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Article

Effectiveness of second-generation direct-acting antivirals in patients infected with hepatitis c virus and factors associated with a nonsustained virological response

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In Brazil, hepatitis C virus (HCV) treatment has gone through several stages until it reached the current schemes. This study aimed to evaluate the clinical, epidemiologic, and effectiveness of treatment with second-generation direct-acting antivirals (DAAs) for HCV-infected patients in southern Brazil. Medical records of a reference center of Uruguaiana-RS/Brazil were evaluated from December 2017 to August 2020. Data collected included demographics, disease severity and comorbidities, genotype, viral load, medications, treatment side effects, and sustained virological response (SVR). A multivariate linear regression model was developed to identify the factors associated with non-sustained virological response. The HCV-infected patients were predominantly male, white, Genotype 1, with initial liver fibrosis (F0/F1), and untreated patients. Laboratory parameters of the liver profile showed significant improvement after completion of treatment with second-generation DAA for 12 weeks. Significant results were found in the Genotype where 7.3 and 6.0 times more chances of Genotype 1a and Genotype 3, respectively, to present detectable SVR compared to Genotype 1b. Variable cardiovascular comorbidity also indicated a higher risk of absence of SVR compared to individuals without this comorbidity. Treatment with second-generation DAAs can contribute to the Brazilian hepatitis C elimination plan proposed by the World Health Organization.

Keywords: Hepatitis C. Aantivirals. Sustained virologic response. Direct antiviral agents.

INTRODUCTION

According to the World Health Organization (WHO) over 58.000,000 people are infected with the hepatitis C virus (HCV) worldwide, and 290,000 die each year from complications (WHO, 2017). From 2000 to 2022, were diagnosed 298,738 cases of hepatitis C in Brazil. Rio Grande do Sul State (RS); southern Brazil leads the Brazilian ranking with 40.8 cases per 100,000 inhabitants (Brasil, 2020). High rates of HCV led Brazil to become one of the signatory countries of the plan to elimination of HCV proposed by the WHO, this first-ever global guidance aims to reduce new infections and mortality by 90 and 65%, respectively, until 2030 (WHO, 2016).

To meet this global goal, the Brazilian Ministry of Health proposed free access to treatment through the Unified Health System (SUS). Treatment consists of the use of interferon-free direct antiviral agents (DAAs), with or without ribavirin, for all individuals with HCV, regardless of the stage and severity of the disease, as these new DAAs significantly reduce adverse events and increase Sustained Virological Response Virological Sustained. (SVR), which corresponds to the cure of HCV

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infection, with a very low probability of late recovery. SVR is generally associated with the normalization of liver enzymes and the improvement or disappearance of necroinflammation and liver fibrosis in patients without cirrhosis. (Brasil, 2019).

From 2015, Brazilian Clinical Protocol of Therapeutic Guidelines for HCV and Co-infections, the second generation of DAAs started to be used, including sofosbuvir (SOF), daclatasvir (DCV), and simeprevir (SIM), representing an important milestone in treating HCV in Brazil, as these new drugs presented SVR rates of around 90%. Subsequently, the Guideline was updated including of Ombitasvir (OMB), Veruprevir (VER), Ritonavir (RIT), Dasabuvir (DSB), ledipasvir (LEDI), and the pangenotypic glecaprevir (GLECA), pibrentasvir (PIB), and velpatasvir (VELPA) (Brasil, 2019).

With their effectiveness proven through clinical trials around the world, observational studies are pivotal to support the evidence in clinical practice and conduct to updates (Ibrahim Mohammed Ebid *et al.*, 2019; Pena *et al.*, 2020). HCV is associated with many factors that can difficulted the treatment, including genotype, disease staging, comorbidities, and the patient's conditions (Pena *et al.*, 2020). Regarding genotypes, type 1 is the most prevalent in Brazil, while the prevalence of genotype 2 is approximately 5% and that of genotype 3 is 30%. Types 4, 5 and 6 occur in isolated cases, with a very low prevalence in the country (Brasil, 2023)

In this sense, there is still a need for research after implementing new treatments for HCV by UHS in order to evaluate their impacts and benefits in the Brazilian population and, specifically, in the southern region. In this context, this study aimed to evaluate the clinical, epidemiologic and effectiveness of the treatment with second generation DAAs for HCV patients in southern Brazil.

METHODS

The Ethics Committee on Human Research of Federal University of Pampa (UNIPAMPA) approved this study under n. #92602618.3.0000.5323. This retrospective cohort study collected and treatment evolution data from patients' medical records at the viral hepatitis outpatient clinic in Uruguaiana (RS) from December 2017 to August 2020.

Patients over 18, both sexes, including HCV 1 (GT1), 1a (GT1A), 1b (GT1B), 2 (GT2) and 3 (GT3) genotypes, were included in the study, the other genotypes occur rarely in Brazil and were not found during the evaluations carried out in the present study. Patients who interrupted the treatment and who did not have SVR results at the end of the analysis were excluded.

Demographic data (sex, age, and self-reported ethnicity), genotype, treatment line, HIV co-infection, smoking, and co-medications data were collected. Liver disease staging was determined using the METAVIR scoring system and obtained by biopsy (F0 - absent fibrosis; F1 - mild fibrosis; F2 – moderate; F3 – advanced; F4 - cirrhosis) or other less invasive methods such as APRI or FIB4 scoring systems (biomarker scales) and liver elastography (Sebastiani, 2014). The presence of comorbidities was assessed according to the Anatomical, Therapeutic, and Chemical (ATC) classification (World Health Organization Collaborating Centre for Drug Statistics Methodology, 2003). Drug interactions were assessed at the first pharmacist interview using the University of Liverpool - Hepatitis C Drug Interactions database.

Laboratory parameters that were evaluated: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, gamma-glutamyl transferase (gamma-GT), baseline glycemia, glycosylated hemoglobin test, serum creatinine levels, triglycerides, total cholesterol and fractions, total bilirubin and fractions. All tests were collected at two moments: before and after the HCV treatment, and a comparison between the different times was performed. For statistical purposes, subjects with both timeline results were evaluated. Viral load was assessed at baseline, at the end, and 12 weeks after to verify SVR.

The therapeutic regimens were those recommended by the Brazilian Clinical Protocol of Therapeutic Guidelines for Hepatitis C and Co-infections (Brasil, 2019) considering: SOF, DCV, OMB/VER/RIT/DAS, SOF/LEDI, SOF/VELA PA and GLECA/PIB according to genotype, associated or not with RBV. RBV was associated with the regimens

mentioned above in patients with medical criteria, an advanced degree of liver fibrosis (>F4), or who had already received DAAs treatment.

The frequency distribution of the demographic, epidemiological, clinical and therapeutic regime used, treatment time and SVR (detectable or undetectable) therapeutic regime was evaluated using SPSS software (version 22.0). The Wilcoxon test was performed to compare pre and post-treatment laboratory parameters; Non -parametric data were presented as a median and interquartile interval. To verify the association with SVR results, Mann-Whitney U test for non-parametric numerical variables, chi-square for variables and the exact fischer test for used user dichotomous variables. Logistic regression analysis was performed to identify risk factors for SVR; $P \leq 0.05$ was considered significant.

RESULTS

Of the 212 medical records, 13 were excluded because the patient passed away or did not receive the result of the SVR exam. Demographic data and laboratory parameters were evaluated from 199 subjects. To analyze the SVR outcome, 15 more records were excluded because they did not present the results or were carried out in private laboratories (Figure 1).

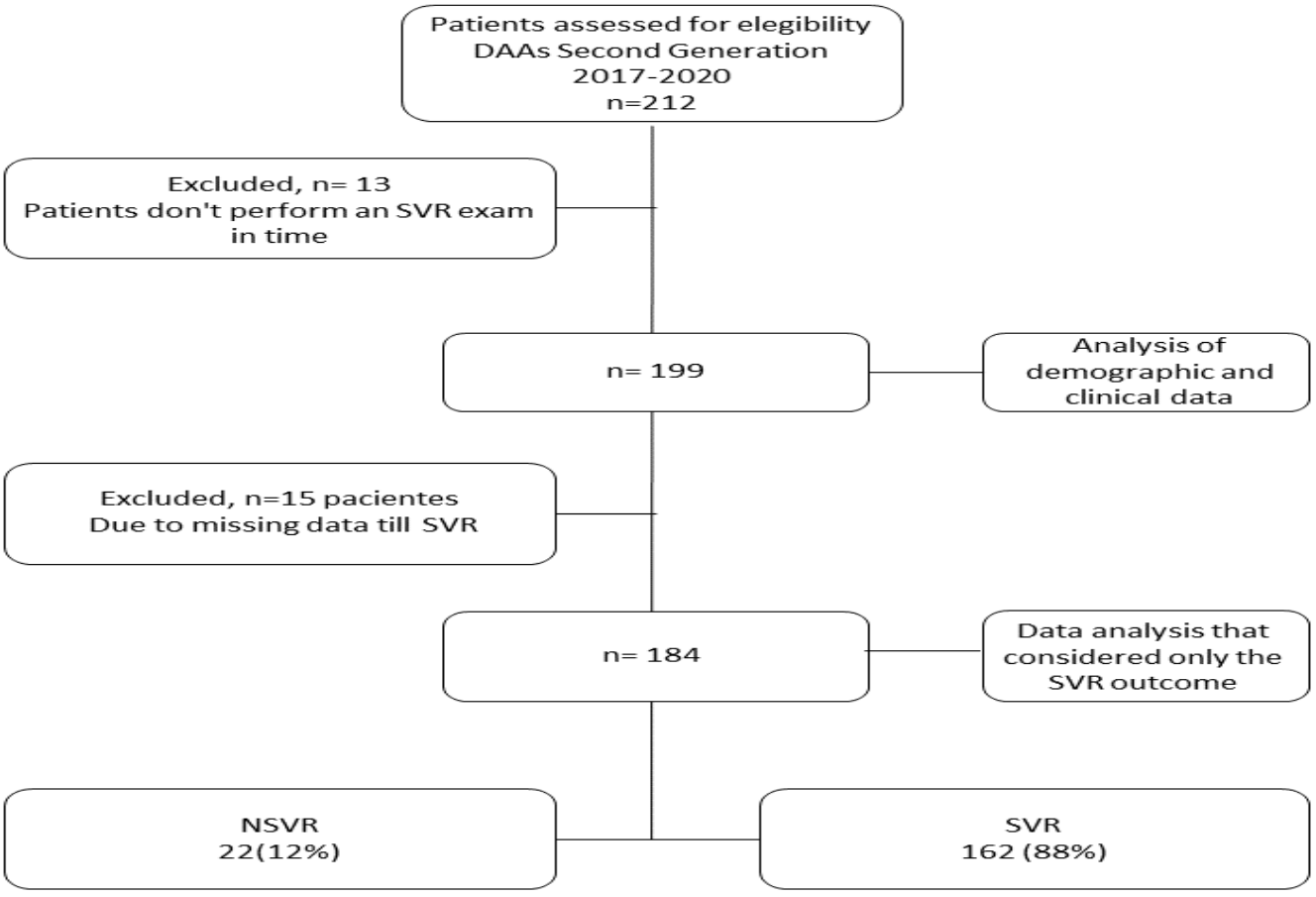

FIGURE 1 - Flowchart of patients diagnosed with HCV at the viral hepatitis outpatient clinic in Uruguaiana from 2017 to 2020 and treated with second-generation direct action (DAAs). NSVR, nonsustained viral response; SVR, sustained viral response.

Demographic and clinical information are shown in Table I. The mean age was 55.08 ± 9.91 years, 68.2% self-reported being white and 55.8% were male. Most of them had initial fibrosis grades of F0-F1 (47.8%) and have not received any treatment before (81.9%). Genotype 1 and its subtypes were the most frequent (63.3%).

TABLE I - Demographic data

Variable	N (%)
Sex	
Female	88 (44.2)
Male	111 (55.8)
Age	
Age (years)	55.08 ± 9.91*
Self-reported ethnicity	
White	125 (62.8)
Yellow	1 (0.5)
Brown	37 (18.6)
Black	36 (18.1)
Genotype	
1	2 (1.0)
1a	51 (25.6)
1b	73 (36.7)
2	11 (5.5)
3	62 (31.2)
Treatment (weeks)	
8	1 (0.5)
12	194 (97.5)
24	4 (2.0)
Fibrosis degree	
F0	64 (32.2)
F1	31 (15.6)
F2	42 (21.1)
F3	37 (18.6)
F4	25 (12.6)
Use of comedications	
Yes	143 (71.9)
No	56 (28.1)
DAAs interaction	
Yes	51 (25.6)
No	148 (74.4)
Comorbidities according to the ATC classification	
Digestive and metabolic system	66 (33.2)
Nervous system	23 (11.6)
Cardiovascular system	76 (38.2)
HIV co-infection	
Yes	15 (7.5)
No	184 (92.5)
Smoking	
Yes	46 (23.1)
No	153 (76.9)
Retreatment	
Yes	36 (18.1)
No	163 (81.9)

* Results expressed are as mean (standard deviation). (n = 199)

We found that 25.6% of patients were using medications that had some potential drug interaction with DAAs. Most patients had comorbidities in the cardiovascular system (38.2%), according to the ATC classification of the drugs used by the patients (WHO, 2003), followed by those that acted in the digestive and metabolic systems (33.2%). Some patients had more than one comorbidity and, for this reason, there was a higher total number (165) in the treatments.

Most patients with genotype 1 and subtypes used the OMB/VER/RIT/DSB (25.6%) and SOF/LED (22.05%) treatment with or without RBV (Table II). On the other hand, individuals with genotype 3 were treated with SOF/DCV (21.1%) with or without RBV.

The frequencies of undetectable SVR, considering the different genotypes and some clinical characteristics, are illustrated in Figure 2. SVR rates above 80% were achieved in all individuals. Regarding GT3 achieved the lowest SVR rate (80.7%). The regimens that had ribavirin associated showed higher SVR undetectable when compared to regimens without this association (Figure 2B).

TABLE II - DAAs regimens used in HCV treatment x genotypes and fibrosis degree

Variables	Treatments					
	SOF/DCV	OMB/VER/ RIT/DSB	GLECA/PIB	GLECA/ PIB/SOF	SOF/LEDI	SOF/VELPA
Genotype 1				1 (0.5%)	1 (0.5%)	
Genotype 1 a	18 (9.4%)	12 (6.0%)	1 (0.5%)	3 (1.5%)	20 (10.0%)	
Genotype 1 b	6 (3.0%)	39 (19.6%)		2 (1.0%)	22 (11.0%)	
Genotype 2	6 (3.0%)					5 (2.5%)
Genotype 3	42 (21.1%)			1 (0.5%)		20 (10.0%)
F0	8 (4,0%)	10 (5,0%)	1 (0,5%)	2 (1,0%)	32 (16,0%)	11 (5,5%)
F1	15 (7,5%)	7 (3,5%)	0 (0%)	0 (0%)	8 (4,0%)	1 (0.5%)
F2	17 (8,5%)	17 (8,5%)	0 (0%)	3 (1,5%)	3 (1,5%)	2 (1,0%)
F3	16 (8,0%)	10 (5,0%)	0 (0%)	2 (1,0%)	2 (1,0%)	7 (3,5%)
F4	7 (3,5%)	5 (2.5%)	0 (0%)	1 (0.5%)	2 (1,0%)	10 (5,0%)

SOF, sofosbuvir; DCV, daclatasvir, OMB, ombitasvir; VER, veruprevir; RIT, ritonavir; DSB, dasabuvir; GLECA, glecaprevir; PIB, pibrentasvir; LEDI, ledipasvir, VELPA, velpatasvir.

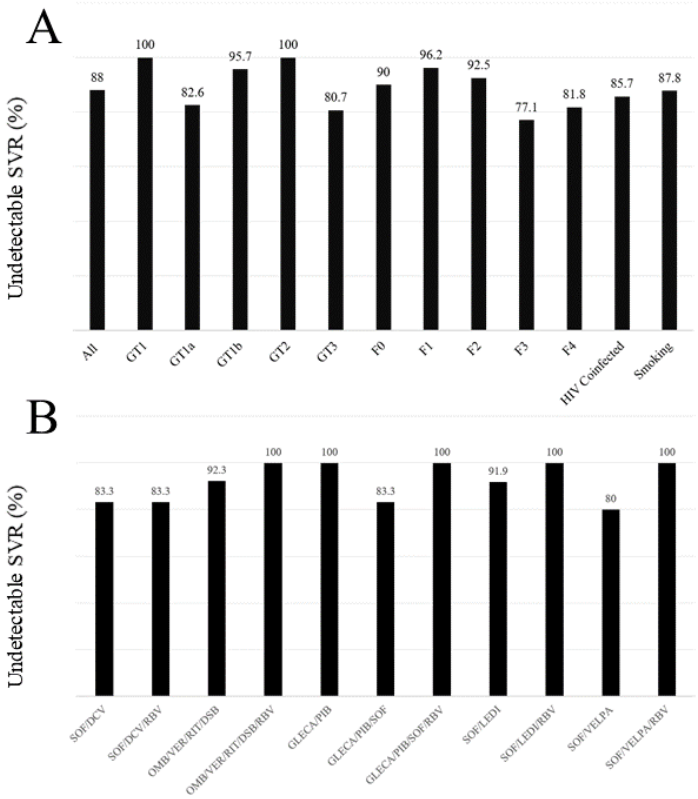

FIGURE 2 - A) Undetectable SVR rates (%) according to patient characteristics and HCV genotypes. GT, genotype; F0-F4, Fibrosis Degree. B) SVR rates according to the therapeutic scheme used.

The influence of using these antivirals on these parameters showed a significantly lower AST, ALT, alkaline phosphatase, gamma-GT, total bilirubin and fractions, and glycated hemoglobin levels. After treatment, hemoglobin levels decreased and total cholesterol, HDL, and LDL showed a significant increase showed in next table.

TABLE III - Pre and post treatment laboratory parameters with DDAs

	Pre-treatment			Post-treatment			Value P[1]
Laboratory exams	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**	
AST (UI/L)	187	72.47	61.50	123	33.80	43.81	<0.001*
ALT (UI/L)	186	77.76	70.20	123	25.63	22.81	<0.001*
Alkaline phosphatase (U/L)	157	133.08	108.22	111	106.39	55.32	0.001*
Gama glutamyl transferase (U/L)	170	86.05	81.41	116	39.57	49.81	<0.001*
Albumin (g/dL)	169	4.35	3.13	113	6.06	7.92	0.806
Hemoglobin (g/dL)	189	14.38	1.71	123	13.98	1.84	0.02*
Creatinine (mg/dL)	175	1.02	1.02	120	0.88	0.35	0.904
Total cholesterol (mg/dL)	178	158.27	45.04	116	182.87	44.77	<0.001*
HDL cholesterol (mg/dL)	174	45.70	14.27	116	46.00	13.29	0.041*
LDL cholesterol (mg/dL)	137	83.26	37.70	73	108.62	35.07	<0.001*
Total bilirubin (mg/dL)	168	0.99	0.61	114	0.79	0.86	<0.001*
Direct bilirubin (mg/dL)	167	0.39	0.32	114	0.31	0.67	<0.001*
Indirect bilirubin (mg/dL)	168	0.61	0.43	114	0.62	1.55	<0.001*
Triglycerides (mg/dL)	176	134.15	65.11	117	137.82	80.02	0.436
Fasting blood glucose (mg/dL)	185	102.77	39.78	118	101.89	39.26	0.758
Glycated hemoglobin (mg/dL)	154	124.47	44.20	112	114.60	46.62	<0.001*

[1]Wilcoxon t-test; *statistically significant values (≤0.05).

The results associating the differences between laboratory parameters in the pre- and post-treatment times with the SVR showed that despite the differences between some of them, e.g., AST, ALT, and alkaline phosphatase, there were no statistically significant differences in the SVR (Table III).

The association between clinical and demographic characteristics with detectable and non-detectable SVR results is listed in Table IV. Among the variables listed, females showed a lower risk of having detectable SVR than males, although there was no significant association ($p>0.05$) and other variables such as age, ethnicity, treatments, among others. In this bivariate analysis, the genotype presented a statistically significant result by Pearson's chi-square test, showing an association between genotype and SVR outcome.

TABLE IV - Association of clinical and demographic characteristics according to the SVR outcome

	Detectable SVR		Undetectable SVR		*P* Value[1]
Variables	**N**	**%**	**N**	**%**	
Sex					
Female	8	9.5	76	90.5	
Male	14	14.0	86	86.0	0.373
Self-reported ethnicity					
Yellow	0	0.0	1	100.0	
White	13	11.5	100	88.5	
Brown	4	11.8	30	88.2	0.963
Black	5	13.9	31	86.1	
Smoking					
No	17	11.9	126	88.1	
Yes	5	12.2	36	87.8	1.000
Age[2]	56.0	10.3	54.8	9.86	0.589°
Genotype					
1	0	0.0	2	100.0	
1a	8	17.4	38	82.6	
1b	3	4.3	67	95.7	
2	0	0.0	9	100.0	
3	11	19.3	46	80.7	0.047*
Treatment					
SOF/DCV	9	16.7	45	83.3	
SOF/DCV/RBV	2	16.7	10	83.3	
OMB/VER/RIT/DSB	3	7.7	36	92.3	
OMB/VER/RIT/DSB/RBV	0	0	12	100.0	
GLECA/PIB	0	0	1	100.0	
GLECA/PIB/SOF	1	16.7	5	83.3	
GLECA/PIB/SOF/RBV	0	0	1	100.0	0.728
SOF/LEDI	3	8.1	34	91.9	
SOF/LEDI/RBV	0	0	1	100.0	
SOF/VELPA	4	20	16	80.0	
SOF/VELPA/RBV	0	0	2	100.0	
Fibrosis degree					
F0	6	10	54	90.0	

TABLE IV - Association of clinical and demographic characteristics according to the SVR outcome

	Detectable SVR		Undetectable SVR		*P* Value[1]
Variables	**N**	**%**	**N**	**%**	
F1	1	6.7	26	96.3	
F2	3	7.5	37	92.5	
F3	8	22.9	27	77.1	0.113
F4	4	18.2	18	81.8	
Use of other drugs					
Yes	17	13.2	112	86.8	
No	5	9.1	50	90.9	0.62
DAAs interactions					
Yes	6	12.5	42	87.5	
No	16	11.8	120	88.2	1.000
Comorbidities					
Digestive and metabolic system					
Yes	6	9.5	57	90.5	
No	16	13.2	105	86.8	0.633
Nervous system					
Yes	7	12.1	51	87,9	
No	15	11.9	111	88.1	1.000
Cardiovascular system					
Yes	12	17.4	57	82.6	
No	10	8.7	105	91.3	0.101
HIV coinfection					
Yes	2	14,3	12	85.7	
No	20	11.8	150	88.2	0.676
Retreatment					
Sim	6	18.2	27	81.8	
Não	16	10.6	135	89.4	0.239

[1]Pearson›s chi-square test with Fisher›s exact test as performed for variables that presented only two categories; [2]Mean and standard deviation; [º]independent T-test. *Statistically significant values (≤0.05).

The multivariable analysis showed a lower risk for females in presenting detectable SVR, even though it was not significant (Table III). It was observed an increase in this risk with increasing age and HIV co-infection. Significant results were found in the genotype where 7.3 and 6.0 times more chances of GT1a and GT3,

respectively, to present detectable SVR compared to GT1b. The presence of cardiovascular comorbidities was also statistically significant, indicating a higher risk of NSVR for those with such diseases compared to those without.

DISCUSSION

This study evaluated the characteristics and results of treatment with DAAs for HCV in clinical and biochemical parameters. Data from clinical trials in daily practice are crucial to verify efficacy and safety in different populations. In this case, specifically in a city of this study, because it has the highest national incidence rate of HCV according to the latest epidemiological report (Brasil, 2020).

The studied population showed clinical and demographic characteristics like others, being predominantly male, elderly, white, presenting initial liver fibrosis grade (F0-F1), and no receiving treatment (Pena *et al*., 2020; Lobato *et al.,* 2019; Pessoa *et al.,* 2018). Regarding genotype, the highest prevalence corresponded to GT1 and its subtypes (63.3%), followed by GT3 (31.2%), corroborating data found at the national level (Brasil, 2020; Pena *et al*., 2020; Pessoa *et al.,* 2018).

Overall, the observed undetectable SVR was 88% (Figure 2A). Second-generation DAAs were highly effective in different clinical situations (Figure 2B). GT3's undetectable SVR rate was the lowest among all others (80.7%), which is consistent with national (Lobato *et al*., 2019) and international data (Mangia *et al*., 2019; Lawitz *et al*., 2013; Nelson *et al*., 2015), which demonstrates that GT3 infection is difficult to treat compared to other genotypes, more related to the genotype than to the treatment itself. These findings are confirmed here, in which the genotype was the only variable that showed a significant association in relation to the SVR outcome, with GT3 having the lowest SVR compared to the other genotypes.

Studies have shown that HCV patients have a high prevalence of comorbidities and use several medications concomitantly (Pena *et al.,* 2020; Louie *et al.,* 2012; Negro, 2014). These facts result in a complex drug interaction. In this sense, is fundamental to know the possible pharmacological interactions and their consequences that can affect adherence to both treatments. The studies reported above corroborate our data, which showed the most patients were taking other medications (71.9%). Of these, 25.6% had some type of interaction with DAA, in addition to most medications acting in the cardiovascular system (38.2%) according to the ATC classification. A total of 26 medications for the treatment of diseases in the cardiovascular system were listed in use by patients, including Losartan (used by 17.8% of patients in the present study) and Atenolol (used by 8.5% of patients in the present study).

Likewise, Pena and colleagues (2020) found the presence of comorbidities in 71.6% of HCV-infected patients and reported that the most common comorbidities were associated with cardiovascular system disorders (38.6%). According to the Brazilian Guideline on Dyslipidemias and Prevention of Atherosclerosis (Faludi AA *et al.,* 2017) the association between OMB/VER/RIT/DAS should not be administered together with some drugs, including Losartan, therefore, in our study, care was taken with patients who reported the use of the drug for the concomitant treatment of diseases of the cardiovascular system, avoiding possible undesirable effects from the interaction, and another treatment was chosen for the patients. All patients who reported using medications with potential interactions with HCV treatments received careful attention and no untoward events were reported.

Regarding the degree of liver fibrosis, higher rates of undetectable SVR (> 90%) were observed in patients at an early stage (F0-F2), proving that the earlier the diagnosis and initiation of treatment, the higher rates of undetectable SVR (Figure 2A), as previously demonstrated (Pena *et al*., 2020; Mangia *et al*., 2019).

Laboratory data is a key factor in HCV-infected patients' diagnosis and follow-up. Analysis of pre- and post-treatment parameters showed significant results in the liver profile tests showed in Table III. Lower AST, ALT, alkaline phosphatase, gamma-GT, total bilirubin, and fractions levels corroborate the literature because higher levels of these enzymes are common in untreated HCV-infected patients due to the damage caused to the cells of the liver parenchyma (Ibrahim Mohammed Ebid *et al.,* 2019; Hajarizadeh *et al.,* 2016). Higher albumin

levels after the end of treatments corroborate Essa and collaborators (2019) after DAA administration in cirrhotic patients, and this can be explained because serum albumin is usually reduced in chronic hepatopathies due to the increased distribution volume of this protein, impaired hepatic synthesis, or even both.

Other laboratory parameters that showed a significant increase after treatment were total cholesterol, HDL and LDL. According to the Brazilian Guideline on Dyslipidemias and Prevention of Atherosclerosis (Faludi AA *et al.,* 2017), the hepatitis C virus has a unique relationship of dependence on lipids, plasma lipoproteins and host cofactors, facilitators of viral replication and results in circulating hypocholesterolemia, explaining the increase in these parameters after completion of DAA treatments. Corroborating these studies, Gong and Cun (2019) describe that the overlap between the HCV replication cycle and lipid metabolism is considered one of the main means by which HCV develops chronic infections efficiently.

Furthermore, the significant decrease in the glycated hemoglobin levels after treatment with DAAs can be justified that HCV infection induces an increase higher insulin resistance (Supplementary information, Table S1). The possible hypotheses include the action of cytokines that induce insulin resistance, such as IL-6 and TNF-α, which are naturally elevated in the presence of inflammation caused by HCV (Milner *et al*., 2014; Bogdanos, Rigopoulou, 2007; Kawaguchi *et al.,* 2007). Recently, HCV infection was discovered to induce gene expression of a protein that has a central role in the insulin signaling pathway (Parolin *et al.,* 2006; Sociedade Brasileira de Diabetes, 2020).

The multivariable analysis presented herein demonstrated the odds ratios of the listed parameters that could present an increased risk of detectable SVR (Supplementary information, Table S2). There were significant findings for genotype and comorbidity associated of the cardiovascular system. GT1a and GT3 showed a higher chance than GT1b in presenting SVR absence. Lobato and collaborators (2019) also verified this lower SVR in GT1a and GT3 in their descriptive study with over 3000 patients from reference centers for HCV treatment in Brazil, as well as Pessoa and collaborators (2018), who demonstrated lower SVR rates for GT1a in cirrhotic and non-cirrhotic patients compared to GT1b treated with DAAs. Regarding comorbidities, the cardiovascular system showed a statistically relevant result, indicating a 3-fold increased risk for patients to have detectable SVR after treatment compared to individuals who did not have this comorbidity. Although the association between chronic HCV infection and cardiovascular disease has yet to be confirmed, higher cardiovascular risk has been considered one of the extrahepatic manifestations of HCV infection and may influence the SVR outcomes of patients treated for HCV (Drazilova *et al.*, 2018).

DAAs represent a significant advance in pharmacotherapy for chronic hepatitis C, both in terms of the therapeutic arsenal available to increase the scope of treatment and in terms of effectiveness. Thus, it is pivotal that further attention is given to disease prevention, early diagnosis, and expanding access to these treatments, which could help Brazil meet the goal eliminating HCV proposed by the WHO.

CONCLUSION

Second generation DAAs provided by Brazilian Clinical Protocol of Therapeutic Guidelines for HCV and Co-infections showed high SVR rates, reflecting the effectiveness previously reported in other studies. The influence of these therapeutic regimens on laboratory parameters, especially liver profile, showed meaningful results after treatment completion. Moreover, statistically relevant results showed that patients with genotypes 1a and 3, as well as with cardiovascular system comorbidity, had a higher risk of detectable SVR at the end of treatment.

These results may contribute to clinical practice, whereby identifying patients with a greater chance of having a detectable SVR and interventions can be made in their clinical follow-up for improvement in response after the end of treatment.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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SUPPLEMENTARY MATERIAL

TABLE SI - Relationship between laboratory tests and SVR

Laboratory exams	Detectable SVR		Undetectable SVR		*P* Value [1]
	*Median difference	Interquartile range	*Median difference	Interquartile range	
AST (UI/L)	-27.0	166.0	-31.0	52.0	0.816
ALT (UI/L)	-18.5	89.7	-35.0	57.0	0.693
Alkaline phosphatase (U/L)	14.0	110.0	-23.0	96.0	0.590
Gama GT (U/L)	-57.0	164.0	-29.0	53.0	0.358
Albumin (g/dL)	0.5	12.3	0.1	1.0	0.346
Hemoglobin (g/dL)	-0.6	2.7	-0.1	1.5	0.271
Creatinine (mg/dL)	-0.4	0.6	0.0	0.4	0.956
Total cholesterol (mg/dL)	14.0	34.0	24.5	54.0	0.449
HDL cholesterol (mg/dL)	7.0	10.0	1.0	15.0	0.418
LDL cholesterol (mg/dL)	-6.0	/	17.0	59.0	0.488

TABLE SI - Relationship between laboratory tests and SVR

Laboratory exams	Detectable SVR		Undetectable SVR		*P* Value [1]
	*Median difference	Interquartile range	*Median difference	Interquartile range	
Total bilirubin (mg/dL)	0.1	1.2	-0.3	0.6	0.344
Direct bilirrubin (mg/dL)	-0.1	0.3	-0.2	0.3	0.066
Indirect bilirrubin (mg/dL)	0.1	1.0	-0.2	0.5	0.344
Triglycerides (mg/dL)	-64.0	112.0	-4.0	65.0	0.465
Fasting blood glucose (mg/dL)	1.0	24.0	1.5	24.8	0.481
Glycated hemoglobin (mg/dL)	-11.5	36.3	-6.0	18.0	0.660

*Difference between the final and initial value/result not calculated in the statistical analysis due to the number of the sample (n=2); [1]Mann-Whitney U test.

TABLE SII - Factors associated with the absence of detectable SVR in DAAs-treated patients

Variable	OR	CI	
		Minimum	Maximum
Sex			
Female	0.63	0.20	2.01
Male	1.00		
Self-reported ethnicity			
Black	1.26	0.40	3.97
Brown	0.73	0.20	2.61
White	1.00		
Age (years)			
65≥	2.20	0.23	20.45
55 - 64	2.43	0.37	15.92
45 - 54	1.54	0.28	8.34
25 - 44	1.00		
Genotype*			
3	6.10	1.70	21.86
1a	7.37	1.46	37.18
1b	1.00		
Fibrosis degree			
F3-F4	2.35	0.67	8.08
F2	0.67	0.11	3.91

TABLE SII - Factors associated with the absence of detectable SVR in DAAs-treated patients

Variable	OR	CI	
		Minimum	Maximum
F0-F1	1.00		
HIV coinfection			
Yes	1.33	0.24	7.54
No	1.00		
Comorbidities - cardiovascular system *			
Yes	3.25	1.04	10.08
No	1.00		
Comorbidities - digestive and metabolic system			
Yes	0.40	0.12	1.29
No	1.00		

Likelihood ratio = -51.36. OR = odds ratio; CI: confidence interval; *statistically significant values ($p \leq 0.05$). (n=172).

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