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Profile of patients with chronic hepatitis C in a public health program in Southern Brazil

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ABSTRACT – **Background** – Chronic hepatitis C (CHC) can progress to cirrhosis and its complications as hepatocellular carcinoma, leading to morbidity and mortality. To know the profile of patients with CHC virus is fundamental to optimize management. **Objective** – To describe the profile of patients with CHC in a public health program in Southern Brazil. **Methods** – A retrospective study was carried out in patients with CHC who underwent treatment against hepatitis C virus in a dispensation and pharmaceutical assistance center of the Public Health Department of the State of Rio Grande do Sul, South Brazil. All medical records of patients attended between December/2015 and December/2016 were evaluated. **Results** – A total of 1,431 records of patients with CHC were evaluated. Males were the most prevalent (802; 56%) patients. The mean age was 58.6±9.9 years, ranging from 18 to 89 years. Genotype 1 was the most frequent (866;60.5%) of the patients. Ninety (6.3%) patients were transplanted from a solid organ, and of these, 73 (5.1%) were transplanted from the liver. The fibrosis evaluation was performed in 1,300 (90.8%) patients. Of these, 566 (39.6%) were evaluated through liver biopsy. Regarding the degree of fibrosis, 779 (54.4%) presented fibrosis grade 4 (cirrhosis). The genotype 3 was the most associated with fibrosis grade 4, and genotype 1 was associated with high viral load. **Conclusion** – The present study made possible the evaluation of the characteristics of patients with CHC in a public health program in South Brazil. There was a predominance of CHC in males, and the mean age was 59 years. They presented a predominance of genotype 1, higher viral load in patients with genotype 1 and greater degree of fibrosis in patients with genotype 3.

HEADINGS – Chronic hepatitis C. Epidemiology. Sustained virologic response.

INTRODUCTION

It is estimated that about 115 million people worldwide have anti-HCV positive antibody, corresponding to a world prevalence of 1.6%. The prevalence of truly viraemic people is estimated at 1.1%, equivalent to about 80 million people in the world with chronic hepatitis C (CHC) infection[1].

The CHC is considered to be of low prevalence in many countries as the United Kingdom, Scandinavia, North America, Western Europe, Australia and South Africa (0.2% to 0.5%). On the other hand, the regions most affected are those in the Mediterranean and Eastern Europe, with a prevalence of 2.3% and 1.5%, respectively[1].

In Brazil, approximately 10,000 cases are notified each year. A population-based study on hepatitis A, B and C virus infections in Brazilian capitals found an anti-HCV prevalence of 2.1% in the Northern Region; 0.7% in the Northeast; 1.3% in the Midwest; 1.3% in the Southeast; 1.2% in the Southern Region; and 0.8% in the Federal District[2].

Hepatitis C vírus (HCV) is primarily transmitted parenterally, more often through the sharing of injection material among illicit drug users, due to the reuse or inadequate sterilization of medical equipment in health services, blood transfusions or blood products without analysis[3].

In general, acute infection is asymptomatic and is rarely associated with a potentially fatal disease. Approximately 15% to 40% of infected people acutely eliminate the virus spontaneously within six months, without the need for any treatment. The remaining 60% to 85% will develop chronic infection if not treated, with a risk of developing cirrhosis in 15% to 30% of cases[4].

The treatment of chronic hepatitis C has undergone rapid evolution. Treatment with direct-acting antiviral drugs (DAA) can cure most people infected with HCV in a short-course (usually 12 or 24 weeks), with sustained virological response rates above 90% in most cases[5-7].

In this context, the objective of this study is to describe the characteristics of patients with HCV in a public reference service in Southern Brazil.

METHODS

A descriptive, retrospective study was carried out in all the CHC patients attended at the Hospital Sanatorio Partenon, a dispensing center for medications used to treat CHC in the Public Health system between December 2015 and December 2016, totaling 1,431 individuals. All the patients who accepted to participate in the research voluntarily and signed the Free and Informed Consent Term were included.

The necessary information for the development of the study were collected from patients' charts after approval by the local Research Ethics Committee under number 1,783,047 (October/2016).

The sex, age, HCV genotypes, viral load, different degrees of fibrosis, and liver or kidney transplantation were evaluated.

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This paper is in accordance with the Declaration of Helsinki, the Universal Declaration on Bioethics and Human Rights, and Resolution 466/12 of the National Health Council of Brazil, approved by the local Research Ethics Committees of the Reference Institutions, respecting the ethical and legal aspects, that regulate the research in Brazil.

The data collected were analyzed in the statistical program Statistical Package for Social Sciences (SPSS®) version 18.0 (SPSS Inc., Chicago, IL). Quantitative variables were presented by mean and standard deviation or median and variation when they were not normally distributed, and were analyzed by Student's t-test. Qualitative variables were presented by frequency and percentage and were analyzed by Pearson's Chi-square test (c^2). The level of significance assumed was 5%.

RESULTS

A total of 1,431 records of patients with CHC were evaluated. Males were the most prevalente (802; 56%) patients. The mean age of the patients was 58.6±9.9 years, ranging from 18 to 89 years. Genotype 1 was the most frequent (866; 60.5%) of the patients. Genotype 2 was observed in 81 (5.7%) patients and genotype 3 in 484 (33.8%) patients (TABLE 1).

TABLE 1. Characteristics of the population (n = 1,431).

Characteristics	
Male gender; n (%)	802 (56.0)
Age years; mean ± SD	58.6 ± 9.9
Genotypes; n (%)	
1	866 (60.5)
2	81 (5.7)
3	484 (33.8)
Transplanted; n (%)	
Liver	73 (5.1)
Kidney	18 (1.2)
Evaluation of fibrosis; n (%)	
Hepatic biopsy	566 (39.6)
Transient hepatic elastography	261 (18.2)
Clinical / laboratory diagnosis	459 (32.1)
Fibrotest	14 (1.0)
NA	131 (9.2)
Degree of fibrosis; n (%)	
2	180 (12.6)
3	341 (23.8)
4	779 (54.4)
NA	131 (9.2)

N: number; m: mean; SD: standard deviation; NA: non available.

Among the patients evaluated, 90 (6.3%) were previously transplanted from a solid organ, of which 73 (5.1%) were liver transplanted, and 18 (1.2%) transplanted from the kidney. Among these, one patient was submmited to liver and kidney transplantation (TABLE 1).

The fibrosis evaluation was performed in 1,300 (90.8%) patients. Of these, 566 (39.6%) were evaluated by liver biopsy, 262 (18.2%) by transient hepatic elastography, and 459 (32.1%) by clinical-laboratory evaluation. Only 14 (1.0%) of the patients had fibrosis evaluated by Fibrotest® and 131 (9.2%) did not evaluate the degree of fibrosis (TABLE 1).

Regarding the degree of fibrosis, 180 (12.6%) of the patients presented grade 2 fibrosis for more than 3 years; 341 (23.8%) had grade 3 fibrosis; and 779 (54.4%) had grade 4 fibrosis (cirrhosis) (TABLE 1).

When the distribution of the different genotypes was evaluated in relation to sex, there was no statistically significant difference (P=0.726; TABLE 2).

Genotypes were analyzed for different degrees of fibrosis, and fibrosis grade 2 fibrosis was associated with genotype 1, grade 3 was associated with genotypes 1 and 2, and grade 4 with genotype 3 (TABLE 2).

TABLE 2. Distribution of genotypes according to sex, different degrees of hepatic fibrosis and viral load.

	Genotype 1 N (%)	Genotype 2 N (%)	Genotype 3 N (%)	*P*
Sex (n=1,431)				0.726
Female	377 (43.5)	39 (48.1)	213 (44.0)	
Male	489 (56.5)	42 (51.9)	271 (56.0)	
Fibrosis (n=1,300)				< 0.001
F2	117 (65.0)*	7 (3.9)	56 (31.1)	
F3	216 (63.3)**	26 (7.6)**	99 (29.0)	
F4	425 (54.6)	39 (5.0)	315 (40.4)***	
Viral load (n=1,227)				0.020
< 600.000	304 (54.3)	30 (5.4)	226 (40.4)§	
≥ 600.000	410 (61.5)#	39 (5.8)	218 (32.7)	

*F2 is associated with Genotype 1; **F3 is associated with Genotype 1 and 2; ***F4 is associated with Genotype 3; # High viral load is associated with Genotype 1; § Low viral load is associated with Genotype 3.

The pre-treatment viral load (PTVL) were evaluated in 1,227 individuals, of which 560 had PTVL <600,000 IU/mL and 667 patients had PTVL > 600,000 IU/mL. Regarding the distribution of genotypes according to viral load, a significant difference was observed in the distribution of genotypes when PTVL was high (≥ 600,000 IU/mL), observing that genotype 1 is associated with high PTVL and genotype 3 was associated with low PTVL (TABLE 2).

On the other hand, there was no difference between the degrees of fibrosis and the high viral load (P=0.559). Of the patients with low PTVL, 41.9% had grade 2 fibrosis, 46% grade 3 fibrosis and 46.4% had grade 4 fibrosis. Of the patients with high PTVL, 58.1% had grade 2 fibrosis, 54% grade 3 fibrosis, and 53.6% had grade 4 fibrosis.

In relation to patients previously submitted to liver transplantation when compared to those not transplanted, mean age was higher (62.1±5.8 vs 58.4±9.9 years respectively; P<0.001), male gender (55.3% vs 69.9% respectively; P=0.009) was less prevalent as well as genotype 1 (45.2% vs 61.2% respectively; P=0.008). There was no difference regarding the PTVL (P=0.162). Advanced fibrosis was observed more frequently in the liver transplanted patients (P=0.011).

DISCUSSION

Hepatitis C virus infection is currently one of the leading causes of chronic liver disease worldwide. Knowing the characteristics of HCV patients may be of interest for the definition of public policy strategies aimed at diagnosis, prevention and treatment.

In the present study, there was a predominance of CHC in the male gender, representing 56.0% of the patients. According to the epidemiological information of the Brazilian Health Department, about 60% of cases of hepatitis C between 1999 and 2011 are male[8]. These results are consistent with the literature, which shows a significant predominance of males in patients with HCV[9-13]. Some authors suggest that the higher prevalence of HCV infection in males can be explained by the fact that men present higher risk sexual behavior in relation to women[13].

Regarding age, the patients included in the present study were between 18 and 89 years old, and the mean age was 58.6±9.9 years. According to Cruz et al.[14] in a study carried out in a Brazilian public health unit on the epidemiological profile of HCV, it was shown that the group most affected was between 40 to 49 years, while in the study by Amaral et al.[12], the highest prevalence was between 46 to 56 years (24.92%).

Regarding the genotypes, several studies have shown that genotype 1 is the most prevalent in the world, followed by genotype 3 and genotype 2 being less frequent[1,15-19]. According to the epidemiological information of the Brazilian Health Department, there is a predominance in the notification of hepatitis C infection of genotype 1 (67.7%), followed by genotypes 3 (25.9%) and 2 (5.7%)[8], similar to the present study, which showed a predominance of genotype 1 followed by 3, genotype 2 being less frequent. However, the results of this study corroborate data from the study that evaluated the distribution of genotypes in Brazil, showing a higher prevalence of genotype 3 in the South region[20].

It was also verified that there was no statistically significant association between sex and genotype distribution in individuals with CHC (P=0.726), in agreement with other authors[9,12,20-22].

Regarding the degree of fibrosis, about 1/3 of the patients did not evaluate fibrosis because they had enough clinical or laboratory evidence for the diagnosis of cirrhosis, or because it was not mandatory to obtain treatment for CHC. Hepatic biopsy was used about twice as much as the hepatic elastography for the evaluation of fibrosis (39.6% vs 18.2%). The majority of patients treated were cirrhotic.

The genotypes were evaluated in relation to the degree of fibrosis, and we observed that advanced fibrosis (F3 and F4) was present in most individuals. Genotype 1 was associated with grade 2 and 3 fibrosis, genotype 2 with grade 3 fibrosis and genotype 3 with grade 4 fibrosis, which has been demonstrated in some studies[23,24].

In the present study, a significant difference was observed in the distribution of genotypes when there was a high viral load, observing that genotype 1 is associated with high viral load and genotype 3 was associated with low viral load. On the other hand, there was no difference between the degrees of fibrosis and the high viral load (P=0.559).

Patients in the present study who had undergone liver transplantation were older patients with advanced fibrosis and less frequently male, with genotype 1 being less present than in the subgroup of non-transplanted patients.

As possible limitations of the study, we emphasize the fact that it is a retrospective study, with its potential methodological limitations. However, the large number of patients included allows to know the characteristics of individuals who had access to CHC treatment in the first year of the Public Protocol implementation using the new DAA, possibly representing patients with more severe liver disease.

In conclusion, the present study made it possible to evaluate the characteristics of patients with CHC in a public health program in South Brazil, who received the DAA recently incorporated by the Brazilian Protocol of the public health system. This research evidenced a predominance of CHC in males, aged between 18 and 89 years, with a predominance of genotype 1, higher viral load in patients with genotype 1 and more advanced degree of fibrosis in patients with genotype 3.

Authors' contribution

Minme R: data collection, writing of text, statistical analysis. Holzmann I: data collection, writing of text. Tovo CV: writing of text, statistical analysis. Almeida PRL: conception of the study, writing of text. All of the authors contributed with the revision and approval of the final version of the manuscript.

Minme R, Holzmann I, Tovo CV, Almeida PRL. Perfil dos pacientes com hepatite C crônica em um programa de saúde pública do sul do Brasil. Arq Gastroenterol. 2018;55(4):403-6.

RESUMO – **Contexto** – A hepatite crônica C (HCC) pode evoluir para cirrose e suas complicações como carcinoma hepatocelular, acarretando morbimortalidade. Conhecer o perfil dos pacientes portadores do vírus da HCC é fundamental para o melhor manejo do tratamento. **Objetivo** – Descrever o perfil dos pacientes portadores de HCC em um programa de saúde pública do sul do Brasil. **Métodos** – Foi realizado um estudo retrospectivo onde foram incluídos os pacientes com HCC que realizaram o tratamento contra o vírus C em um polo de dispensação e assistência farmacêutica da Secretaria Estadual da Saúde do Estado do Rio Grande do Sul, Brasil. Foram avaliados todos os prontuários dos pacientes tratados entre dezembro/2015 e dezembro/2016. **Resultados** – Foram avaliados 1.431 registros de pacientes portadores de HCC. O sexo masculino foi o mais prevalente (802; 56%) pacientes. A idade média dos pacientes foi de 58,6±9,9 anos, com variação de 18 a 89 anos. O genótipo 1 foi o mais frequente, em 866 (60,5%) dos pacientes. Noventa (6,3%) pacientes eram transplantados de órgão sólido, sendo que 73 (5,1%) eram transplantados de fígado. A avaliação de fibrose foi realizada em 1.300 (90,8%) pacientes. Dentre estes, 566 (39,6%) foram avaliados através de biópsia hepática. Em relação ao grau de fibrose, 779 (54,4%) apresentavam fibrose grau 4 (cirrose). Os genótipos foram analisados em relação aos diferentes graus de fibrose, sendo observado que o genótipo 3 está associado com o grau 4 de fibrose. O genótipo 1 está associado com alta carga viral. **Conclusão** – O presente estudo possibilitou a avaliação do perfil dos pacientes portadores de HCC em um programa de saúde pública do Brasil. Houve uma predominância de HCC no sexo masculino, e a média de idade foi de 59 anos. Apresentam um predomínio do genótipo 1, maior carga viral nos pacientes portadores do genótipo 1 e maior grau de fibrose nos portadores de genótipo 3.

DESCRITORES – Hepatite C crônica. Epidemiologia. Resposta viral sustentada.

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