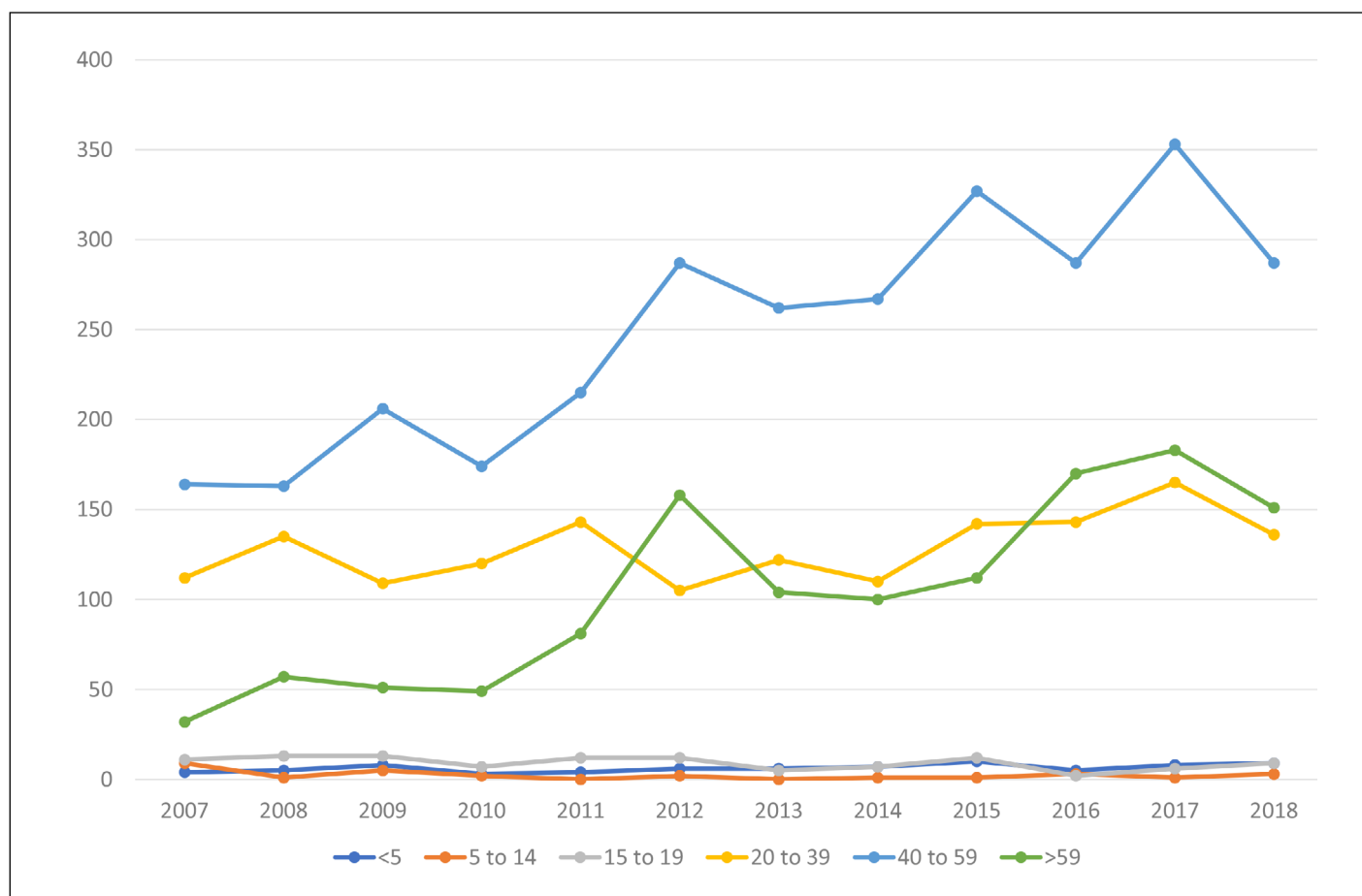
Data collection was carried out in stages, including the variables shown in SINAN, which were incorporated into Excel spreadsheets (Microsoft Excel for Office 365 MSO 2016).

The Cusick non-parametric test⁽⁶⁾, available through the Stata 6.0 nptrend command (Statacorp, College Station, USA, 1999), was applied to test the time trend for the total case series and for each age group. The value of statistical significance was set at 5%.

As it is a documentary and electronic research, based on public domain data, available on public electronic websites, there was no need for submission to the Research Ethics Committee.

RESULTS

Between the years 2007 and 2018, 6,199 cases of acute HCV were reported in Brazil, totaling 3.1% of HCV infection notifications to SINAN (**Figure 1**). There was a progressive increase in notifications, ranging from 332 (2007) to 716 (2017). Of these cases, 70.2% affected people over 40 years of age. The variation in the annual incidence rate was from 0.17 cases per 100 thousand inhabitants in 2007 to 0.28 in 2018, reaching statistical significance ($p = 0.005$). When analyzed by age group, this growth trend was significant for children under 5 years of age ($p = 0.025$) and among those over 40 years ($p = 0.008$), as shown in **Table 1**.



SINAN: National System of Notifiable Diseases (*Sistema de Informação de Agravos de Notificação*).

Source: MS/SVS/DCCI - Department of Chronic Conditions and Sexually Transmitted Infections.

Figure 1 – Total cases of acute hepatitis C notified to the National System of Notifiable Diseases between 2007 and 2018, by age group (in years).

Table 1 – Incidence rate of notifications of acute hepatitis C (/100 thousand inhabitants) to the National System of Notifiable Diseases by age group (in years), from 2007 to 2018, and analysis of temporal tendency using the Cusick test.

Year	Age range (in years)						Total
	<5	5–14	15–19	20–39	40–59	>60	
2007	0.02	0.03	0.06	0.18	0.41	0.18	0.17
2008	0.03	0.01	0.07	0.21	0.39	0.31	0.19
2009	0.05	0.01	0.07	0.17	0.48	0.27	0.20
2010	0.01	0.006	0.04	0.18	0.40	0.25	0.18
2011	0.03	0	0.07	0.22	0.48	0.40	0.23
2012	0.04	0.006	0.07	0.15	0.63	0.74	0.29
2013	0.04	0	0.03	0.18	0.56	0.47	0.25
2014	0.05	0.003	0.04	0.16	0.56	0.43	0.24
2015	0.07	0.003	0.07	0.21	0.68	0.47	0.29
2016	0.03	0.001	0.01	0.21	0.58	0.68	0.29
2017	0.03	0.003	0.03	0.24	0.70	0.70	0.34
2018	0.06	0.01	0.05	0.20	0.56	0.56	0.28
Cusick*	+2.23	-1.47	-1.68	+1.04	+2.64	+2.64	+2.82
p-value	0.025	0.140	0.093	0.297	0.008	0.008	0.005

*positive values of the non-parametric Cusick test show an upward trend. Negative values indicate a downward trend. $p \geq 0.05$ indicates stability. Source: National System of Notifiable Diseases (*Sistema Nacional de Agravos de Notificação*; www.datasus.gov.br).

DISCUSSION

Analysis of the cases reported as acute hepatitis C in the studied period showed that there has been an increase in the incidence of notifications, mainly due to cases in individuals over 40 years of age. Other authors have already demonstrated the aging of detected cases of hepatitis C in Brazil^(7,8). Most of these cases are chronic infections, acquired many years before, which have remained asymptomatic for decades⁽⁸⁾. With the control of the main HCV transmission modes — namely: transfusion of blood products and reuse of syringes and needles —, a significant decrease in new infections was expected. However, this is not what was observed in the present survey.

It is expected, with the control of the main modes of HCV transmission in Brazil, that new infections (acute cases) are limited to individuals belonging to very restricted risk groups, such as intravenous drug users and sex workers with many partners and poor adherence to barrier methods, especially those with HIV⁽⁹⁾. Therefore, an increase in the number of chronic cases would be expected, but not in the number of acute ones. Add to that the fact that notifications higher for people above 40 years old, and even above 60 years old, age groups in which the risk behaviors mentioned above are not so frequent. These risk groups should be more common between 20 and 39 years of age, whose growth was not significant. This could mean that a portion of these cases over 40 years of age are not actually new infections, but people with an old infection who were mistakenly diagnosed as acute cases, due to the technical difficulty of laboratory confirmation of acute infections in people whose serological status was not previously known.

Another explanation for the increase in cases over 40 years of age would be a relative increase in the importance of sexual transmission in relation to the most effective modes of transmission mentioned^(9,10). The increase in the expectation and quality of life of the Brazilian population has caused sexual activity to continue until more advanced ages, which could generate sexually transmitted infections

and be acquired later. The progressive decrease in adherence to safe sex among groups who have sex with many partners may also contribute to the increase of new infections, as seen recently in relation to hepatitis A among men who have sex with men⁽¹¹⁾. In any case, it would still be difficult to explain why the same phenomenon is not happening to individuals between 20 and 39 years of age.

Among acute cases under 5 years of age, 89% occurred in children under 1 year of age, which suggests vertical transmission. However, this is an infrequent mode of HCV transmission, ranging from 4.2 to 7.8%⁽¹²⁾. One possible explanation is that some of these cases are due to the maternal transfer of antibodies through breastfeeding and are not real infections. A study by Tovo et al.⁽¹³⁾ showed that there is a clear association between maternal viral load and risk of HCV vertical transmission. However, there is no information regarding the maternal situation of HCV in cases reported at this age.

A limitation of the present study is the underreporting of cases. Every epidemiological surveillance system around the world is flawed, as there are operational difficulties in getting all health professionals to report detected cases. However, the Brazilian surveillance system has managed to reduce underreporting. And linking the supply of medication for the treatment of HCV infection to the notification of the case, in several Brazilian states, has reduced underreporting.

Another limitation is the difficulty in diagnosing acute hepatitis C. In addition to being largely asymptomatic, recent HCV infection does not have any specific serological or molecular markers to differentiate between its acute and chronic phases in clinical practice⁽¹⁴⁾. Thus, to be sure that an HCV infection is recent, it is necessary to know the patient's previous serological status, in which the individual was negative for anti-HCV and HCV deoxyribonucleic acid, allowing the detection of seroconversion. Consequently, acute infections are more often detected in patients who are part of cohorts of risk groups that are already being followed and have known serological status, such as drug addicts, people living with HIV or patients in hemodialysis programs.

The increased number of cases over the age of 60 raises doubts as to whether these are really acute infections, considering the lack of a specific laboratory tool for diagnosing recent infection in people with unknown previous serological status. An increase in cases over 40 years old could also mean greater importance of sexual transmission, but it would not explain the non-increase between 20 and 39 years old. Brazil is experiencing an important upsurge in sexually transmitted infections, notably syphilis, a consequence of relaxation regarding the practice of safe sex. Despite the possible inconsistencies and weaknesses in the notification systems, these numbers are of concern, justifying efforts to review the notified cases of acute HCV infection to achieve better classification and clarifications on contagious routes. The WHO target for HCV control by 2030 is to reduce new infections by 90%⁽¹⁵⁾. Counseling and popular education measures may be needed to control HCV circulation.

CONCLUSION

Although there are not many cases of acute hepatitis C reported annually, there is a progressive increase in the incidence of acute cases of HCV infection, suggesting that the circulation of the agent remains active and causing concern.

Authors' contributions

KHBN, LHBS, OSV and FJDS contributed to the study design and data interpretation. LHBS and OSV created the figures and the table. KHBN wrote the first version of the text. FJDS performed the statistical analysis and revised the first version of the text, giving it its final shape. All authors read and agreed to the final form of the article and its conclusions.

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Conflict of interests

No conflict of interests to declare.

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Correspondence address:

FRANCISCO JOSÉ DUTRA SOUTO

Hospital Universitário Júlio Müller

Rua Luis Philippe Pereira Leite, s/n – Alvorada Cuiabá (MT), Brasil.

CEP: 78048-092

E-mail: fsouto@terra.com.br

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