O MUNDO DA SAÚDE

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Trend analysis of new hepatitis C cases in Brazil: 2011 to 2019

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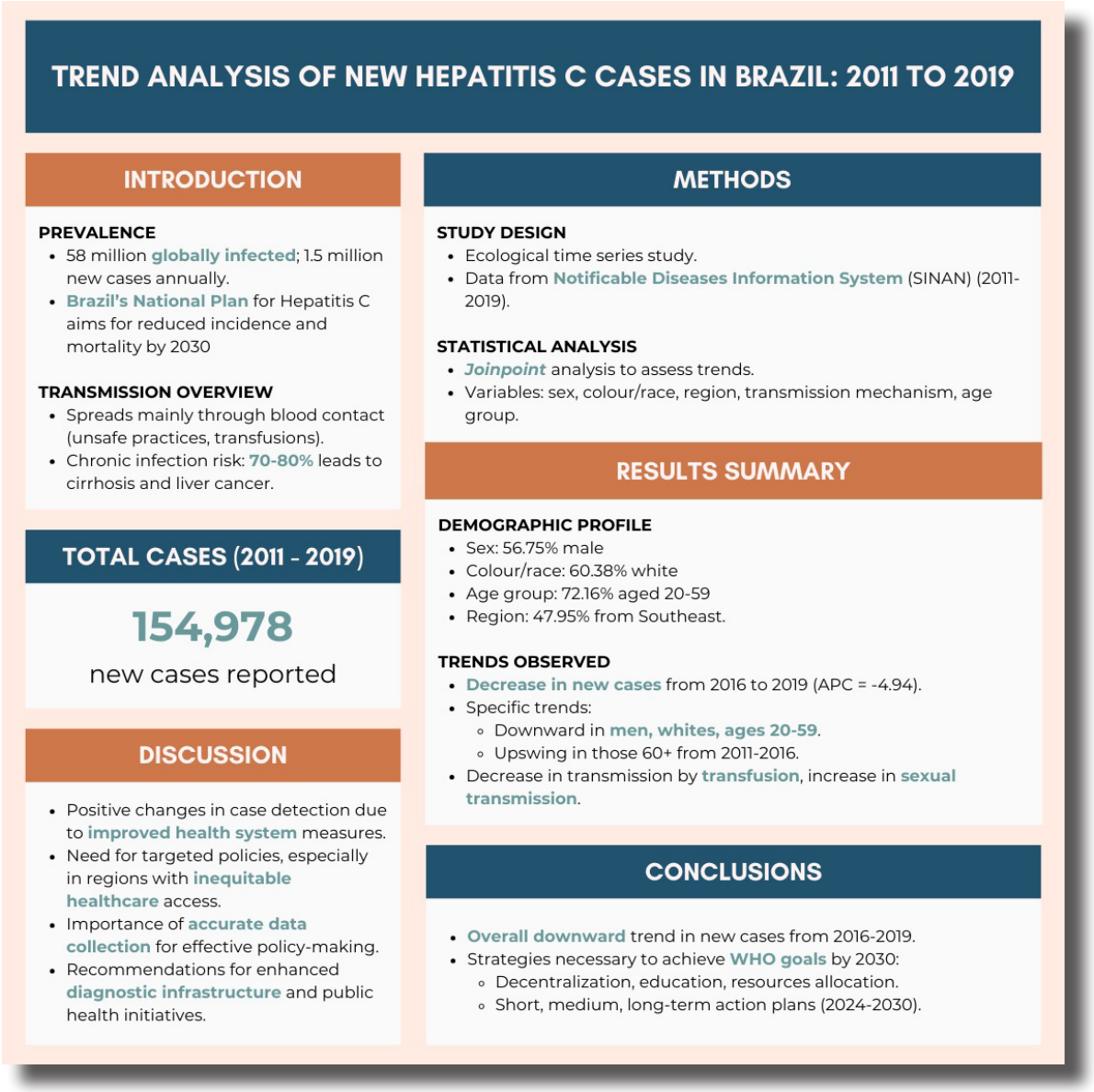
Graphical Abstract



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Abstract

Hepatitis C virus (HCV) infection is a disease transmitted through exposure to the blood or other body fluids of infected people as a result of unsafe health practices and care, unscreened blood transfusions, injecting drug use, and sexual practices without the use of condoms. This study aims to analyse the trend in new cases of hepatitis C in Brazil from 2011 to 2019. Data were collected from HCV cases registered in the Notifiable Diseases Information System in all regions of Brazil from 2011 to 2019. The information collected included the following variables: sex, colour/race, region of notification, transmission mechanism and age group. A trend analysis was then performed using the Joinpoint programme with a 5% significance level. In Brazil, 154,978 new cases of hepatitis C were reported. Regarding the trend of new hepatitis C cases in Brazil between 2011 and 2019, a decreasing trend was observed between 2016 and 2019. The data analysed in the study showed that new cases of hepatitis C in Brazil are on a downward trend, especially among men, whites, children under one year of age, people aged 20-59 years, and in the southern and central-western regions of the country. Despite being a notifiable disease, several variables remain blank, highlighting the low quality of information collection. Brazil faces significant barriers to eradicating the disease by 2030. Overcoming these barriers will require investment in infrastructure and comprehensive public policies, as well as an integrated approach that regional the various variables involved.

Keywords: Hepatitis C. Epidemiology. Communicable Disease Control.

INTRODUCTION

Hepatitis C virus (HCV) infection is a disease that spreads mainly through direct contact with infected blood, and most infections occur through exposure to blood resulting from unsafe injection practices, unsafe healthcare, unscreened blood transfusions, injecting drug use, and sexual practices that lead to exposure to blood. Estimating the spread of the virus based on the rate of development of molecular diversity suggests that this infection has existed for between 500 and 2,000 years. This makes it a significant global health issue in many countries[1].

Acute HCV infection often progresses to a chronic form in 70-80% of cases, increasing the risk of serious complications such as liver cirrhosis and cancer. Yet, advances in the development of population screening tools and effective treatments have paved the way for high-impact interventions aimed at reducing the disease burden. The ultimate goal is to end viral hepatitis as a public health threat by 2030, as set by the World Health Organization[1,2].

Globally, an estimated 58 million people are chronically infected with the hepatitis C virus, with around 1.5 million new infections occurring every year. The WHO estimated that in 2019, approximately 290,000 people died from hepatitis C, mainly from cirrhosis and hepatocellular carcinoma (primary liver cancer). Direct-acting antiviral drugs (DAAs) can cure more than 95% of people with hepatitis C infection, but access to diagnosis and treatment is low. There is currently no effective vaccine against hepatitis C[1,2].

The World Health Organization (WHO) has set an ambitious goal to tackle hepatotropic viruses, with the aim of reducing new infections by 90% and mortality associated with these viruses by 65% by 2030. In line with this proposal, Brazil has developed a National Plan for the Elimination of Hepatitis C, which aims to expand access to prevention, diagnosis and treatment of the disease. This plan involves collaboration between the federal, state and municipal levels of government, seeking to reduce both the incidence and mortality from hepatitis C[1,3].

Studies carried out in Brazil have identified an increase in the detection of hepatitis C cases, but a decrease in mortality[4,5]. However, one of the main challenges faced in Brazil is the high cost of access to health care, aggravated by profound regional inequalities, which generate disparities in the

diagnosis and treatment of hepatitis C[3,4,5]. Thus, this study aims to analyze the trend of new cases of hepatitis C in Brazil from 2011 to 2019.

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METHODS

This was an ecological time series study of new cases of hepatitis C. Data were collected from hepatitis C cases registered in the Notifiable Diseases Information System (*Sistema de Informação de Agravos de Notificação* (SINAN) *em todas as regiões do Brasil)* in all regions of Brazil, from 2011 to 2019 (data extracted on 01 Aug, 2023). The information is available until 2020, but due to the pandemic, the notification of new cases has greatly reduced (almost one third compared with the mean number of cases of the previous years) and had a significant impact on the estimates obtained in the statistical analyses. Because of that it was decided to remove 2020 data.

The data collected includes information on the following variables: sex, colour/race, region of notification, transmission mechanism, and age group. Subsequently, the data was entered into Microsoft Excel to carry out the statistical analyses. The trend analysis of the data on the number of new cases of Hepatitis C, from 2011 to 2019, was carried out using Joinpoint analysis[6]. Joinpoint analysis is a segmented line regression model with continuous trend changes, and the joinpoints represent the times at which the changes occur[6]. The analyses considered the yearly count of hepatitis C cases as the dependent variable. A general model was built, as well as models adjusted according to the variables gender, age group, color/race, and region (independent variables). The time series was composed by[9] time points which could result in a maximum number of one joinpoint[7]. The models were adjusted after applying the logarithmic transformation to the dependent variable and considering constant variance and uncorrelated errors. The use of the logarithmic transformation to the dependent variable make it possible to transform a skewed distribution into an approximately Normal distribution and allows for easier interpretation of the results[8]. In a log-linear model it is estimated the annual percentage change (APC). The APC refers to the percentage change of the rates of the dependent variable in relation to the rate of the previous year[9].

The results of the analyses show the APC measures, with the respective confidence intervals. There is an increasing trend when significant positive APC values are observed and a decreasing trend when significant negative APC values are observed[10]. These analyses were carried out using the Joinpoint Regression Program 5.0.2 software[11] and a 5% significance level was considered.

Since the data is secondary, publicly accessible, unrestricted, and without identifying the study participants, the research was exempt from evaluation by the Research Ethics Committee, following the Resolution of the National Health Council No. 510 of April 7, 2016.

RESULTS

In Brazil, 154.978 new cases of hepatitis C were reported between 2011 and 2019. The profile was male (56.75%), white (60,38%), aged between 20 and 59 (72,16%), living in the Southeast (47.95%) and the mechanism of action was blank in 57.67% of the reports, followed by injecting drug use (10,95%). (Table 1).

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Table 1 - New cases of hepatitis C by sex, colour/race, age group, region of Brazil and mechanism of action, 2011-2019.

Variable	N	%
Sex		
Male	87956	56.75
Female	67022	43.25
Colour/Race		
Caucasian	82249	60.38
Black	12494	9.17
Yellow	1120	0.82
Brown	39996	29.36
Indigenous	353	0.26
Age group		
< 1	651	0.42
1 to 9	253	0.16
10 to 19	1379	0.89
20 to 59	111862	72.16
60 or more	40880	26.37
Region		
North	7710	4.97
Northeast	12913	8.33
Southeast	74346	47.95
South	53047	34.21
Midwest	7027	4.53
Mechanism of action		
Ignored/Blank	89416	57.67
Use of injectable drugs	16984	10.95
Sexual	15169	9.77
Transfusion	13261	8.54
Work-related accident	592	0.37
Vertical	419	0.26
Hemodialysis	932	0.60
Household	768	0.47
Dental care	3867	2.58
Person/Person	1846	1.19
Surgical Treatment	5546	3.58
Water/Foods	90	0.05
Others	6159	3.97

Source: DATASUS. Notifiable Diseases Information System of the Brazilian Unified Health System (SUS) from 2011 to 2019.

Regarding the trend of new cases of Hepatitis C in Brazil between 2011 and 2019, there was a downward trend between 2016 and 2019 (APC = -4.94; 95% CI = -12.15; -0.61). In this same period of time it was observed a downward trend in men (APC = -5.09; 95% CI = -10.11; -1.86), whites (APC= -6.82; 95% CI = -17.00; -0.92), and among people aged 20 to 59 (APC = -6.47; 95% CI = -13.72; -2.02) (Table 2).

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Table 2 - Trend analysis of new hepatitis C cases by sex, colour/race, age group and region in Brazil, 2011-2019.

Sex	Tendency	Period	APC	Lower limit	Upper limit
Male	1	2011-2016	1.35	-0.29	6.11
	2	2016-2019	-5.09	-10.11	-1.86
Female	1	2011-2016	-7.98	-7.98	15.09
	3	2016-2019	-17.72	-17.72	3.54
Race/Ethnicity					
Caucasian	1	2011-2016	-0.06	-4.05	11.29
	2	2011-2019	-6.82	-17.00	-0.92
Black	1	2011-2017	3.05	-7.12	24.94
	2	2017-2019	-5.66	-21.54	7.82
Brown	1	2011-2017	4.04	1.95	10.70
	2	2011-2014	-6.77	-12.51	1.24
Yellow	1	2011-2014	-6.58	-25.37	18.70
	2	2014-2019	6.85	-15.98	34.03
Indigenous	1	2011-2013	28.53	-4.88	81.35
	2	2013-2019	-1.93	-31.05	16.95
Age Group					
< 1	1	2011-2017	0.51	-4.27	13.75
	2	2017-2019	-14.01	-24.90	-1.29
1 to 9	1	2011-2013	5.75	24.57	65.28
	2	2013-2014	-16.30	-47.93	9.30

to be continued...

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... continuation table 2

Sex	Tendency	Period	APC	Lower limit	Upper limit
10 to19	1	2011-2014	-10.78	-25.22	4.85
	2	2014-2019	1.44	-13.76	21.33
20 to 59	1	2011-2016	-1.46	-4.56	6.14
	2	2016-2019	-6.47	-13.72	-2.02
60 or more	1	2011-2016	7.17	2.20	20.78
	2	2016-2019	-1.65	-13.89	5.71
Region					
North	1	2011-2013	26.36	0.02	62.83
	2	2013-2019	-2.38	-24.48	6.58
Northeast	1	2011-2015	-1.01	-11.40	8.21
	2	2015-2019	2.20	-6.56	14.82
Southeast	1	2011-2017	-2.48	-16.26	26.49
	2	2017-2019	-9.79	-30.00	7.45
South	1	2011-2015	5.90	3.05	13.09
	2	2015-2019	-3.11	-9.16	-0.46
Midwest	1	2011-2016	3.11	0.38	11.33
	2	2016-2019	-6.15	-13.64	-1.03

Source: DATASUS. Notifiable Diseases Information System of the Brazilian Unified Health System (SUS) from 2011 to 2019.

Also regarding to age it was observed downward trend in the period of 2017 to 2019 among people aged with less than one year (APC = -14.01; 95% CI = -24.90; -1.29) and an upward trend in the period of 2011 to 2016 among people age with 60 or more years (APC = 7.17; 95% CI = 2.20; 20.78). An upward trend was observed in the period of 2011 to 2017 in browns (APC = 4.04; 95% CI = 1.95; 10.70). In terms of region, downward trends were observed in the South and Centre-West regions (Table 2).

DISCUSSION

The study found that new cases of hepatitis C in Brazil are on the decline, especially among men, whites, children under one year of age, people aged 20 to 59, and in the southern and central-western regions of the country.

Compulsory notification of hepatitis C in Brazil was implemented in 1996, with strict criteria for confirming cases. In 2015, these criteria were relaxed to include individuals with at least one reactive test (Anti-HCV or HCV-RNA), increasing the sensitivity of surveillance and resulting in an increase in detection rates[3], especially in the South and Southeast regions[12], where there is greater access to healthcare and prevalence of injecting drug use[13].

The expansion of the use of rapid tests and the change in confirmation criteria have allowed for greater detection in areas with less health infrastructure[3,14]. However, the Ministry of Health recommends that anti-HCV results be complemented with the use of an assay for direct detection of the viral agent, since around 80% of those infected become chronic carriers, which reinforces the importance of accurate diagnosis and continuous surveillance[3].

A time analysis study carried out in Brazil from 2008 to 2018 identified an upward trend in the hepatitis C detection rate[5].A meta-analysis study found that the prevalence of hepatitis C was higher among men who have sex with men[15], and another variable associated with the male profile was risk behavior and injecting drug use[16], corroborating the profile identified in Brazil.

The profile of people affected by hepatitis C in the period from 2011 to 2019 was predominantly made up of individuals aged between 20 and 59, a figure that is in line with findings from previous international studies[17]. However, it is crucial to note that there was a notable increase in the incidence of Sexually Transmitted Infections among people aged 60 and over during this period[18]. This increase can be associated with several factors, including lower levels of education and income, the influence of personal beliefs, older people's self-perception of their sexual health, and the reluctance of health professionals to address STI-related issues with this age group. As a result, the lack of education and access to adequate information has contributed to inappropriate sexual behavior among the elderly, which in turn has driven up infection rates in Brazil[18].

It is necessary to implement health policies aimed at sexuality and sexually transmitted infections (STIs) in the elderly population, covering actions such as the inclusion of the sexual history approach during home care, the continuous training of health professionals to deal with this issue, and the development of STI screening campaigns. In addition, public policies should focus on deconstructing prejudices related to sexuality in the elderly, as well as promoting sexual health, guaranteeing comprehensive, stigma-free care for this age group[19].

The Southeast and South regions of Brazil have stood out for having proportionally better hepatitis C surveillance systems, as well as wider access to detection and treatment tests, compared to the North, Northeast, and Central-West regions. Studies such as that by Brito *et al.*[5] have shown that the availability of health resources and infrastructure in these more developed regions of the country has allowed for a more effective response in the fight against hepatitis C, with a greater reach of testing campaigns and early diagnosis. This has contributed significantly to reducing the burden of the disease in these regions, mitigating the impact of hepatitis C on public health.

In contrast, the North, Northeast, and Midwest regions of Brazil face significant challenges due to limited health resources and infrastructure, which have highlighted regional disparities in the implementation of surveillance programs and access to hepatitis C testing and treatment, resulting in higher rates of underreporting and late diagnosis in these areas[4,5]. However, this study found that the Cen-

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tral-West region is showing a downward trend in new cases, and we recommend analysing the main programmes and activities implemented in recent years that have positively contributed to this decrease. Lack of financial resources and poor health infrastructure are barriers that still need to be overcome to improve hepatitis C control in these regions, demonstrating the need for more comprehensive public policies and investments to balance regional inequalities in tackling this disease in Brazil.

Regarding the transmission mechanism, most of the fields are blank, revealing the weakness in the completeness of the information system, which could be used as a basis for public health policies to intervene in the transmission chain. Despite being a compulsorily notifiable condition, several variables remain open, which shows the poor quality of the recording of this information. The findings indicate a change in the main source of infection, with a reduction in transfusion transmission between 2011 and 2019 and an increase in sexual transmission and drug use. However, the difficulty in determining the true source of infection is evident, reflected in the increase in cases with unknown origin over the period[5].

A meta-analysis study carried out in the Eastern Mediterranean region identified that the prevalence of hepatitis C is higher in people who inject drugs, corroborating this work. Nine countries provided needle and syringe exchange program services and seven countries provided opioid agonist treatment services, mostly with very low, low, or unclear coverage[20]. In Brazil, there is no uniformity in the distribution of "anti-drug" kits, since each city establishes its specific health policy, and those that provide these kits with the aim of harm reduction are often the target of significant criticism. This criticism often leads to controversy over the distribution, with allegations that this practice represents an incentive on the part of the public authorities to continue using substances.

Strategies to reduce geographical inequalities in the management of hepatitis C in Brazil aim to promote greater equity in the diagnosis, treatment and prevention of the disease. Among the main measures proposed are the decentralization of laboratories, the expansion of the supply of rapid tests in areas with less infrastructure and the implementation of telemedicine to provide clinical support to health professionals in remote regions. In addition, regional educational campaigns, continuous training of health professionals (including the importance of properly filling in the Notification System) and the active search for cases in at-risk populations are recommended, as well as intersectoral coordination to ensure the equitable distribution of resources and medicines and subsidies to expand access to the most modern treatments, such as direct-acting antivirals.

CONCLUSION

Regarding the trend in new cases of hepatitis C in Brazil between 2011 and 2019, a decrease was observed between 2016 and 2019, mainly among men, whites, children under 1 year of age, people aged 20-59 years, and in the southern and central-western regions of the country.

In order to eradicate hepatitis C by 2030, it is essential to target investments in key areas such as diagnostic infrastructure, training for health professionals, telemedicine and awareness campaigns. Decentralizing laboratories and expanding the supply of rapid tests are essential, especially in regions with less access to health services. In addition, the continuous training of professionals and the implementation of telehealth technologies will guarantee clinical support in remote areas. Educational campaigns also play a crucial role in raising awareness among the population about prevention and the importance of early diagnosis.

A strategic timetable should be established, starting with short-term actions (2024-2025) to decentralize laboratories and launch educational campaigns, followed by a medium-

-term one (2026-2027) to expand training and telemedicine. In the long term (2028-2030), it is necessary to consolidate the diagnostic and treatment infrastructure, ensuring equity in access. To deal with regional disparities, equitable resource allocation and intersectoral coordination are essential. These coordinated actions are fundamental to achieving the goals of eliminating hepatitis C and promoting equitable access to care throughout Brazil.

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CRediT author Statement

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