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HEPATITIS C CARE PATHWAY IN CEARÁ: TACKLING THE DISEASE AND PROSPECTS FOR ELIMINATION

LINHA DE CUIDADOS DA HEPATITE C NO CEARÁ: ENFRENTAMENTO DA DOENÇA E EXPECTATIVAS DE ELIMINAÇÃO

LÍNEA DE CUIDADOS DE LA HEPATITIS C EN CEARÁ: ENFRENTAMIENTO DE LA ENFERMEDAD Y PERSPECTIVAS DE ELIMINACIÓN

Luiz Alberto de Freitas Júnior[1], *Larissa Peixoto Teixeira*[2], *Danilo Dias Avancini*[3], *Francisco Sérgio Rangel de Paula Pessoa*[4], *Ítalo José Mesquita Cavalcante*[5], *José Milton de Castro Lima*[6], *Elodie Bomfim Hyppolito*[7]

ABSTRACT

Objective: To evaluate the hepatitis C care cascade in Ceará by diagnosing the current stage of the state regarding the World Health Organization's elimination targets. **Methods:** Retrospective, ecological, analytical study assessing hepatitis C in Ceará from 2000 to 2024 regarding case notifications, treatments, liver transplants, and deaths. Local, state, and national databases were used. **Results:** It is estimated that 44,837 individuals have been infected with hepatitis C in Ceará. Only 2,893 cases were reported from 2000 to 2023. Of these, 1,734 (61.8%) patients were treated with direct-acting antiviral drugs. There were 560 liver transplants and 560 deaths reported due to hepatitis C. **Conclusions:** Ceará reported a small fraction of the estimated hepatitis C cases and treated most of them. The low number of deaths and notifications suggests the need to expand testing and surveillance for this disease in Ceará, aiming for elimination by 2030.

Keywords: *Hepatitis C; Mortality; Epidemiologic surveillance; Adherence to treatment; Liver transplantation.*

RESUMO

Objetivo: Avaliar a linha de cuidado da hepatite C no Ceará, realizando um diagnóstico de qual estágio o estado se encontra em relação às metas de eliminação da Organização Mundial da Saúde. **Métodos**: Estudo retrospectivo, ecológico, analítico, avaliando a hepatite C no Ceará entre 2000 a 2024 quanto às notificações de casos, tratamentos, transplantes de fígado e óbitos. Foram utilizadas bases de dados locais, estaduais e nacionais. **Resultados**: Estima-se que existam 44.837 indivíduos tenham se contaminado por hepatite C no Ceará. Apenas 2.893 casos foram notificados de 2000 a 2023. Destes, 1734 (61,8%) pacientes foram tratados com as drogas antivirais de ação direta. Foram notificados 560 transplantes hepáticos e 560 óbitos por hepatite C. **Conclusões**: O Ceará notificou uma pequena parcela dos pacientes estimados com hepatite C e tratou a maior parte deles. O baixo número de óbitos e notificações de hepatite C sugerem a necessidade de ampliação da testagem e vigilância para essa doença no Ceará, objetivando a eliminação deste agravo até 2030.

Descritores: *Hepatite C; Mortalidade; Vigilância Epidemiológica; Submissão ao Tratamento; Transplante de Fígado.*

RESUMEN

Objetivo: Evaluar la cadena de atención de la hepatitis C en Ceará, realizando un diagnóstico del estado actual en relación con las metas de eliminación de la Organización Mundial de la Salud. **Métodos:** Estudio retrospectivo, ecológico y analítico que evalúa la hepatitis C en Ceará entre 2000 y 2024 en cuanto a notificaciones de casos, tratamientos, trasplantes de hígado y defunciones. Se utilizaron bases de datos locales, estatales y nacionales. **Resultados:** Se estima que 44.837 individuos se han infectado con hepatitis C en Ceará. Solo 2.893 casos fueron notificados entre 2000 y 2023. De estos, 1.734 (61,8%) pacientes fueron tratados con fármacos antivirales de acción directa. Se notificaron 560 trasplantes hepáticos y 560 defunciones por hepatitis C. **Conclusiones:** Ceará notificó una pequeña fracción de los casos estimados de

[1] Universidade Federal do Ceará, Faculdade de Medicina. Fortaleza/CE - Brasil.
[2] Universidade de Fortaleza, Faculdade de Medicina. Fortaleza/CE - Brasil.
[3] Universidade Federal do Ceará, Faculdade de Medicina. Fortaleza/CE - Brasil.
[4] Secretaria da Saúde do Estado do Ceará, Hospital Geral de Fortaleza. Fortaleza/CE - Brasil.
[5] Secretaria da Saúde do Estado do Ceará, Laboratório Central do Estado do Ceará. Fortaleza/CE - Brasil.
[6] Universidade Federal do Ceará, Faculdade de Medicina, Departamento de Medicina Clínica. Fortaleza/CE - Brasil.
[7] Universidade Federal do Ceará, Hospital Universitário Walter Cantídio. Fortaleza/CE - Brasil.

hepatitis C y trató a la mayoría de ellos. El bajo número de defunciones y notificaciones sugiere la necesidad de ampliar la detección y vigilancia de esta enfermedad en Ceará, con el objetivo de su eliminación para 2030.
Descriptores: *Hepatitis C; Mortalidad; Vigilancia epidemiológica; Adherencia al tratamiento; Trasplante de Hígado.*

INTRODUCTION

Hepatitis C virus (HCV) infection is a major public health concern in Brazil and worldwide, historically representing the leading indication for liver transplantation (LT), followed by non-alcoholic steatohepatitis and alcoholic liver disease[1-2]. Most patients were infected before the 1980s through parenteral exposure (such as blood transfusions or intravenous drug use), a period preceding the implementation of universal precaution measures and anti-HCV serological screening in blood banks[3]. Currently, new cases primarily occur via parenteral routes among people who use drugs and healthcare professionals exposed to occupational accidents, as well as through sexual transmission in individuals with multiple partners or sexually transmitted infections. Vertical transmission during childbirth or breastfeeding is less common[4].

In 2015, it was estimated that 71 million people globally were living with hepatitis C, with the majority undiagnosed or without access to treatment[3]. Approximately 55% to 85% of infected individuals develop chronic infection, and about 20% of these progress to cirrhosis within 20 to 30 years. Among those with cirrhosis, 1% to 4% per year develop hepatocellular carcinoma (HCC)[4].

The introduction of second-generation direct-acting antivirals (DAAs) in 2014 significantly reduced HCV-related mortality and liver transplantation rates. These agents were incorporated into the Brazilian Unified Health System (SUS) in October 2015[5]. Prior to that, treatment was based on interferon and ribavirin, which were associated with low sustained virologic response (SVR) rates and significant adverse effects such as fever, flu-like symptoms, and depression[6].

Several studies have attempted to estimate the disease prevalence in various regions. Salari et al. (2022), in a meta-analysis, estimated a global prevalence of 1.8%, contrasting with World Health Organization (WHO) data suggesting a rate above 3%[7]. In Latin America, the prevalence of anti-HCV antibodies was estimated at 1.23%[8]. In Brazil, Pereira et al. (2013) reported prevalence rates ranging from 0.5% to 1.38%, with figures between 1.7% and 3.4% in the Northeast[8-9].

According to the Brazilian Ministry of Health (MoH), the estimated prevalence of hepatitis C in the general population is 0.53% (anti-HCV positive) and 0.31% (HCV-RNA positive)[1011]. It is further estimated that approximately 700,000 people in Brazil have active HCV infection, are potentially eligible for treatment, but remain unaware of their condition[12].

In 2016, the WHO World Health Assembly approved the Global Health Sector Strategy on Viral Hepatitis, which set the goal of eliminating hepatitis C as a public health threat by 2030, a goal to which Brazil is a signatory[13]. Targets for hepatitis C include a 90% reduction in new cases, treatment of 80% of diagnosed individuals, and a 60% reduction in mortality, using 2015 as the baseline year[14-15].

Given the approach of the deadline, this study aims to assess the hepatitis C care continuum in the state of Ceará by analyzing detection, treatment, and mortality data and estimating the state's progress toward disease elimination.

METHODS

This is a retrospective, ecological, analytical, quantitative, and descriptive study. The number of reported hepatitis C cases was obtained from the Notifiable Diseases Information System (SINAN) between 2000 and 2023, as well as from the Department of HIV/AIDS, Tuberculosis, Viral Hepatitis, and Sexually Transmitted Infections (DATHI), through the Epidemiological Surveillance Unit of the Health Secretariat of the State of Ceará (SESA-CE).

The case definition of hepatitis C was based on positivity in molecular tests (quantitative or qualitative HCV-RNA) and/or serological tests (anti-HCV). Until 2014, detection of HCV-RNA was required for case notification; from 2015 onward, serological positivity (anti-HCV) alone was deemed sufficient.

Mortality data related to hepatitis C (2000–2023) were obtained from the Mortality Information System (SIM). Epidemiological bulletins published by SESA and the Brazilian Ministry of Health (MoH) were also consulted. Information regarding DAA treatment in Ceará (October 2015 to December 2023) was obtained from the SESA Pharmaceutical Assistance Coordination and hospital pharmacies of São José Infectious Disease Hospital (HSJ), Walter Cantídio University Hospital (HUWC/UFC), and Fortaleza General Hospital (HGF/SESA).

Data on liver transplants performed due to HCV were directly collected from transplant teams at HUWC/UFC and HGF/SESA-CE.

Proportion calculations were conducted to analyze notification and mortality rates, based on the population of Ceará, estimated at 8,794,957 inhabitants according to the 2021 census by the Brazilian Institute of Geography and Statistics (IBGE).

To estimate the expected number of cases, a national prevalence of 0.5% was used as a proxy, a strategy supported by widely accepted epidemiological methodologies such as those employed in the Global Burden of Disease (GBD) studies, which apply the DisMod-MR 2.1 statistical model for subnational projections using national and regional data. In contexts of limited local data, as in the present study, hierarchical extrapolation is considered valid for population-level inference, including in Brazil and for diseases such as viral hepatitis[16].

The study was approved by the Research Ethics Committee of HUWC/UFC under CAAE 81962424.8.0000.5045, in accordance with the principles of the Declaration of Helsinki. Data not covered by the approved protocol are publicly available through official epidemiological surveillance sources.

RESULTS

INCIDENCE AND PREVALENCE

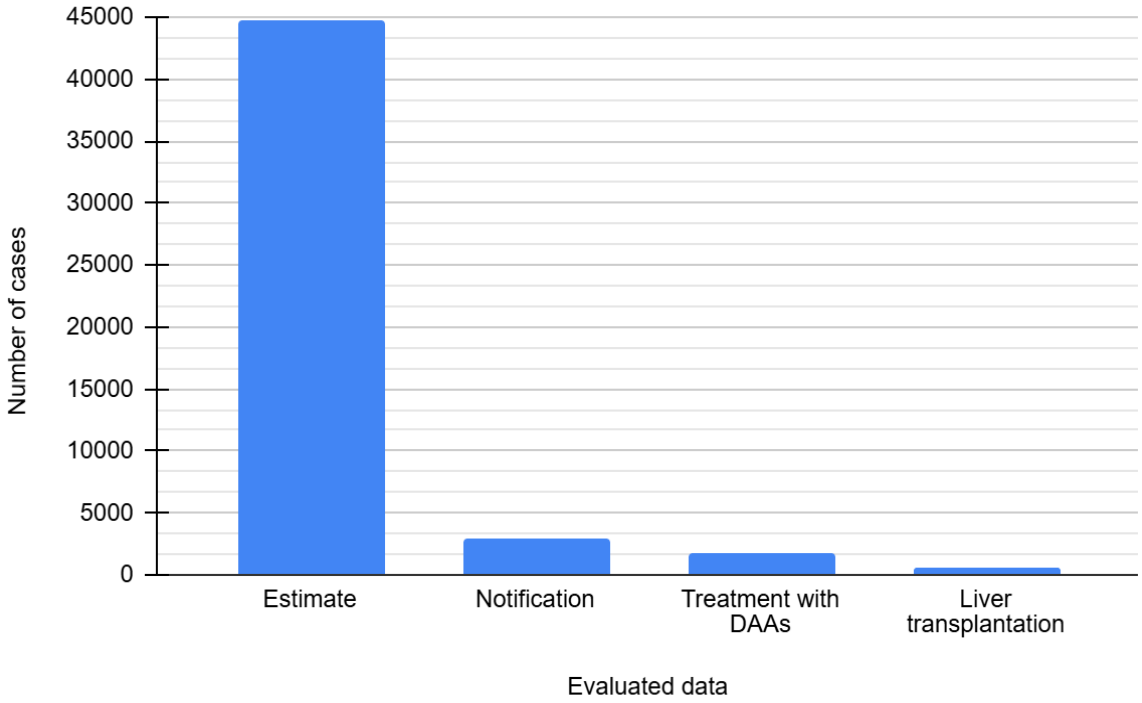
Throughout the historical series, hepatitis C consistently showed higher detection rates than hepatitis A and B, with temporal variations. In 2023, the most recent year with complete data, the detection rate was 2.3 cases per 100,000 inhabitants[17]. According to

DATHI/SINAN, from 2000 to 2023, a total of 2,893 cases of hepatitis C were reported in Ceará, with 237 cases in 2015 and 210 in 2023—an 11% reduction.

Considering only cases confirmed by both anti-HCV and detectable PCR, 2,076 notifications were recorded. When including individuals with either anti-HCV positivity or detectable HCV-RNA, the total reached 4,051 notified cases in the state[18].

Based on an estimated prevalence of 0.5% and the state population according to the 2021 census, approximately 44,837 individuals in Ceará are estimated to be infected with hepatitis C. Therefore, even under the broadest diagnostic criteria, the number of notified cases represents a significantly smaller fraction of the estimated total (Figure 1).

Figure 1 - Hepatitis C Care Pathway In Ceará



Source: authors' elaboration

TREATMENT

A total of 1,734 patients were treated with DAAs according to records from HSJ, HUWC, HGF, and other services—approximately 60% of the cases reported to SINAN. Notably, only 26.3% of treated patients resided in the interior regions of the state[19].

The average number of treatments dispensed per month declined over time: in 2019, HSJ dispensed an average of 9 treatments monthly, while in 2023, this number dropped to 2. This study did not include patients treated with pegylated interferon and ribavirin, regimens used before 2015.

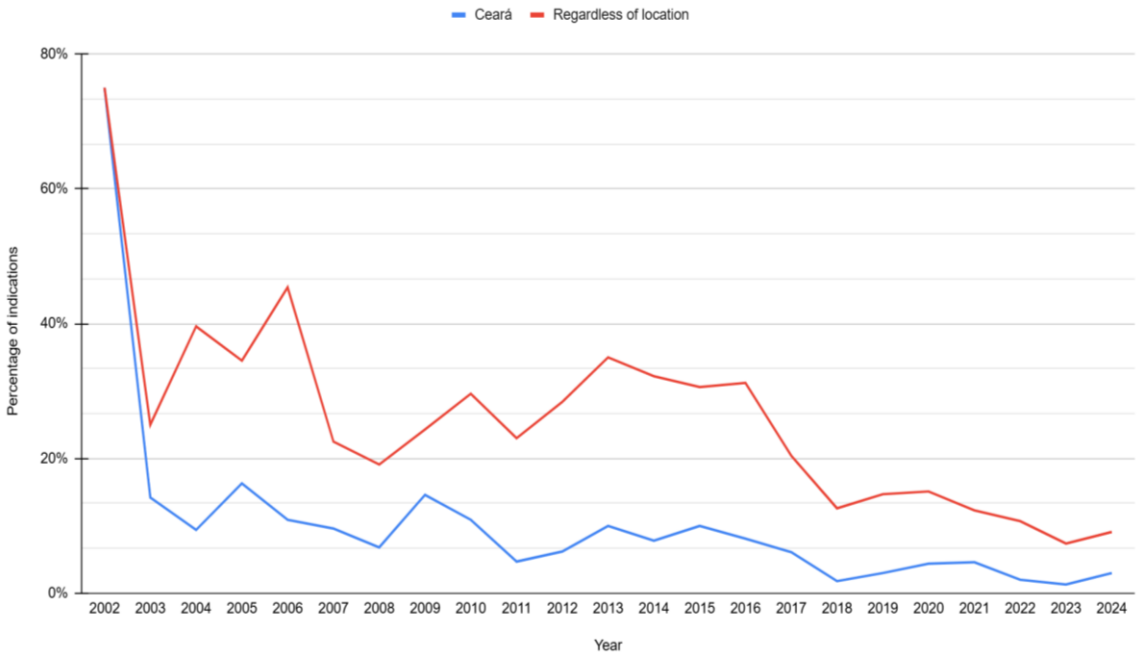
LIVER TRANSPLANTATION

Ceará has two active liver transplant teams. Between May 2002 and December 2024, the team at HUWC/UFC performed 2,521 transplants, of which 560 (22%) were indicated for hepatitis C - the second leading etiology after alcoholic liver disease. Indications for HCV showed a progressive decline over the years, reaching the lowest

percentage in the historical series in 2023, even when analyzing only patients from within the state (Figure 2).

At HGF, 798 transplants were performed between December 2009 and December 2024. However, the exact number of transplants performed due to hepatitis C at this unit could not be determined as of the time of this report[19].

Figure 2 - Evolution of the percentage of liver transplants for HCV performed by the HUWC-UFC team (2002–2024), stratified by recipient origin



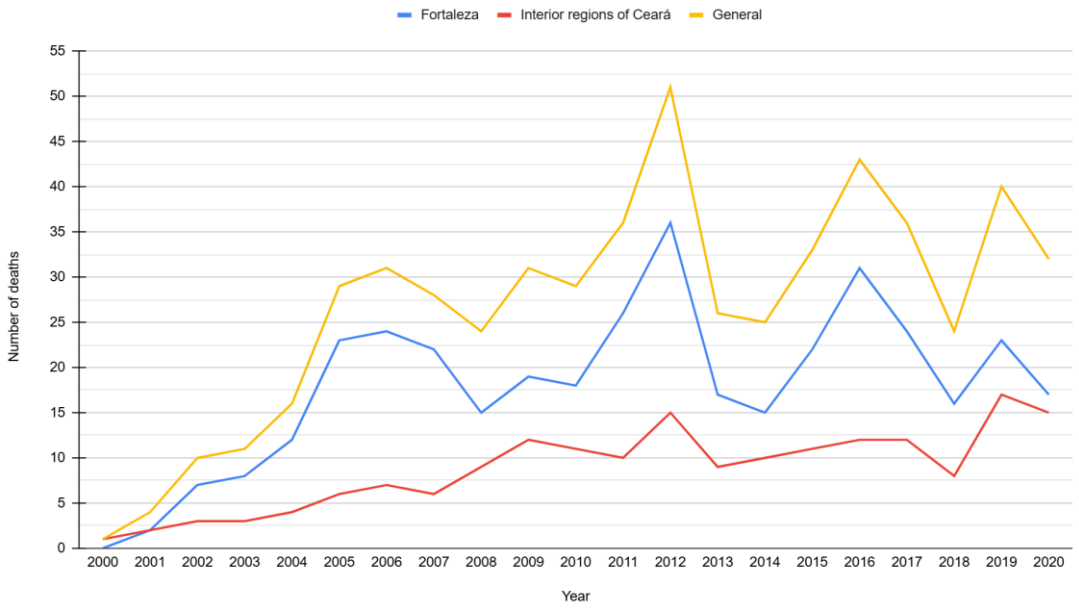
Source: HUWC-UFC Liver Transplant Team RedCap Database (2025)

MORTALITY

Although the absolute number of hepatitis C–related deaths increased in Brazil between 2000 and 2022, the national mortality coefficient decreased to 0.5 deaths per 100,000 inhabitants in 2022[3]. In Ceará, this figure was 0.2—the same observed in 2015, which is the WHO's reference year[17].

According to SIM, 560 hepatitis C–related deaths were recorded in Ceará between 2000 and 2020, with a higher concentration in the capital compared to inland municipalities, except in the first year of the series. During this period, 75 out of 184 municipalities (40.8%) reported at least one death, with notable concentrations in the capital, its metropolitan area, and the Cariri region[19-20]. The local and temporal distribution of deaths is shown in Figure 3, with similar trend lines for Fortaleza and inland municipalities. Since 2015, data show fluctuations without a clear downward trend.

Figure 3 – Distribution of Hepatitis C–related deaths in Ceará by location (2000–2020)



Source: authors' elaboration

DISCUSSION

Understanding the hepatitis C care continuum in Ceará requires a historical review of the assistance provided to individuals with this condition in the state. Until recently, only three specialized outpatient clinics for viral hepatitis operated in Fortaleza: the pioneering clinic at HUWC/UFC, the General Hospital of Fortaleza (HGF), and the São José Hospital for Infectious Diseases (HSJ). Subsequently, additional services were incorporated into patient care, including the Integrated Medical Care Center (NAMI) at the University of Fortaleza (UNIFOR), the outpatient clinic at Unichristus, three polyclinics (Lusmar Veras, Eloy Costa, and Dr. Luiz Carlos Fontenele), and the Reference Center for Infectious Diseases in Sobral[21].

Despite the limited number of decentralized services, Ceará was among the first Brazilian states to begin dispensing DAAs, in October 2015. After decades of interferon- and ribavirin-based therapies—characterized by low efficacy and high toxicity—the free availability of highly effective and well-tolerated antiviral medications marked a significant milestone in the fight against hepatitis C. Local studies have documented cure rates around 96%, even among transplanted and HIV-coinfected patients[22-23].

One of the main limitations of this study is the temporal heterogeneity of the data sources analyzed. Nevertheless, cross-referencing the available data allowed us to estimate the state's progress toward hepatitis C elimination.

The estimated number of HCV cases in Ceará was considerably higher than the number of cases reported to SINAN, suggesting significant underdiagnosis. The incidence rate also remained below the national average. According to the 2023 Viral Hepatitis Epidemiological Bulletin, detection rates in Ceará and its capital were approximately 2.5 and 5 cases per 100,000 inhabitants, respectively, while the national average was 7.63. Two hypotheses may explain this scenario: local underreporting or overestimation of national prevalence relative to the Ceará context.

The first hypothesis is supported by the literature. Previous studies have identified structural weaknesses in hepatitis C surveillance in Brazil, with substantial underreporting of cases[24]. The second hypothesis is less plausible considering that most treatments were concentrated in the capital, possibly due to limited testing capacity in inland municipalities and barriers to accessing specialized care. This situation reflects the socioeconomic disparities and inequalities in healthcare access seen across different regions of the country[25].

Underreporting may also affect cases of HIV coinfection. Although the Ministry of Health reported a decline in HCV-HIV coinfection prevalence from 8% in 2011 to 7.3% in 2022[3], a study by Távora et al. (2008) at HSJ—a reference center for HIV/AIDS in Ceará—found 6.9% of patients were coinfected, with 5.4% presenting active HCV infection[26].

Regarding mortality, the limited number of notifications restricts the evaluation of real trends in death reduction. Challenges in testing and surveillance in inland areas contribute to this bias. Hyppolito et al. (2025) showed lower HCV-related mortality rates outside Brazilian capitals, particularly in municipalities with low Human Development Index (HDI), which may reflect deaths due to cirrhosis or HCC without a confirmed HCV diagnosis[27].

Analysis of the mortality coefficient shows stability between 2015 and 2023 (0.2 deaths per 100,000 inhabitants), a value that falls short of the WHO target of a 60% reduction, indicating a slow pace toward disease elimination.

Although 60% of reported patients were treated with DAAs, this figure remains below the 80% target. The decline in the number of treatments at HSJ (see Results), without a proportional decrease in detection rates, suggests possible undertreatment. This hypothesis is consistent with findings from other studies linking such scenarios to insufficient funding and inadequate healthcare infrastructure[28].

Indications for liver transplantation due to hepatitis C have shown a downward trend in Ceará—a phenomenon attributed to the efficacy of DAAs in controlling hepatic inflammation and preventing disease progression. This pattern mirrors international trends[29]. The reduction in transplant indications represents a positive outcome, demonstrating the local health system's capacity to provide effective curative treatment.

Considering that hepatitis C is a condition that can be diagnosed using widely available methods and treated with effective, safe, and free therapies, it is essential to develop strategies to address weaknesses across different levels of care in identifying and treating infected individuals early. With fewer than five years remaining until the WHO's 2030 target, the current pace in Ceará remains insufficient to achieve hepatitis C elimination.

CONCLUSION

The analysis of the hepatitis C care continuum in the state of Ceará reveals a scenario of underreporting and underdiagnosis, with the number of reported cases and deaths falling below the estimates provided by the Ministry of Health. This highlights the urgent need to strengthen diagnostic and surveillance strategies, particularly in municipalities located outside the state capital.

The proportion of patients treated with direct-acting antivirals (DAAs) corresponds to the majority of notified cases, representing a significant advance. However, the decline in the number of treatments in recent years points to a possible decrease in the detection of new cases or failures in referring diagnosed patients for treatment, both of which warrant attention from public health authorities. A reduction in HCV-related liver transplant indications was also observed following the incorporation of DAAs, indicating a positive impact of the new therapies on the natural history of the disease.

Despite the progress made, the data analyzed show that the state remains far from achieving the goal of eliminating hepatitis C as a public health problem, as proposed by the World Health Organization. Priority strategies include expanding anti-HCV and HCV-RNA testing in primary healthcare units, strengthening case reporting, and decentralizing access to specialized treatment. Making antiviral therapy available at the same location where the diagnosis is made, fully integrated into the primary care network, is an essential measure to accelerate progress toward eliminating hepatitis C in Ceará by 2030.

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