

## ORIGINAL ARTICLE

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# Association between anxiety and depression in metabolic dysfunction-associated steatotic liver disease (MASLD)

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## HIGHLIGHTS

- Depression and anxiety have also been a very frequent disorder worldwide; however, few are the studies which relate anxiety to MASLD.
- Data by the WHO demonstrate that Brazil has the highest rate of anxiety (9.3%) and is one of the main countries with high numbers of depression cases (5.8%).
- Recent studies have shown a link between depression and MASLD, as well as a close link between anxiety and MetS, suggesting a higher probability of patients with MASLD having anxiety.
- However, the link between depression, anxiety and MASLD is still inconsistent, since some studies show a positive association, and others did not reach any association.

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**ABSTRACT – Background** – This study aimed to assess the frequency and intensity of anxious and depressive symptoms in patients diagnosed with metabolic dysfunction-associated steatotic liver disease (MASLD). **Methods** – This is a descriptive and cross-sectional study, resulting from 106 patients from the Hepatology outpatient clinic at the *Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo* (HC-FMUSP), São Paulo, Brazil without a history of alcohol abuse, verified by the alcohol use disorders identification test (AUDIT). These were assessed using the sociodemographic data sheet, Hospital Anxiety and Depression Scale (HADS), Hamilton Anxiety Rating Scale (HAM-A), and Hamilton Depression Scale (HAM-D). **Results** – A total of 69.8% were women and 30.2% were men, with a mean age of 61 years. The majority (71.7%) discovered MASLD through routine exams, presenting as comorbidities: Type 2 diabetes mellitus (59.4%), Dyslipidemia (49.1%), Arterial hypertension (68.9%), Obesity (61.3%) and Metabolic syndrome [MetS (63.2%)]. The HADS scale indicates 34% probability of anxiety and 33% depressive symptoms. The Hamilton's scales of intensity indicates 63.9% severe anxiety and 54.3% severe depression. There is also a relationship between anxiety, depression and the female gender, as well as between depression and MetS. **Conclusion** – The findings point to the presence of anxiety and depression in more than one third of MASLD patients, most with severe symptoms. The group is concentrated in the elderly, with many comorbidities, including MetS. There was a positive correlation between anxiety, depression and being female; also, being significant between MetS and depression.

**Keywords** – Anxiety, depression, metabolic dysfunction-associated steatotic liver disease, MASLD.

## INTRODUCTION

Metabolic dysfunction-associated steatotic liver disease (MASLD) is one of the most common hepatic diseases and it is estimated to affect 25% of the global population. It is considered a chronic illness and it consists in the accumulation of fat in the liver of individuals who do not present a significative history of alcohol consumption, the presence of liver diseases or hereditary disorders<sup>(1-3)</sup>. The abnormal retention of fat in the liver is called steatosis and when there is inflammation and damage of the hepatocytes (hepatocellular ballooning), it becomes Metabolic dysfunction-associated steatohepatitis (MASH). Even though it is considered a benign condition, this disease may develop into more advanced forms, such as: fibrosis, cirrhosis and hepatocellular carcinoma, which may require of a liver transplant<sup>(1,4,5)</sup>.

This disease is closely associated with metabolic syndrome (MetS), which includes several diseases, such as arterial hypertension, abdominal obesity, dyslipidemia, resistance to insulin, intolerance to glucose and type 2 diabetes mellitus (T2DM), and it is also a risk factor for the development of cardiovascular diseases<sup>(6)</sup>. Metabolic comorbidities are chronic diseases compromise patients' physical and psychological health, causing an adverse impact on their quality of life. This way, patients are even more vulnerable to suffering from cognitive and self-esteem difficulties and from anxiety and depression. Research conducted by Elwing et al. (2006) showed a higher prevalence of anxiety and depression in patients with MASLD throughout their lifetime in comparison to the control population<sup>(7,8)</sup>.

Data presented by the World Health Organization (WHO) (2017) in 2015 demonstrate that Brazil has the highest rate of anxiety (9.3%), and is one of the main countries with high numbers of depression cases (5.8%). However, the prevalence of anxiety and depression in the global population may vary between studies, according to the diversity of tests and instruments used. In general hospitals, anxiety and depression rates range from 20% to 34%<sup>(9,10)</sup>, while among patients with MASLD, they range from 10% to 25%<sup>(11,12)</sup>.

Evidences suggest that depression is associated with a higher risk of mortality, chronic and cardio-

vascular diseases and MetS. These factors, as a consequence, have a great impact on MASLD patients' lives and on healthcare systems<sup>(13,14)</sup>. Besides depression, anxiety has also been a very frequent disorder worldwide, however, few studies associate anxiety to MASLD<sup>(15-17)</sup>. One recent study, however, conducted in the United States, showed a link between depression and MASLD, as well as a close link between anxiety and MetS, suggesting a higher probability of patients with MASLD having anxiety<sup>(18)</sup>.

However, the link between depression, anxiety and MASLD is inconsistent, since some studies show a positive association<sup>(19,20)</sup>, and others did not<sup>(18,21)</sup>. This study aimed to assess the frequency and intensity of anxious and depressive symptoms in patients diagnosed with MASLD.

## METHODS

### Patients

This research had 110 participants enrolled and in follow-up at the Hepatology outpatient clinic at the *Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo* (HC-FMUSP), São Paulo, Brazil. Among the 110 participants evaluated, four presented a compatible score to harmful use of alcohol on the Alcohol Use Disorders Identification Test (AUDIT). Therefore, they were removed from the protocol, and this study was conducted with 106 participants.

Inclusion criteria were the following: adults (over 18 years of age) from both sexes and races with a diagnosis of MASLD, stabilized in terms of physical illness, to the point that it did not affect the application of the instruments (evaluated by medical report).

Exclusion criteria, for their turn, consisted of: excessive alcohol consumption (defined by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association) as a daily alcohol consumption of >20 g for women and of >30 g for men<sup>(2)</sup>, which was evaluated by the patient's doctor during an appointment, according to the alcohol consumption results on the AUDIT screening test<sup>(22)</sup> the use of illicit substances, considered as medical information on the patient's report; and refusal to participate to the study.

## Procedures

Once a week, over a 6-months period, patients who attended a medical or nutritional appointment were randomly invited to participate in this study, and the ones who accepted signed the free and informed consent form.

After evaluating the criteria of inclusion and exclusion, the tests were applied by the psychologist researcher following each instrument's and scale's instructions.

An extra care was taken to consider patients' possible use of anxiolytics and/or antidepressants; also, the questions were read out loud by the examiner, since most of the patients had difficulties reading. The application lasted about 40 minutes with each patient.

In cases whose results revealed anxiety and/or depression symptoms, patients were welcomed by active listening, given orientations and forwarded to specialized services.

## Demographic and clinical data

The following patients' data was registered: a) sex b) age c) education level d) comorbidities: T2DM, arterial hypertension, dyslipidemia, obesity [body mass index (BMI)], and MetS; and e) use of psychotropic medication.

The data was collected from the patients' reports and from a questionnaire they answered on the same day the scales and tests were applied. The BMI and abdominal circumference calculations to the MetS classification were done by nutritionists.

The BMI classification of patients up to 65 years old was defined according to the WHO parameters in the Seidell and Flegal (1997)<sup>(23)</sup> study, while patients above 65 years old were classified according to the patterns established by Lipschitz (1994)<sup>(24)</sup>. This way, both were grouped according to these classifications.

## Alcohol consumption evaluation by alcohol use disorders identification test AUDIT

The WHO developed this instrument aiming to track excessive ingestion of alcoholic drinks and to identify individuals who would benefit from alcohol consumption reduction or abstinence.

The scoring considers the following risk-level zones: Zone I (0–7 points: low-risk drinking or ab-

stinence); Zone II (8–15 points: (alcohol use in excess of low-risk); Zone III (16–19 points, harmful drinking); and Zone IV (above 20 points: possible alcohol dependence). In this study, patients; who reached a Zone II punctuation or above were excluded<sup>(22)</sup>.

## Anxiety and depression scales

Two instruments were used to evaluate anxiety and depression: The Hospital Anxiety and Depression Scale (HADS) identifies the presence of anxious and depressive symptoms, and the Hamilton's scales evaluate the intensity of the anxious and depressive symptomatology.

### Hospital anxiety and depression scale HADS

The HADS was validated and translated to Brazilian Portuguese and aims to identify mild levels of affective disorders in non-psychiatric environments. It is a self-applicable instrument, composed by 14 multiple-choice items, from which seven question were focused on evaluating anxiety and seven focused on evaluating depression, considering the patient's past week. Each question may vary from zero to three points, with a maximum score of 21 points in each subscale. The cut-off point is the following: 0–8: unlikely anxious and depressive symptomatology, 9–21 likely anxious and depressive symptomatology<sup>(9,25)</sup>.

### Hamilton Anxiety Rating Scale HAM-A

This scale was developed in 1959 and translated to Brazilian Portuguese in 1998 by Moreno and Moreno. It is composed by 14 items equally divided into two groups, one for anxious mood symptoms and another for physical anxiety symptoms, considering the past seven days. Each item may vary in a scale from 0 to 4, according to the intensity and frequency of the symptoms (0=absent, 1=mild, 2=medium; 3=strong, 4=maximum). The total score varies from 0 to 56 points, in which 0–17 is considered the minimum, 18–24 mild, 25–30 moderate and 31–56 severe anxiety<sup>(26,27)</sup>.

### Hamilton Depression Rating Scale HAM-D

This scale was developed in 1960 and translated to Brazilian Portuguese in 1998 by Moreno and Moreno.

Hamilton's depression scale is used to evaluate the presence and the intensity of depressive symptoms in the past seven days. It has three versions, with 17, 21, or 24 items, respectively. In this study we chose the 17-items version. The HAM-D scale items approach somatic symptoms, cognitive symptoms, motor symptoms, anxiety, mood and social symptoms. The punctuation is the following: 0–7 points – minimum; 8–17 points – patients with mild depression; 18–24 points – moderately depressed patients, and above 25 points – severely depressed patients<sup>(26-28)</sup>.

### Statistical analysis

The data analysis process of this study started with a descriptive exploration, resulting in frequency tables for qualitative variables, combined with a proportional confidence interval (CI95%). We calculated descriptive statistics, including mean and standard deviation, medians and minimum and maximum to summarize continuous and discrete quantitative variables.

To study the distribution of qualitative variables according to the Anxiety and Depression groups in the HADS scales and the Hamilton's scales, we used the chi-square test, or Fischer's exact test, when needed.

All tests took into consideration a bidirectional  $\alpha$  of 0.05 and a confidence interval (CI) of 95%, and were performed with the computational support of the following software: R (<https://www.r-project.org/>), IBM SPSS 25 (Statistical Package for the Social Sciences) and Excel 2016 ® (Microsoft Office).

## RESULTS

Of the 106 patients included, 74 (69.8%) were women and 32 (30.2%) were men and the age ranged from 19 to 88 years, with a mean of  $61 \pm 13$ . It was found that all patients (100%) have comorbidities, the most common being T2DM (59.4%), dyslipidemia (49.1%), arterial hypertension (68.9%), obesity (61.3%) and/or MetS in 63.2% of patients.

The average weight of patients is 82 kg, ranging from 44 kg to 133 kg. BMI had an average of 31.8 kg/m<sup>2</sup>, with an average waist circumference of 107.6 cm. Therefore, patients were classified according to their BMI, in which 3.8% of patients are underweight, 13.2% are at adequate weight, 21.7% are overweight and 61.3% are obese.

Most participants (71.7%) discovered MASLD through routine exams and did not have a psychiatric history (75.2%), but 10.4% of patients use anxiolytics and 31.3% use antidepressants.

Through the HADS scale, it was found that most participants were unlikely to have anxious symptoms (66%). With the HAM-A scale, it was possible to classify patients likely to have anxiety, with 5.6% being minimal, 16.7% mild, 13.9% moderate and 63.9% severe. Regarding depression, the HADS scale showed that 33% of patients were likely to have the disease. The classification by the HAM-D scale showed 17.1% mild, 28.6% moderate and 54.3% severe.

Therefore, considering the number of patients who were already using psychiatric drugs (n=44) and the number of patients with anxious/depressive symptoms in this study (n=71), 27 new cases were discovered.

After statistical analysis of the HAD scale for anxiety, we found a relationship between sex and anxiety ( $P=0.013$ ), with a higher prevalence in females. Regarding the HAD scale for depression, it was also possible to verify the correlation between sex and depression ( $P=0.045$ ), with a higher prevalence in females. The degree of obesity and metS did not present statistically significant results in the association between such variables and anxiety/depression according to the HAD scale, as shown in TABLES 1 and 2.

When evaluated according to the Hamilton Anxiety Scale, it was observed that patients had a correlation between sex and anxiety ( $P=0.001$ ), with a higher prevalence in females. Regarding the Hamilton Scale for depression, it was not possible to establish an association between sex and depression ( $P=0.499$ ), but we identified a statistically significant relationship between depression and metS ( $P=0.019$ ), as shown in TABLES 3 and 4.

## DISCUSSION

We have observed a higher rate of women in this study, which matches general statistics of patients in this clinic. This result diverges from literature, which indicates that MASLD is twice more likely to affect men than women<sup>(29-31)</sup>. However, there are controversies, since some recent studies have proven that the disease is more frequent in women<sup>(32-34)</sup>.

**TABLE 1.** Descriptive statistics of the qualitative characteristics evaluated in the study stratified according to the HADS Anxiety Scale including absolute and relative frequency, 95% confidence interval and descriptive level.

HADS Scale - anxiety (HADS-A)	Absence of anxiety		Presence of anxiety		*P-value
	n	% (CI95%)	n	% (CI95%)	
<b>Sex</b>					
Male	27	38.6% (27.8%–50.2%)	5	13.9% (5.5%–27.8%)	0.013
Female	43	61.4% (49.8%–72.2%)	31	86.1% (72.2%–94.5%)	
<b>Obesity degree</b>					
Under weight	4	5.7% (2.0%–13.0%)	0	0.0%	0.601
Eutrophy/adequate	9	12.9% (6.6%–22.1%)	5	13.9% (5.5%–27.8%)	
Overweight/Pre-Obesity	14	20.0% (12.0%–30.5%)	9	25.0% (13.2%–40.7%)	
Severe obesity	43	61.4% (49.8%–72.2%)	22	61.1% (44.8%–75.7%)	
<b>Metabolic syndrome</b>					
No	23	32.9% (22.7%–44.4%)	16	44.4% (29.2%–60.6%)	0.290
Yes	47	67.1% (55.6%–77.3%)	20	55.6% (39.4%–70.8%)	

\*The Fisher-exact P-value.

**TABLE 2.** Descriptive statistics of the qualitative characteristics evaluated in the study stratified according to the HADS Depression scale including absolute and relative frequency, 95% confidence interval and descriptive level.

HADS Scale - depression (HADS-D)	Absence of depression		Presence of depression		*P-value
	n	% (CI95%)	n	% (CI95%)	
<b>Sex</b>					
Male	26	36.6% (26.1%–48.2%)	6	17.1% (7.5%–32.0%)	0.045
Female	45	63.4% (51.8%–73.9%)	29	82.9% (68.0%–92.5%)	
<b>Obesity degree</b>					
Under weight	3	4.2% (1.2%–10.8%)	1	2.9% (0.3%–12.6%)	0.899
Eutrophy/adequate	9	12.7% (6.5%–21.9%)	5	14.3% (5.7%–28.5%)	
Overweight/pre-obesity	17	23.9% (15.2%–34.8%)	6	17.1% (7.5%–32.0%)	
Severe obesity	42	59.2% (47.5%–70.0%)	23	65.7% (49.2%–79.7%)	
<b>Metabolic syndrome</b>					
No	23	32.4% (22.4%–43.8%)	16	45.7% (30.1%–62.0%)	0.204
Yes	48	67.6% (56.2%–77.6%)	19	54.3% (38.0%–69.9%)	

\*The Fisher-exact P-value.

**TABLE 3.** Descriptive statistics of the qualitative characteristics evaluated in the study, stratified according to the Hamilton Anxiety Scale, including absolute and relative frequency, 95% confidence interval and descriptive level.

Hamilton Anxiety Scale (HAM-A)	Minimum		Slight		Moderate		Severe		*P-value
	n	% (CI95%)	n	% (CI95%)	n	% (CI95%)	n	% (CI95%)	
<b>Sex</b>									
Male	0	0.0%	4	66.7% (28.6%–92.3%)	1	20.0% (2.3%–62.9%)	0	0.0%	0.001
Female	2	100.0%	2	33.3% (7.7%–71.4%)	4	80.0% (37.1%–97.7%)	23	100.0%	
<b>Obesity degree</b>									
Under weight	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0.173
Eutrophy/adequate	1	50.0% (6.1%–93.9%)	2	33.3% (7.7%–71.4%)	0	0.0%	2	8.7% (1.9%–25.1%)	
Overweight/pre-obesity	0	0.0%	2	33.3% (7.7%–71.4%)	0	0.0%	7	30.4% (14.8%–50.7%)	
Severe obesity	1	50.0% (6.1%–93.9%)	2	33.3% (7.7%–71.4%)	5	100.0%	14	60.9% (40.6%–78.6%)	
<b>Metabolic syndrome</b>									
No	1	50.0% (6.1%–93.9%)	4	66.7% (28.6%–92.3%)	3	60.0% (20.9%–90.6%)	8	34.8% (18.0%–55.1%)	0.431
Yes	1	50.0% (6.1%–93.9%)	2	33.3% (7.7%–71.4%)	2	40.0% (9.4%–79.1%)	15	65.2% (44.9%–82.0%)	

\*The Fisher-exact P-value.



**TABLE 4.** Descriptive statistics of the qualitative characteristics evaluated in the study, stratified according to the Hamilton Depression Scale, including absolute and relative frequency, 95% confidence interval and descriptive level.

Hamilton Scale - depression (HAM-D)	Minimum		Slight		Moderate		Severe		*P-value
	n	% (CI95%)	n	% (CI95%)	n	% (CI95%)	n	% (CI95%)	
<b>Sex</b>									
Male	0	0.0%	1	16.7% (1.9%–55.8%)	3	30.0% (9.3%–60.6%)	2	10.5% (2.3%–29.7%)	0.499
Female	0	0.0%	5	83.3% (44.2%–98.1%)	7	70.0% (39.4%–90.7%)	17	89.5% (70.3%–97.7%)	
<b>Obesity degree</b>									
Under weight	0	0.0%	0	0.0%	1	10.0% (1.1%–38.1%)	0	0.0%	0.282
Eutrophy/adequate	0	0.0%	2	33.3% (7.7%–71.4%)	1	10.0% (1.1%–38.1%)	2	10.5% (2.3%–29.7%)	
Overweight/pre-obesity	0	0.0%	1	16.7% (1.9%–55.8%)	3	30.0% (9.3%–60.6%)	2	10.5% (2.3%–29.7%)	
Severe obesity	0	0.0%	3	50.0% (16.7%–83.3%)	5	50.0% (22.4%–77.6%)	15	78.9% (57.4%–92.4%)	
<b>Metabolic syndrome</b>									
No	0	0.0%	3	50.0% (16.7%–83.3%)	8	80.0% (49.7%–95.6%)	5	26.3% (10.8%–48.4%)	0.019
Yes	0	0.0%	3	50.0% (16.7%–83.3%)	2	20.0% (4.4%–50.3%)	14	73.7% (51.6%–89.2%)	

\*The Fisher-exact P-value.

It is valid to consider that women are much more aware of their own health and look for help more often than men. Some authors suggest that this is due to men's socialization, in which self-care is not a common male practice<sup>(35-37)</sup>. Moreover, Lonardo et al. (2019)<sup>(38)</sup> showed that the condition is more common in women after menopause ( $\geq 50$ –60 years old), when they are more likely to develop the main MASLD risk factors, such as weight gain and dyslipidemia<sup>(39)</sup>.

Most patients in this study have identified the disease through routine checkups (71.7%). This is not uncommon, and it happens because it is an asymptomatic and silent condition. Therefore, the suspicion arises only after alterations in routine checkups, such as in blood test results (hepatic alteration) or in ultrasounds<sup>(40,41)</sup>.

Facing this problem, associations such as the European Association for the Study of the Liver (EASL) and the Latin American Association for the Study of the Liver (ALEH) have already recommended that medical doctors require screening exams to the high-risk population, such as to obese patients and those with MetS<sup>(42,43)</sup>. Routine checkups done in primary care may help detecting the disease early, and it may prevent comorbidities and worsening of the clinical picture, directing them to appropriate treatment<sup>(44)</sup>.

Most of the participants in our study presented MetS or at least one risk factor for developing it. Previous studies showed that the more MetS-related-diseases a patient has, the more likely it is that their liver disease worsens. Besides, we have observed that the increase in the number of MetS components may be related to a lower survival rate<sup>(2,45)</sup>.

Regarding mental health, anxiety and depression are the most frequent psychiatric disorders among patients with MASLD, however, the link between these points is still ambiguous, since some studies found a positive link between depression and MASLD, while others did not reach any significant association<sup>(18,20,21,46,47)</sup>. Moreover, according to Filipovi et al. (2018), some studies related depression to MASLD's histological severity, while other studies denied the link between them. This link could not be achieved in this research due to its low statistical power<sup>(48)</sup>.

Anxiety and depression rates in our patients were high (34% and 33%, respectively), and higher than in previous studies that used the same scales, which showed an anxiety rate of 19.6%, a depression rate of 24.5% and a 10.7% rate for both disorders<sup>(11,49)</sup>. Although most patients have not reached a significant likelihood of psychiatric disorders, most of those who did present them are already in a severe clinical condition.

It is necessary to take into consideration that this study was performed in a tertiary hospital, in which patients have shown a more severe clinical picture and a longer diagnosis period. Therefore, most of them may suffer from anxiety and/or depression for a long time, but have not had a chance for early detection and appropriate treatment. This way, at the time of this evaluation, they presented a more severe psychological state<sup>(12)</sup>. Therefore, the importance of psychological assessment in these patients is given, in which 27 new cases were discovered in this work, which can be followed up.

Some issues made the analysis more difficult, such as the small sample size and the presence of other concomitant chronic liver diseases<sup>(20,21)</sup>. Besides, it is important to highlight that the instruments used in this research required only the patients' own answers, but not the psychologist's perception of their attitude. Therefore, other types of instruments could have led to even more severe results, had some aspects beyond the objective test questions been considered.

In our study, anxiety in patients with MASLD has a close link to women, and this finding was also described Labenz et al. (2019)<sup>(50)</sup>. However, other studies did not meet this result and, therefore, there is no literature consensus of this link, since few are the researches on this subject<sup>(15,51)</sup>.

While the prevalence of MASLD is higher in men, according to literature, the prevalence of depressive symptoms is higher among women, which confirms our study and is consistent with previous findings. The difference between sexes when it comes to anxiety and depression may be due to biological and/or social factors that diverge between men and women<sup>(51,52)</sup>.

In the past decades, women have gone through professional, social and familiar transformations inside a rigid and restrictive culture towards them – as a consequence, they may end up having higher chances of developing depressive and anxious pictures due to the combination of stressors inside the biopsychosocial dynamics<sup>(53)</sup>.

Other studies also mentioned epigenetics, that is, genetics combined with environmental factors, which can lead to the development of depression and anxiety. Moreover, we must also consider biological differences, mainly when it comes to the endocrine

system and feminine sexual hormones, which may alter the development and the course of anxious and depressive disorders<sup>(54)</sup>.

In accordance to our study, recent studies have pointed out a significative link between depression and metabolic diseases, as shown in Jung et al. (2019)<sup>(19)</sup> and Repousi et al. (2018)<sup>(55)</sup> researches. The exact mechanisms that involve the link between depression and MetS are not so well known; however, some hypotheses have been brought up in this matter, such as unhealthy lifestyle, including unhealthy eating habits and low physical activity<sup>(56)</sup>.

Other studies approached some points that depression and MetS have in common, such as dysregulation of the hypothalamic-pituitary-adrenal axis with final hypothalamic inflammation<sup>(57)</sup>, the association with low-grade chronic inflammation<sup>(58)</sup> and the likelihood of these diseases' progression being related to oxidative stress<sup>(59,60)</sup>. Besides, one of the main factors that may contribute to the development and progression of MASLD is resistance to insulin. This way, we speculate that this factor could unleash depression-related processes<sup>(19)</sup>.

We have observed that the progression of a liver disease interferes with patients' physical and mental health, drastically reducing their quality of life. As a consequence, patients may present psychological and behavioral changes, therefore making it necessary to change their habits and the way they deal with these problems. This may also cause many conflicts and internal feelings, increasing their need for medical and psychological support<sup>(61)</sup>.

It is known that, currently, MASLD treatment includes mainly changes in lifestyle with physical exercise, healthy food and weight loss. However, these may be difficult goals to be reached and maintained, since they require more than a mere behavioral change, and patients may encounter physical, social, and economic barriers. These points do not only refer to an individual issue, and may directly influence them, positively or negatively<sup>(62)</sup>.

Thinking of depressed patients, it is known that they tend to manifest less-healthy behaviors, such as: an inflammatory diet, rich in palatable foods or fast food, high food ingestion for seeking pleasure; a sedentary lifestyle, sleep alterations and low adherence to treatment<sup>(63)</sup>.

Pleasure among individuals with anxiety and depression is lower, making the intake of sweets – a big source of pleasure – difficult to be reduced or ceased. One of the physiological explanations for this movement is that some hormones act as neurotransmitters – like dopamine, serotonin and oxytocin – directly on mood and affection regulation. This way, changes in these systems may lead to mood or behavior changes: when people go through a stressful situation or emotional exhaustion, especially those who present anxiety and depression, they may increase the intake of such foods to compensate the deficiency caused by the hormonal alteration<sup>(64)</sup>.

Still regarding food habits change, the recommendation is that patients with MASLD follow a Mediterranean diet, however, they may regard it as more expensive or more difficult to prepare<sup>(65)</sup>. Therefore, it is necessary to plan, supervise and structure a new diet for each patient, according to their limitations (Johnson, 2013)<sup>(66)</sup>. Some authors suggest that changing food habits may prevent and be therapeutical for mental illnesses, such as anxiety and depression<sup>(67)</sup>.

Anxious and depressed patients need some level of supervision for better support and encouragement that they will be able to initiate and maintain their new routines in the lifestyle change plan<sup>(68)</sup>. Thus, it is essential to establish real goals to each patient, considering that the more we know one patient and adjust to their possibilities and needs, the higher is their adherence to treatment<sup>(69)</sup>. Regarding physical activity, it may not be appropriate to every depressed patient because some may have physical limitations or limiting beliefs, so making the imposition of physical exercise could actually reduce its adherence<sup>(70,71)</sup>. For these patients, it is important to consider and put into practice some motivation and adherence strategies<sup>(72)</sup>.

MAFLD patients have lower adherence to treatment since it usually requires commitment and continuity. Some factors contribute to the difficulty in adhering to treatment, such as the lack of social support, the presence of psychiatric diseases and changes in a lifestyle that had been established long before, requiring much more effort to change it<sup>(73,74)</sup>. This way, a multidisciplinary follow-up is needed, mainly when it comes to psychology, for being able to intervene directly on patients' personal motivation, willpower, self-esteem, and beliefs<sup>(75)</sup>.

The approach to the causal relationship between clinical manifestations at the level of organic processes, characterized as expressions of symptoms or physical signs and their representation in the sphere of affective-emotional processes, should not be considered as cause-effect mechanisms between them, but rather, as simultaneous expressions of the same phenomenon of the individual, in a more global and integrated context of the human being in the psychosomatic view (2010)<sup>(76)</sup>. Therefore, this psychosomatic approach of the professional to the individual should be considered within a bio-psycho-social context, thus, integrating the individual at a certain time of his relationship with his internal and relational world<sup>(76-78)</sup>.

In cases whose results revealed anxiety and/or depression symptoms, patients were welcomed by active listening, given orientations and forwarded to specialized services. The psychology professional can also help minimize the distance between the doctor's and/or nutritionist's speech and the patient's daily habits, a usually frustrating issue to the patient who cannot follow what is required by the health professionals. Besides, the psychologist can help the patient understand which emotions may directly interfere on their eating habits and why, adjusting and offering them new ideas to deal with non-physiologic desires<sup>(79,80)</sup>.

## CONCLUSION

We have identified the presence of anxiety and depression in most of the participants of this study, and that most of them present severe symptomatology. We have also observed that this group is concentrated on the elderly, with many comorbidities and the presence of MetS. The link between anxiety, depression and participants' sex was positive to women, but not significant for obesity or most of the comorbidities. There was a significant link between MetS and depression.

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## Authors' contribution

Botacin EC: collected the data and wrote the manuscript. Duarte SMB: Duarte SMB: collected the data and helped with the revision of the manuscript. Stefano JT: wrote and helped with the revision of the manuscript. Barbosa MED: collected the data, Pessoa MG: collected the data and Oliveira CP: study design, wrote, and helped with the revision of the manuscript.

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Botacin EC, Duarte SMB, Stefano JT, Barbosa MED, Pessoa MG, Oliveira CP. Associação entre ansiedade e depressão na Doença hepática esteatótica associada à disfunção metabólica (MASLD). *Arq Gastroenterol.* 2024;61:e23128.

**RESUMO – Contexto** – Este estudo teve como objetivo avaliar a frequência e a intensidade dos sintomas ansiosos e depressivos em pacientes com diagnóstico de doença hepática esteatótica associada à disfunção metabólica [do inglês: *Metabolic dysfunction-associated steatotic liver disease* (MASLD)]. **Métodos** – Trata-se de um estudo descritivo e transversal, resultante do acompanhamento de 106 pacientes do Ambulatório de Doença Hepática Esteatótica Associada à Disfunção Metabólica (A2MG700) da Disciplina de Gastroenterologia Clínica do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HC-FMUSP), São Paulo, Brasil, sem história de abuso de álcool, verificada pelo *Alcohol Use Disorders Identification Test* (AUDIT). Foram avaliados os dados sociodemográficos, Escala hospitalar de ansiedade e depressão [do inglês: *Hospital Anxiety and Depression Scale* (HADS)], Escala de avaliação de ansiedade de Hamilton [do inglês: *Hamilton Anxiety Rating Scale* (HAM-A)] e Escala de depressão de Hamilton [do inglês: *Hamilton Depression Scale* (HAM-D)]. **Resultados** – Um total 69,8% dos indivíduos eram do sexo feminino com idade média de 61 anos. A maioria dos indivíduos avaliados (71,7%) descobriu a doença por meio de exames de rotina e apresentavam diabetes mellitus tipo 2 (59,4%), dislipidemia (49,1%), hipertensão arterial (68,9%), obesidade (61,3%) e síndrome metabólica [SM (63,2%)]. A análise da escala HADS demonstrou probabilidade de ansiedade em 34% dos participantes e 33% de sintomas depressivos. A escala de intensidade de Hamilton demonstrou que 63,9% dos indivíduos apresentavam ansiedade severa e 54,3% depressão severa. Observamos também relação entre ansiedade, depressão e o sexo feminino, assim como, entre depressão e SM. **Conclusão** – Nossos achados demonstram a presença de ansiedade e depressão em mais de 1/3 dos indivíduos com MASLD avaliados e a maioria apresenta sintomas graves. O grupo era composto por pacientes idosos e com comorbidades, incluindo SM. Observamos correlação positiva entre ansiedade, depressão e sexo feminino, sendo significativa entre SM e depressão.

**Palavras-chave** – Ansiedade; depressão; doença hepática esteatótica associada à disfunção metabólica.

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