

## Early diagnosis of hepatitis C by primary health care

## Diagnóstico precoce da hepatite C pela atenção primária à saúde

## Diagnóstico precoz de la hepatitis C por parte de la atención primaria a la salud

Received: 17/01/2020

Approved: 04/09/2020

Published: 03/03/2021

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This is an exploratory, descriptive, cross-sectional, retrospective study with an epidemiological approach, carried out in primary health care units in the city of Uberaba between 2014 and March of 2017. It aimed to know the prevalence and positivity of the Anti-hepatitis C antibody in adult population over 40 years. 17,845 people were tested using the immunochromatographic test and then the 131 positives were tested for genotyping and liver fibrosis staging. It was found 0.73% of positives, 79.3% of whom were born in the 1950s to 1970s; and 24% had moderate liver fibrosis, advanced liver fibrosis or cirrhosis. The most cited forms of transmission were drug use (any route); multiple sexual partners and transfusions, hemodialysis or organ transplantation. It is important to train professionals in the primary care network on the importance of hepatitis C, its early diagnosis and priority risk groups, in addition to providing greater access to diagnosis.

**Descriptors:** Primary health care; Hepatitis C; Prevalence; Epidemiology; Early diagnosis.

Trata-se de um estudo exploratório, descritivo, transversal, retrospectivo, de abordagem epidemiológica, realizado nas unidades de atenção primária à saúde de Uberaba entre 2014 e março de 2017, com objetivo de conhecer a prevalência e positividade do anticorpo Anti-hepatite C na população adulta acima de 40 anos. Foram testadas 17.845 pessoas através do teste de imunocromatográficos e, depois, aos 131 positivos aplicou-se o teste de genotipagem e estadiamento da fibrose hepática. Encontrou-se 0,73% de positivos, sendo 79,3% nascidos nas décadas de 1950 a 1970; e 24% apresentavam fibrose hepática moderada, avançada ou cirrose. As formas de transmissão mais citadas foram uso de drogas (qualquer via); múltiplos parceiros sexuais e transfusões, hemodiálise ou transplante de órgãos. É importante capacitar os profissionais da rede de atenção primária sobre a importância da hepatite C, de seu diagnóstico precoce e dos grupos de risco prioritários, além de propiciar a ampliação do acesso ao diagnóstico.

**Descritores:** Atenção primária à saúde; Hepatite C; Prevalência; Epidemiologia; Diagnóstico precoce.

Se trata de un estudio exploratorio, descriptivo, transversal, retrospectivo, con enfoque epidemiológico, realizado en las unidades de atención primaria a la salud de Uberaba entre 2014 y marzo de 2017, con el objetivo de conocer la prevalencia y positividad del anticuerpo contra el virus hepatitis C en la población adulta mayor de 40 años. Un total de 17.845 personas se sometieron a la prueba inmunocromatográfica, y después se aplicó una prueba de genotipado y estadificación de la fibrosis hepática a los 131 positivos. Se encontró 0,73% positivos, de los cuales 79,3% nacieron entre los años 1950 y 1970; y el 24% tenían fibrosis hepática moderada, avanzada o cirrosis. Las formas de transmisión más citadas fueron el consumo de drogas (por cualquier vía); las parejas sexuales múltiples y las transfusiones, la hemodiálisis o el trasplante de órganos. Es importante formar a los profesionales de la red de atención primaria sobre la importancia de la hepatitis C, su diagnóstico precoz y los grupos de riesgo prioritarios, así como aumentar el acceso al diagnóstico.

**Descritores:** Atención primaria de salud; Hepatitis C; Prevalencia; Epidemiología; Diagnóstico precoz.

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## INTRODUCTION

It is estimated that around 70 million people are infected with the hepatitis C virus (HCV) in the world, which today is considered a global public health problem by the World Health Organization (WHO)<sup>1</sup>.

Hepatitis by virus C is a curable disease, but it is often underdiagnosed. It is associated with several hepatic and extrahepatic manifestations, including malignant tumors<sup>2,3</sup>. It progressed to chronic hepatitis in 55 to 85% of cases, of which 30% of patients develop liver cirrhosis in about 20 years, and 2 to 4% of these develop into hepatocellular carcinoma every year. The natural history of HCV is affected by several demographic, virological, clinical and lifestyle factors. It is important to understand the determinants of the virus's impact to plan appropriate strategies for detection, prognosis and treatment<sup>4</sup>.

International goals were established for the elimination of viral hepatitis as a threat to public health by the year 2030, underscoring the urgent need to improve the search for cases. The need to increase the diagnosis of HCV has also become more relevant as a result of the increasing availability and success of direct-acting antiviral treatment.

Globally, only 15 to 20% of individuals with chronic HCV infection are currently considered aware of their diagnosis, and even fewer are receiving treatment<sup>5</sup>. Under these circumstances, WHO, through the Global Health Sector Strategy on Viral Hepatitis 2016–2021: Towards Ending Viral Hepatitis, establishes that it is crucial to develop a strong strategic information system to understand viral hepatitis epidemics and develop an effective response<sup>6</sup>.

In 2012, the United States Centers for Disease Control and Prevention recommended the use of tests for all individuals born between 1945 and 1965 (Baby Boomers), because about three quarters of HCV infections were identified in this age group by the National Health and Nutrition Survey (NHANES)<sup>7,8</sup>.

In 2019, the Ministry of Health (MH) published the Plan for Elimination of Hepatitis C in Brazil (*Plano para Eliminação da Hepatite C no Brasil*), which aims to expand access to prevention, diagnosis and treatment of hepatitis C. It involved the participation of all three spheres of government for the reduction of new infections and mortality. The following were also defined: development of communication and health education actions that promote diagnosis in the population older than 40 years of age and priority groups; construction of a line of care for viral hepatitis and strengthening of epidemiological surveillance<sup>9</sup>.

The MH proposes an increase in the number of people tested, prioritizing groups according to their vulnerability, for example: people with HIV/AIDS, incarcerated individuals, drug users, people with multiple sexual partners and those on dialysis, among others must be tested at least once a year. For people aged 40 or older, those with tattoos and/or piercings, those exposed to biological material, and children of a carrier mother, testing is recommended at least once in their lives<sup>9</sup>.

In Brazil, studies show that the diagnosis of HCV increases in prevalence after the fourth decade of life, and the diagnosis happens between the ages of 46 and 60 years in almost half of the patients, with peak prevalence at the age of 50-60 years. Population-based prevalence study carried out in Brazilian capitals between 2005 and 2010 found a global prevalence of Anti-HCV of 1.38% (95% CI 1.12% -1.6%) and, for the Southeast region of the country, the prevalence found was 1.27%<sup>10-12</sup>.

According to the results of the epidemiological survey, the state of Minas Gerais has an identified prevalence of 2.47% for the Macroregion of the Triângulo Sul<sup>13</sup>. This result needs to be questioned, since the behavior of grievance at the national level is projected to reduce incidence. Considering the local organization of health services, assistance network, critical and intellectual mass of the region (training centers and medical and health faculties), in addition to the economy of the region, the indicator found must be questioned.

In a recent investigation with 24,085 adults who live in the Macro-region of Triângulo Sul in the state of Minas Gerais, they were tested for the Anti-HCV antibody, with a prevalence of

0.76%. Most positive individuals were born between 1951 and 1980, and the most prevalent risk groups were those who share needles and syringes for drugs and/or medicines, are or have been incarcerated and have tattoos or piercings<sup>14</sup>.

It is observed the existence of scientific productions that define the prevalence of the virus at the international and national levels. However, few studies describe this prevalence in specific locations. This knowledge is a crucial aspect for the management of actions, strengthening of initiatives: case tracking, active search, monitoring and insertion of patients, in the appropriate treatment segments. Thus, this study aims to know the prevalence and positivity of the Anti-hepatitis C antibody in the adult population over 40 years.

## METHOD

This is an exploratory, descriptive, cross-sectional, retrospective study with an epidemiological approach.

The data analyzed in this study are part of the Hepatitis C Diagnosis Expansion Program at the Hepatitis Outpatient Clinic of the Hospital de Clínicas of the Universidade Federal do Triângulo Mineiro (HC-UFTM), in partnership with the Brazilian Society of Hepatology (*Sociedade Brasileira de Hepatologia* - SBH), carried out between 2014 to March 2017 in order to track new cases of Hepatitis C in the city of Uberaba.

The program's proposal, in addition to the diagnosis of Hepatitis C, was to train the health care network to identify risk groups. The triage nurses, members of the Primary Care teams, were previously trained on the importance of early diagnosis and complications of the disease, on the performance of tests and filling in a control form for positive and negative, including the recording of test losses, as well as sociodemographic and epidemiological data of positives, such as decade of birth, gender and risk groups.

The minimum age to participate in the campaign was 18, with individuals over 40 being intentionally encouraged.

The rapid tests used were immunochromatographic for qualitative detection of specific antibodies against HCV in human serum, plasma or whole blood (ALERE HCV® Code 02FK10); having 100% sensitivity and 99.4% specificity, according to manufacturer information.

To the individuals who tested positive for Hepatitis C, the health agents welcomed them and offered the follow-up at the HC-UFTM Hepatitis Outpatient Clinic with the assistance team. Following the Clinical Protocol and Therapeutic Guidelines for Hepatitis C and Co-infections (*Protocolo Clínico e Diretrizes Terapêuticas para Hepatite C e Coinfecções* - PCDT) of the MH implanted in service, molecular biology research (quantitative RNA-HCV and genotyping) for the C virus was carried out for these patients, in addition to liver fibrosis staging.

The quantitative research of RNA-HCV was carried out by the Macrorregional Laboratory of Uberaba, linked to the State Department of Health, it is done by the RT-PCR method in real time, using the Real Time HCV® kit from the Abbott laboratory; and the genotyping of the virus was developed by the Centro de Genomas, in partnership with the State Health Department of Minas Gerais, carried out using the RT-PCR method in real time, using the HCV Real Time Genotype II® kit from the Abbott laboratory.

Still within the PCDT, the staging of the degree of fibrosis was performed for all patients infected with HCV, co-infected or not with HIV, in order to characterize absence or presence of advanced disease and definition of the therapeutic strategy. This could be done by any of the available methods: APRI or FIB4, liver biopsy or hepatic elastography<sup>16</sup>.

According to IBGE, the location of this study, Uberaba, has an estimated population of 333,783 people in 2019, with a demographic density in 2010 (last census) of 65.43 inhabitants/km<sup>2</sup>. In 2017, the average monthly salary was 2.6 minimum wages. GDP per capita in 2016 was R\$ 41,360.17, 97.2% of households have adequate sanitation, 90.7% of urban households on public roads with afforestation and 31.5% of urban households on public roads with urbanization (presence of manhole, sidewalk, pavement and curb)<sup>15</sup>. In order to assess the

general prevalence of Hepatitis C, the 17,845 people tested in that period were considered.

As for the distribution by year and sociodemographic and epidemiological profile, positive cases for Anti-HCV were considered. Duplicate tests, tests performed on people who did not live in the city and also information related to people who presented negative results for the rapid testing of Anti-HVC were excluded from the analysis.

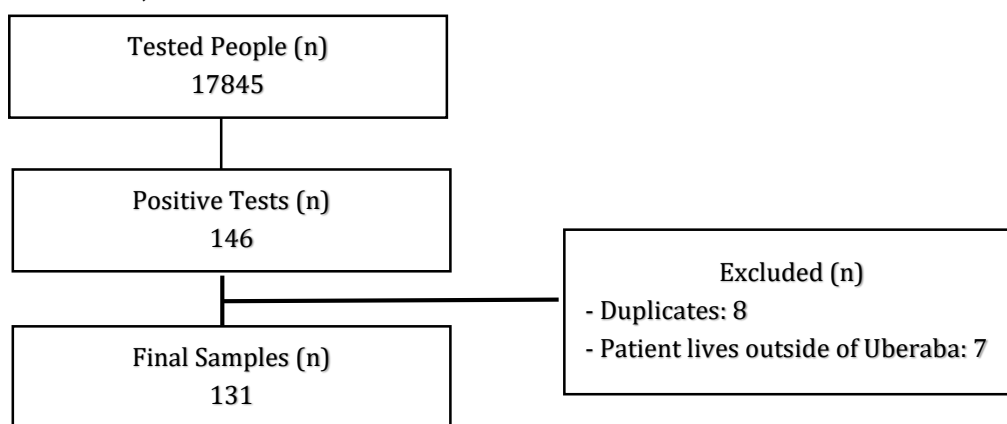
Univariate descriptive statistical analysis was used based on absolute and percentage frequencies and the results were organized in tables and graphs. Excel® and StatSoft software. Inc. (2007) - STATISTICA were used.

The project was approved by the Research Ethics Committee of the Universidade Federal do Triângulo Mineiro in accordance with the Brazilian resolution of the National Health Council No. 466/2012, which deals with research on human beings, under registration with CAAE No. 68312717.5.0000.5154 and opinion of approval no. 2,394,876.

## RESULTS

According to data from the Hepatitis C Diagnosis Expansion Program at the HC-UFTM Hepatitis Clinic in partnership with SBH, carried out between 2014 and March 2017, 400 rapid tests for the detection of hepatitis C were distributed to each of the 30 Basic Health Units (UBSs) existing in the Municipality in 2014, totaling 12,000 tests, when the testing started. Subsequently, the Municipal Health Secretariat and HC-UFTM promoted campaigns in squares and boardwalks, integrating Hepatitis C testing with other events such as World Health Day, Health Week, Pink October, Blue November, among others, with a total of 17,845 tests performed (Figure 1).

**Figure 1.** Flowchart of the tested population, exclusions and final sample from 2014 to 2017. Uberaba, Minas Gerais, 2020.



For the follow-up of the target population, the 131 positive cases were welcomed by the previously trained Primary Care teams and sent to the HC-UFTM Hepatitis Outpatient Clinic, without a waiting line to schedule appointments.

At the outpatient clinic, these patients were instructed on the importance of the diagnosis even in the asymptomatic phase, the risks of the absence of medical monitoring and the therapeutic possibilities. After anamnesis and physical examination, the complementary exams recommended by the PCDT 2012, updated in 2015, 2017, 2018 and 2019, were requested. Municipal Primary Care Directorate. Thus, absences from consultations were reduced.

The city of Uberaba is divided into Sanitary Districts I, II and III (Figure 2). Of the 17,845 tests carried out, 8,106 people had their addresses recorded, with the housing district identified. For the rest of the people tested (9,739) it was not possible to recover their home address. Of the 131 positives, it was possible to recover the address of 125 (Table 1).

**Figure 2.** Sanitary districts of Uberaba/MG, Brazil. 2020.



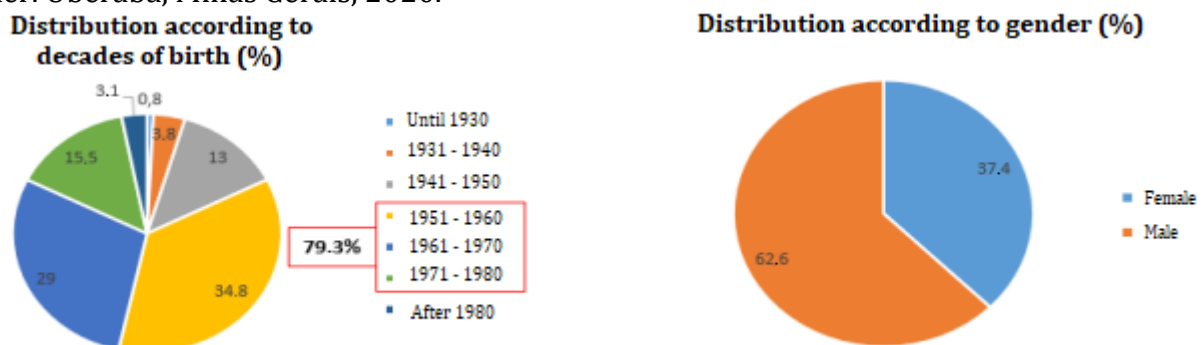
Source: POWER MAP. Key: I - Sanitary district I; II – Sanitary district II; III – Sanitary district III.

**Table 1.** Prevalence of Anti-HCV reagent according to district of residence. Uberaba, Minas Gerais, 2020.

Sanitary districts	Positive tests (n)	Tests performed (n)	Prevalence in district (%)
DS I Abadia	62	2,738	2.26
DS II Mercês	28	3,183	0.87
DS III Boa Vista	35	2,185	1.60
No address	6	9,739	0.06
<b>Total</b>	<b>131</b>	<b>17,845</b>	<b>0.73</b>

The present study found 0.73% of Anti-HCV positive in 17,845 people tested in the city of Uberaba. Among the positives, 62.6% were men and 79.3% were born in the 1950s, 1960s and 1970s (Graph 1). A quarter of the positive for Anti-HCV had moderate, advanced fibrosis or cirrhosis and 71.3% had genotype 1 of the virus (Graph 2).

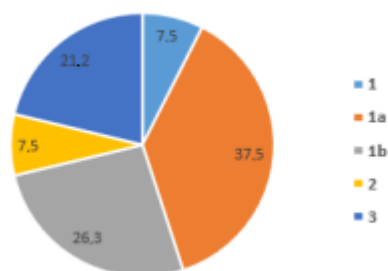
**Graph 1.** Anti-HCV positive from 2014 to March 2017, according to the decade of birth and gender. Uberaba, Minas Gerais, 2020.



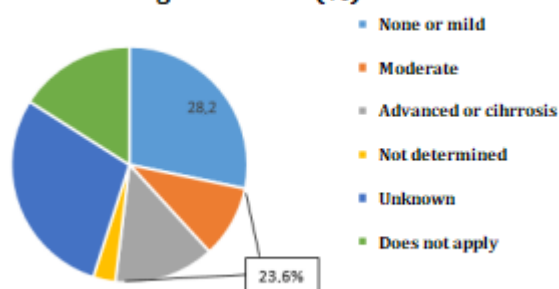


**Graph 2.** Anti-HCV positive from 2014 to March 2017, according to virus C genotype and fibrosis stage. Uberaba, Minas Gerais, 2020.

**Distribution according to genotype (%)**



**Distribution according to stage of fibrosis (%)**



Regarding forms of transmission (risk groups), some people had more than one possible way of acquiring the virus, while others belonged to no identifiable risk group (Table 2). The most cited forms of transmission were: 1) current or previous use of drugs (by any means); 2) multiple sexual partners without a condom; 3) blood transfusion or blood products, hemodialysis or organ transplantation (iatrogenic transmission). To a lesser extent, the following risk groups were identified: tattoos or piercings; surgery or injection with non-disposable material; having HBV and/or HIV (Table 2).

**Table 2.** Forms of transmission or risk groups of people positive for Anti-HCV from 2014 to March 2017. Uberaba, Minas Gerais, 2020.

Risk group*	n	(%)
User of illicit drugs	24	18.32
Multiple sexual partners	23	17.55
Blood transfusion/Dialysis or Transplant	20	15.26
Tattoo/Piercing	14	10.68
Iatrogeny (syringes/surgery)	10	7.63
Has HIB and/or HBV	9	6.87
Occupational risk	6	4.58
Carrier in the family	5	3.81
Incarcerated	3	2.29
Mother is a carrier	2	1.52
Homeless	1	0.76
No risk group identified	46	35.11

\* Some people belonged to more than one age group, while some people belonged to none.

## DISCUSSION

With the availability by the Ministry of Health (MH) of direct acting antivirals, potent and safe medications for the treatment of hepatitis C, what has been causing concern is the large number of undiagnosed cases. Strategies to deal with this are necessary and researchers have tried to find the best cost-effectiveness for the diagnosis, prevention and eradication of HCV in the world.

In the municipality of Uberaba, Minas Gerais, the strategies recommended by the WHO were applied, later included in the Plan for the Elimination of Hepatitis C in Brazil, which recommend training the primary care network to diagnose the disease<sup>6,9</sup>.

The prevalence of the serological contact marker for Hepatitis C (Anti-HCV) found here (0.73%) is in line with the estimate by the MH in 2018 (0.70%), differing from previously published data, extracted from serological surveys carried out in Brazil and in the state of Minas Gerais (1.27% for Minas Gerais and 2.47% for the Triângulo Sul macro-region, respectively)<sup>12,13</sup>.

Regarding the age group of HCV carriers identified, it was observed that these individuals were born in decades similar to that described in countries such as Switzerland, USA, Spain and Brazil itself, where it was identified that those born after the Second World War had greater risk of exposure to the virus<sup>17-20</sup>. Such a finding can guide public policies for the eradication of the C virus in the municipality and shows the importance of diagnostic investigation in these age groups at all points of the health care network.

As for gender, the MH Epidemiological Bulletin, published in 2019, shows that the ratio between men and women has been falling, having dropped to 1.2 in 2018. The present study found a ratio of 1.7 with a higher prevalence for men in the central municipality of the Macrorregião do Triângulo Sul<sup>21</sup>.

The distribution of C virus genotypes among the positive ones that performed the molecular biology exams follows the same trend published for Brazil. Genotype 1 is the most prevalent in the Brazilian population, followed by genotypes 3 and 2. No genotype 4 or 5 was found<sup>20</sup>.

As for the staging of fibrosis, a Brazilian study published in 2014 showed an association between age at diagnosis and the degree of liver damage in hepatitis C, that is, the older the patient, the greater the degree of fibrosis. The present study showed that a quarter of the positive for Anti-HCV already had moderate or severe fibrosis. Knowing that Hepatitis C is a silent disease, that older people have a higher risk of advanced fibrosis or cirrhosis and are the same in which the prevalence is higher, it is urgent to expand the diagnosis and therapeutic interventions<sup>10</sup>.

This reality requires different preparation of health teams and the system in their different points of care, since health services must be prepared for rise of complications among infected populations, as well as for the management of the epidemic and its consequences. This fact makes it crucial to detect cases among the general population and identify who are the people who live with the virus and do not know.

The present study had as its main focus people over 40 years of age, that is, those born until the 1980s. However, in relation to the probable way of acquiring the virus, the most cited forms of transmission were precisely those for which the MH recommends annual testing, given the great potential for transmission, namely: current or previous use of drugs; multiple sexual partners and blood transfusion or blood products, hemodialysis or organ transplantation (iatrogenic transmission). Having tattoos or piercings; having undergone surgery or receiving injections with non-disposable material; having HBV or HIV are also part of the priority groups recommended for testing by MH<sup>9,16</sup> and were present in the study.

It is important to note that the law that prevented the reuse of syringes and needles was enacted in 1996<sup>22</sup>, although disposable products have been subject to importation since the 1970s. Therefore people born before the 1990s probably received injections with non-disposable material, and have no memory of it. Thus, during the interviews conducted by the researchers, this information may not have received the necessary importance.

The higher prevalence of positives in Sanitary District I in the municipality cannot be explained by this study, but such a finding should not be overlooked. The social vulnerability, demographic density, habits and living conditions of residents of the neighborhoods in the region deserve further investigation.

There are still global and national challenges to be faced in achieving this goal, which include inadequate surveillance data, limited prevention program coverage, few people aware of their hepatitis status and little access to treatment, drugs and diagnoses to most, public health approach to hepatitis is lacking, and unequal government leaderships and commitments<sup>6,23-25</sup>.

## CONCLUSION

The present study made it possible to know the prevalence of Hepatitis C in the municipality of Uberaba in the state of Minas Gerais, and the distribution by decade of births, risk groups and socio-demographic and epidemiological data of people tested with a positive result for HCV.

This study has as a limitation the fact that it is linked to a program that did not aim to systematize the evidence, but rather to expand the diagnosis, serve people with positive results, in addition to training the health care network.

However, the results of the research point out relevant results that can be used to guide the main groups to be tested in the city of Uberaba, such as males, living in the Sanitary District I and born in the 1950s, 1960s and 1970s. Such groups should have the attention of the Health Care Network redoubled regarding the disease Hepatitis C.

From the analysis of retrospective data from the Hepatitis C Diagnosis Expansion Program in Uberaba, it is possible to emphasize the importance of such initiatives. The Program, which found a general prevalence of 0.73%, reaching 2.26% in certain Health Districts, meets the Plan for the Elimination of Hepatitis C in the Ministry of Health.

It is important to train professionals in the primary care network on the importance of hepatitis C, its early diagnosis and priority risk groups, in addition to providing greater access to the diagnosis goals of WHO and MH.

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**Associate Editor:** Vania Del Arco Paschoal

#### CONTRIBUTIONS

**Cristina Cunha Hueb Barata Oliveira** and **Geisa Perez Medina Gomide** contributed to the design, collection and analysis of data, writing and review. **Gilberto Araújo Pereira** and **Rodrigo Juliano Molina** participated in the conception, collection and analysis of the data.

#### How to cite this article (Vancouver)

Gomide GPM, Molina RJ, Pereira GA, Oliveira CCHB. Early diagnosis of hepatitis C by primary health care. REFACS [Internet]. 2021 [cited in *insert day, month and year of access*]; 9(Suppl. 1):271-280. Available from: *insert access link*. DOI: *insert DOI link*

#### How to cite this article (ABNT)

GOMIDE, G. P. M.; MOLINA, R. J.; PEREIRA, G. A.; OLIVEIRA, C. C. H. B. Early diagnosis of hepatitis C by primary health care. **REFACS**, Uberaba, MG, v. 9, p. 271-280, 2021. Suppl. 1. DOI: *insert DOI link*. Available from: *insert access link*. Access in: *insert day, month and year of access*.

#### How to cite this article (APA)

Gomide, G.P.M., Molina, R.J., Pereira, G.A., & Oliveira, C.C.H.B. (2021). Early diagnosis of hepatitis C by primary health care. *REFACS*, 9(Suppl. 1), 271-280. Retrieved in *insert day, month and year of access* from *insert access link*. DOI: *insert DOI link*.

