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HIGH RATE OF DEPRESSION IN PATIENTS WITH CHRONIC HEPATITIS C

Taxa elevada de depressão em pacientes com hepatite C crônica

Alta tasa de depresión en pacientes con hepatitis C crónica

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ABSTRACT

Objective: To describe the frequency of depression in patients with hepatitis C (HCV) and relate to the biological variables and liver function. **Methods:** cross-sectional, descriptive study with a quantitative approach, which assessed depression using the criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) and the association with biological and liver function variables in 85 patients HCV chronically infected indicated for direct-acting antiviral therapy (DAA) between May 2018 and May 2019. **Results:** depression was detected in 47.1% of patients, predominantly mild depression (95%). However, depression occurred independently of biological characteristics, such as gender, age, education, associated comorbidities and liver function, such as degree of fibrosis and viral genotype. **Conclusions:** the frequency of depression was high in patients with HCV and had no statistical relationship with biological characteristics and liver function, suggesting that active search for depression could be a valuable strategy in managing these patients.

Descriptors: Depression, Hepatitis C, DSM-V, Chronic hepatitis C.

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RESUMO

Objetivo: Descrever a frequência de depressão em pacientes com hepatite C (HCV) e relacionar com as variáveis biológicas e função hepática. **Métodos:** estudo transversal, descritivo, de abordagem quantitativa, que avaliou a depressão utilizando os critérios do Manual de diagnóstico e estatístico de transtornos mentais (DSM-V) e a associação com as variáveis biológicas e de função hepática em 85 pacientes com HCV crônica indicados para a terapia antiviral de ação direta (DAA) entre maio de 2018 e 2019. **Resultados:** detectou-se depressão em 47,1% dos pacientes, predominantemente depressão leve (95%). Entretanto a depressão ocorreu de forma independente das características biológicas, como sexo, idade, escolaridade, comorbidades associadas e da função hepática, como grau de fibrose e genótipo viral. **Conclusões:** a frequência de depressão foi alta em pacientes com HCV e não teve relação estatística com as características biológicas e função hepática, sugerindo a busca ativa da depressão como estratégia na condução destes pacientes.

Descritores: Depressão, Hepatite, DSM-V, Hepatite C crônica.

RESUMEN

Objetivo: Describir la frecuencia de depresión en pacientes con hepatitis C (VHC) y relacionarla con variables biológicas y función hepática. **Métodos:** estudio descriptivo transversal con abordaje cuantitativo, que evaluó la depresión utilizando los criterios del Manual Diagnóstico y Estadístico de los Trastornos Mentales (DSM-V) y la asociación con variables biológicas y de función hepática en 85 pacientes con VHC crónico indicados para tratamento com terapia antiviral de acción directo (AAD) entre mayo de 2018 y 2019. **Resultados:** se detectó depresión en el 47,1% de los pacientes, predominantemente depresión leve (95%). Sin embargo, la depresión se produjo independientemente de las características biológicas, como el sexo, la edad, la educación, las comorbilidades asociadas y la función hepática, como el grado de fibrosis y el genotipo viral. **Conclusiones:** la frecuencia de depresión fue alta en pacientes con VHC y no tuvo relación estadística con características biológicas y función hepática, sugiriendo la búsqueda activa de depresión como estrategia en el manejo de estos pacientes

Descriptores: Depresión, Hepatitis C, DSM-V, Hepatitis C crónica.

INTRODUCTION

It is estimated that around 71 million people are infected with the hepatitis C virus (HCV) worldwide, and approximately 400 thousand die each year due to complications of this disease. In Brazil, the number of people chronically infected with HCV is estimated to be around 650,000. The highest detection rates have been observed in males, with a reduction in the sex ratio over the years.[1-2] Neuropsychological and neurocognitive impairment are frequently reported by patients with chronic HCV infection. These changes occur regardless of HCV genotype and even in the absence of structural brain damage. According to epidemiological studies, about one-third of chronically HCV-infected individuals have depression, which represents a frequency 1.5 to 4 times higher compared to depression alone. [3-5]

Depression is a serious and highly prevalent medical problem throughout the population. According to the World Health Organization (WHO), the prevalence of depression in the primary health care network is 10.4%, either alone or associated with a physical disorder. It ranks fourth among the main causes of burden, accounting for 4.4% of the burden of disease during life. It ranks first when considering time lived with disability over a lifetime (11.9%) and is the leading cause of disability, with more than 300 million people suffering from this condition.[4]

Depression in HCV used to be related to symptoms induced by Interferon (IFN) treatment, but has regained prominence with the new drug therapies, the direct-acting antivirals (DAA), as depression rates have remained high (20-50%) after their implementation. Therefore, understanding and diagnosing depression are still crucial points in the DAA era.[5-6] Even in the face of this reality, the search for and treatment of depression in HCV patients is not routinely practiced, leading to impairments in treatment adherence, functionality, and quality of life.[2] Studies of groups with nurses administering medications, of multidisciplinary interventions, and of programs incorporating cognitive-behavioral therapy have improved adherence to treatment and depressive symptoms with simultaneous improvement in sustained virologic response (SVR).[7-9] In addition to mood disorders, low education, common in patients in the public health network, also interferes in adherence to treatment of HCV and other chronic comorbidities, as it limits the understanding of the treatment. [2-3]

In HCV patients, depression can be directly related to the viral infection or be a comorbidity, and it becomes opportune to diagnose it regardless of the cause and effect relationship in HCV patients. The high prevalence of depression, both in Brazil and worldwide, in these patients raises questions about characteristics that can be considered risk and protection factors for the development of this disease.[2,4,10-12]

Thus, this study aims to describe the frequency of depression in patients with hepatitis C (HCV) and relate it to biological variables and liver function. This work is part of the research project developed in the Hepatology service of HUGG and becomes even more important, since it is an opinion-forming university hospital that intends to benefit patients and the service.

METHODS

This is a cross-sectional, descriptive study with a quantitative approach. Data were collected during the consultation prior to HCV treatment with DAA in the period from May 2018 to May 2019 at HUGG, located in the Tijuca neighborhood, northern zone of Rio de Janeiro, RJ, Brazil. The gastroenterology and hepatology service has accreditation from the Ministry of Health to act as an HCV treatment center. The pre-treatment consultation was used as a strategy to ensure evaluation just before the start of therapy and try to ensure follow-up and reassessment with adequate follow-up in the service.

Patients were included in the research: duly registered in the gastroenterology and hepatology outpatient clinic of HUGG; with confirmed diagnosis of chronic HCV infection (with Anti-HCV reagent for more than six months and confirmed with HCV-RNA detectable for more than six months), even if coinfected by HIV; patients who fit the DAA therapy protocol, according to the recommendations of the Clinical Protocol and Therapeutic Guidelines (PCDT) for Hepatitis C and co-infections of the Ministry of Health , which are part of a national list forwarded to the Ministry of Health and had their medications released during the research period. Patients coinfected with hepatitis B and acute HCV were excluded.

To diagnose depression, the criteria of the Diagnostic and Statistical Manual of Mental Disorders in its fifth edition (DSM-V) were used, and then, in patients with depression, the Hamilton scale was applied as a screening to classify depression into mild (score between 7 and 17), moderate (score between 18 and 24), or severe (above 25 points). In addition, all patients answered a data collection questionnaire with the following information: sex, age, educational level, religion, comorbidities, medications in use, route of infection, HCV genotype and viral load, degree of liver fibrosis, liver function (modified Child-Pugh grading scale for prognostic evaluation). Education was divided by the length of study into equal or greater than eight years (≥ 8 years) and less than eight years (< 8 years) of study.

All data were tabulated in Excel® 2013 spreadsheet and for statistical analysis we used BioStat 5.3® and Prism 5. We used descriptive statistics with the absolute number and percentage of patients for categorical variables and the mean for continuous variables. We used Fisher's exact test or Chi-square to test the association between variables. This work is part of the research project "Global and cognitive assessment in elderly people with hepatitis C virus infection before and after treatment with DAA regimen", approved by the Research Ethics Committee of the Gaffree and Guinle University Hospital of HUGG on May 30, 2019, under CAAE: 12630419.0.0000.5258 and opinion 3.358.238. All participants signed the Informed Consent Form (ICF).

RESULTS

In a previous study, our group evaluated the cognitive impairment caused by HCV in the 85 participants of this study, whose main biological characteristics have already been described.10 Briefly, the mean age of the patients was 58.1 years, 50 (58.8%) were female, and 60 (70.6%) had studied 8 or more years. The predominant genotype was type 1 (93%), with a mean viral load of 112,298 copies and considered compensated in the disease prognostic classification (Child A; 95.3%). Depression was diagnosed in 40 (47.1%) patients, of whom 38 (95%) had mild depression, according to the Hamilton score, and two (5%) had moderate depression.

Next, an association between depression and the biological variables of the study participants was sought. The variables age, sex, and ethnicity were equally distributed between the groups with and without depression, as were education and religion (Table 1). The analysis of lifestyle-related variables and the presence of other diseases revealed that sedentary patients with multiple comorbidities and those who used more than three medications predominated, however, it was not possible to observe a statistical association with depression, **Table 1**.

Table 1- Association of biological variables and depression.

Variables	Variable Subdivisions	Total number of patients n (%)	Depression YES	Depression NO	p-value
Total		85 (100%)	40 (47,1%)	45 (52,9%)	
Age	≥ 60 years old	44 (51,8%)	23 (52,3%)	21 (47,7%)	0,3865
	< 60 years old	41 (48,2%)	17 (41,5%)	24 (58,5%)	
Gender	Male	35 (41,2%)	17 (48,6%)	18(51,4%)	0,6639
	Female	50 (58,8%)	23 (46%)	27 (54%)	
Education	≥ 8 years old	60 (70,6%)	30 (50%)	30 (50%)	0,4778
	< 8 years old	25 (29,4%)	10 (40%)	15 (60%)	
Ethnicity	Blacks	16 (18,8%)	6 (37,5%)	10 (62,5%)	0,1314
	Grizzlies	27 (31,8%)	17 (63%)	10 (27%)	
	Whites	42 (49,4%)	17 (40,5%)	25 (59,5%)	
Religion	Yes	76 (89,4%)	37(48,7%)	39 (51,3%)	0,4907
	No	9 (10,6%)	3 (33,4%)	6 (66,6%)	
Sedentary lifestyle	Yes	53 (62,3%)	27 (51%)	26 (49%)	0,3794
	No	32 (37,7%)	13 (40,6%)	19 (59,4%)	
Associated Comorbidities	None	3 (3,5%)	0	3 (100%)	0,2301
	One or Two	18 (21,2%)	8 (44,4%)	10 (55,6%)	
	Three or more	64 (75,3%)	32 (50%)	32 (50%)	
Medications in use	None	19 (22,4%)	11 (57,9%)	8 (42,1%)	0,1444
	One or Two	28 (32,9%)	9 (32,2%)	19 (67,8%)	
	Three or more	38 (44,7%)	20 (52,6%)	18 (47,4%)	
Degree of Fibrosis	F0-F1	30 (35,3%)	15 (50%)	15 (50%)	0,9493
	F2	28 (32,9%)	12 (42,9%)	16 (57,1%)	
	F3	13 (15,3%)	6 (46,2%)	7 (53,8%)	
	F4	14 (16,5%)	7 (50%)	7 (50%)	
Child-Pugh Scale	=A5	80 (94%)	36 (45%)	44 (55%)	0,1827
	>A5	5 (6%)	4 (80%)	1 (20%)	
HCV genotype	1	6 (7%)	4 (66,6%)	2 (33,4%)	0,4332
	1A	21 (24,7%)	8 (38,1%)	13 (61,9%)	
	1B	50 (58,8%)	24 (48%)	26 (52%)	
	1A/1B	2 (2,35%)	2 (100%)	0 (0%)	
	2	0	0	0	
	3	5 (5,9%)	2 (40%)	3 (60%)	
	4	1 (1,25%)	0	1 (100%)	

Assessing the depressive episodes and correlating them to the degree of hepatic fibrosis, half of the patients with F0-F1 and F4 and close to 45% of the patients in F2 and F3 presented depression, and no association was observed between the degree of fibrosis nor the Child-Pugh prognostic scale, **Table 1**. Finally, relating the cases of depression found in the sample to HCV genotypes, genotypes 1A/1B and 1 had more than 50% of patients with depression, genotypes 1A and 1B between 30% and 50%, and the patient with genotype 4 had no depression, (**Table 1**). No association was observed between the variables depression and HCV genotype (p = 0.4332), **Table 1**, not even when we analyzed only genotypes 1, 1A and 1B, the most prevalent genotypes in the population (p = 0.445).

DISCUSSION

The present study sought to describe the prevalence of depression in patients with HCV treated at HUGG and to search for an association between depression and social and biological factors. Almost half of the patients presented

symptoms of depression, corroborating the findings of other studies that reveal a prevalence that varies between 20 and 50% in patients with HCV, while the prevalence in the general population is around 10%.[1,4,11-13] The frequency of depression was high in our study in the pre-treatment period, reinforcing that the active search for depression should be part of the care routine. It is believed that the high rate of mild depression and the low rates of moderate and severe depression are due to the fact that many patients are looking forward to the opportunity to start treatment with AADs and the possibility of a cure.[14-15]

In São Paulo, researchers followed 58 HCV patients before and after treatment with DAAs. The data from the pre-treatment evaluation are similar to those found in our population, that is, high rates of depression and neurocognitive alterations, however, the post-treatment analysis of the São Paulo group shows significant improvement of some neurocognitive symptoms in patients who achieved HCV eradication, but the frequency of depressive symptoms did not show a statistically significant decrease.[16] As the interface of psychic and cognitive symptoms is a frequent and relevant situation in clinical practice, the improvement of neurocognitive symptoms without improvement of depressive symptoms should be highlighted, because the evaluation of these symptoms with integrated tests is important and should be stimulated aiming at improving quality of life during and after HCV infection.[10,17]

The average age found is as expected, since it follows the statistical data from Brazil and the world. It speaks in favor of the length of the disease, which is long, and the chronicity of HCV, where patients are submitted to risk factors for depression, which include social stigma and negative expectations about the prognosis.[1,3,8,18]

In the general population, females are more affected by depression in a 2:1 ratio. Here, we found no statistically significant difference between men and women, which differs from the literature, and we can postulate that the direct action of the virus on the central nervous system is the main explanation, which reinforces that regardless of gender, the search for a diagnosis of depression is fundamental.[1,19]

The occurrence of depression is strongly associated with social and economic indicators, such as low income and education levels. It was expected that the high level of education in this population would be a protective factor, but this did not happen. It is possible that some biological factors, such as the HCV inflammatory-infectious process and chronicity are more relevant for the outcome than those analyzed here.[11,18]

The analysis of viral characteristics showed that in this research, the absolute majority had genotype 1, the most prevalent in Brazil and worldwide, and similar to other studies, the cases of depression were not related to genotype.[1,2,16] The high viral load was expected in this population, because all patients were awaiting the release of DAAs by the Brazilian Ministry of Health, according to the national protocol.[1-2,20-21]

The number of comorbidities and sedentary lifestyle are expected for the average age of the population.[22] Although we did not find a statistical association with depression, these variables may impair the interpretation of neuropsychological tests, since the symptoms of depression may be linked to another disease, demonstrating once again the importance of depression screening and the need to develop studies that seek to elucidate these interactions.[23] The degree of fibrosis also had an equitable distribution between patients with and without depression, indicating that liver dysfunction did not impair the evaluation. The results of the Child-Pugh scale reinforce this idea, since with most patients in Child A5 and it is clear that encephalopathy did not interfere with these results and shows that depressive symptoms were independent of the degree of fibrosis.[12-13,19,23]

The descriptive design, cross-sectionality, and small number of subjects limit the understanding of causality between depression and HCV, as well as the generalization of these data to the entire population. Even so, our data resemble the literature on the topic, presenting a high prevalence of depression in patients with HCV, strengthening the idea that one cannot ignore the high rates of depression in patients with chronic HCV because it can negatively interfere in the quality of life and in the outcomes of the disease and that the development of more studies that seek to understand the cause and effect relationship of these diseases should be encouraged.

CONCLUSIONS

Our results show that the frequency of depression is high in patients with HCV. We also highlight that the frequency of depression was independent of gender, education, HCV genotype, degree of fibrosis, and associated comorbidities. Together, these data indicate the need to establish as a national routine the assessment of depression in HCV patients, especially those assisted by the Unified Health System (SUS), which present socioeconomic frailties and limited access to comprehensive care.

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