

Anxiety and depression in patients with post-COVID-19 comorbidities

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Abstract

Background: The COVID-19 pandemic has brought significant impacts on mental health, increasing conditions such as anxiety and depression. The negative impact was even bigger among the population with chronic illnesses like diabetes, hypertension, and obesity. Fear of contamination, social isolation, lack of medical follow-up, and changes in lifestyle have contributed to the worsening of these disorders. **Objective:** The aim of this study was to assess anxiety and depression levels and quality of life in individuals with pre-existing comorbidities post COVID-19. **Methods:** This is a cross-sectional study with a descriptive and analytical approach. The study included 125 individuals divided in healthy group and chronically ill group. Behavioral and clinical characteristics were evaluated, such as physical activity after COVID-19, smoking, alcohol consumption, pre-existing comorbidities, and symptoms of anxiety and depression. **Results:** The study highlighted that the patients with diabetes and hypertension suffered the most from anxiety and depression possibly due to the higher susceptibility to coronavirus infection and the negative impact of these pre-existing conditions on mental health. In hypertensive individuals, the complex interaction between emotional stress, anxiety, and cardiovascular system dysregulation contributed to increased levels of anxiety and depression. Obesity, besides a risk factor for severe COVID-19, it also negatively impacted the immune system and had adverse effects on mental health, with an increase in depressive and anxious symptoms. **Conclusion:** This study emphasizes the need of special care to at-risk groups to minimize adverse impacts on mental health and improve the quality of life of individuals with pre-existing comorbidities post COVID-19.

Keywords: Anxiety; depression; chronic diseases.

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BACKGROUND

The emergence of a pandemic can cause psychosocial disruption in response to a threat. The World Health Organization (WHO) warns that at least one-third of the population exposed to a pandemic may suffer psychopathological manifestations, depending on the magnitude of the event and the degree of vulnerability. The first reaction is panic, a sudden and extraordinary fear that can influence behavior and decision-making⁽¹⁾. Since the emergence of Coronavirus Disease 2019 (COVID-19) in December 2019, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has infected more than 500 million people worldwide. Severe respiratory symptoms, high mortality rates, and rapid transmissibility have made COVID-19 a serious illness that has had a negative impact on physical and mental health. During the pandemic, many

people felt severe anxiety and fear of getting sick, which led to a range of mental health symptoms, including lack of motivation, anhedonia, exhaustion, irritability, and sleep disturbances. Depression and anxiety during COVID-19 have been leading causes of a global health-related burden and will have long-term economic and social consequences⁽²⁾.

COVID-19 Mental Disorders Collaborators (2020)⁽³⁾ reported that the emergence of the COVID-19 pandemic has raised many questions about the effects on mental health through its direct psychological effects and long-term economic and social consequences.

COVID-19 has spread throughout most of the world's population, with significant health consequences and mortality among those who become infected. In addition to the direct effects of COVID-19, the pandemic has created an environment in which many determinants of mental health have also been affected. Social restrictions, lockdowns, school and business closures, loss of livelihoods, decreased economic activity, and shifting priorities of governments in their attempt to control COVID-19 outbreaks have had the potential to affect the mental health of the population substantially.

Survivors of COVID-19 may experience persistent symptoms related to cardiopulmonary, neurological, and psychological sequelae, among others, for a long time. The definition of this condition is still uncertain. Still, the persistence of symptoms for more than 12 weeks after acute infection has been called post-COVID syndrome (or long COVID) and has an essential impact on quality of life and health status, which can negatively influence activities of daily living and return to work, with consequences for the mental health of these patients⁽⁴⁾.

It is essential to determine the main risk groups for any disease, accentuated during a pandemic, especially for professionals to make decisions. Associated chronic diseases are called comorbidities and appear when a patient, during their evolution, suffers from some underlying disease⁽⁵⁾. Furthermore, the comorbidity of chronic diseases has been another risk factor for mental health problems during the COVID-19 pandemic. A multinational, multicenter study reported that healthcare professionals with comorbid chronic diseases, such as hypertension, hyperlipidemia, and diabetes mellitus, had greater susceptibility to psychological problems than those without comorbidities. The incredible difficulty in accessing medical care during the pandemic is an essential reason for the increase in depression and anxiety associated with chronic illnesses⁽²⁾. This study hypothesizes that individuals with previous comorbidity and who had COVID-19 have a higher prevalence of anxiety and depression, as well as a worsening quality of life. Therefore, this article aims to verify the rates of anxiety and depression and the quality of life in people with previous comorbidity after COVID-19.

METHODS

This is a cross-sectional observational study with a descriptive and analytical approach, which sought to verify the rates of anxiety and depression and quality of life in four groups that are an Obesity Group (OBSG), a Systemic Arterial Hypertension Group (SAHG), a Diabetes Mellitus Group (DMG) and Control Group (CG). The research complied with resolution 466/2012 and its supplementary 510/2016 of the National Health

Council and was approved by the Research Ethics Committee of the Federal University of Delta do Parnaíba, under opinion n.º. 5,393,151. One hundred twenty-five volunteers participated in the study, with a confirmed diagnosis of infection with the new coronavirus, positive PCR or serology for at least three and a maximum of 12 months and who had not undergone rehabilitation during this period; aged between 18 and 59 years old, of both sexes; and individuals who reside and have been notified in Parnaíba (PI), Brazil. The exclusion criteria were patients who did not agree to participate in the research; patients with psychological/emotional/neurological impairment that makes it impossible to respond to the applied methodological instruments; with a history of pneumonia, flu accompanied by fever, body pain or diarrhea and anosmia for less than 15 days; who were diagnosed with any comorbidity after being infected by SARS-COV-2 and patients who are in Post-Covid rehabilitation or have undergone treatments for post-Covid comorbidities in the last 03 months. In the Epidemiological Surveillance Sector of the Municipality of Parnaíba (PI) Brazil, the "investigation files for SG suspected of coronavirus disease 2019" were analyzed and selected, valid throughout the national territory for notification of COVID-19 cases in each municipality, according to the research inclusion criteria. Next, the personal data of each patient and the UBS receiving assistance were collected. A search for people positive for COVID-19 was also carried out in the Clinical Analysis laboratory of the Federal University of Delta do Parnaíba (UFDFPar), Parnaíba (PI), Brazil. Soon after, the volunteers were contacted which they were explained about the project, and requested, according to the availability of each individual, that they attend the Pain Neuromodulation and Sensorimotor Performance Laboratory (LANDS) at UFDFPar, with a scheduled time and scheduled date, complying with all health safety protocols, on which the Free and Informed Consent Form (TCLE) was requested to be signed, and the assessment instruments were applied individually. Furthermore, participants received guidance on post-Covid-19 care, the need for monitoring, and the importance of post-Covid-19 rehabilitation. Each patient is also individually advised about their current clinical condition and comorbidity.

Initially, the researchers prepared a sociodemographic and clinical questionnaire to investigate gender, age, education, self-declared race/color, marital status, occupation, and religion. This was followed by questions about behavioral and clinical characteristics such as physical activity after COVID-19, smoking, alcohol consumption, previous comorbidities, date of positive test for COVID-19, symptoms presented, sequelae, hospitalization, immunization for COVID-19, number of doses, and presence of reinfection with SARS-COV-2.

Symptoms of anxiety and depression were assessed using the Brazilian version of the Beck Depression Inventory (BDI) for depression and the Visual Analogue Scale (VAS) for anxiety, respectively. BDI is a self-assessment measure of depression consisting of 21 items, whose intensity varies from zero to 3, with higher scores indicating more depressive symptoms⁽⁶⁾. The VAS for general anxiety is assessed using a 100 mm long horizontal line. The extreme left end means no anxiety, and the extreme right end means the worst possible anxiety⁽⁷⁾.

The sample calculation was estimated according to official data on cases confirmed by the State Department of Health of the State of Piauí (<http://www.saude.pi.gov.br/>)

and official data on the total population of Parnaíba (PI), Brazil. Considering the period from 03/20/2020 to 02/21/2022, there were 19,206 confirmed cases in the population of Parnaíba (PI), Brazil. Adopting a confidence interval and precision value of 95% and ± 0.07 , respectively, the minimum sample size was estimated at 86 subjects. However, considering losses resulting from non-responders, the estimated sample was 100 individuals.

The graphpadprism5 program was used to perform statistics between the groups. Initially, the data were tabulated in Excel and presented as mean and standard deviation, in addition to the statistical test used: Kruskal-Wallis with Dunn's post-test.

RESULTS

A total of 137 individuals, 125 of whom met eligibility criteria for the study, with 81 participants being part of the Control Group (CG), 19 being part of the Obesity Group (OBS), 17 being part of the Arterial Hypertension Group Systemic (SAH) and 8 are part of the Diabetes Mellitus Group. There was loss of follow-up, as 12 volunteers had other comorbidities not analyzed in this study. Of the total sample, there were 125 individuals, 81 (CG), 19 (OBSG), 17 (SAHG) and 8 (DMG).

In the participants studied, the most prevalent gender in all groups was female, giving a total of 91 participants (72.8%) and the average age in all variables was 41.75 years (± 5.5 years), as can be seen in Table 1.

Table 1. Demographic data of the groups studied

Variables	CG (n=81)	SAHG (n=17)	OBSG (n=19)	DMG (n=8)	Total/mean (n=125)
Gender Female	65 (80,2%)	9 (52,9%)	12(63,2%)	5 (62,5%)	91 (72,8%)
Gender Male	16 (19,8%)	8 (47,1%)	7 (36,8%)	3 (37,5%)	34 (27,2%)
Age (years) mean (sd)	37 ($\pm 11,9$)	48 ($\pm 8,6$)	38 ($\pm 13,0$)	45,5 ($\pm 5,4$)	41,75 ($\pm 5,5$)

CG: Control Group; OBSG: Obesity Group; SAHG: Arterial Hypertension Group; DMG: Diabetes Mellitus Group; sd: Standard deviation.

Regarding the habits and addictions of the study participants, of the total number of participants in the variables, 49 (39.2%) participants are alcoholics, with the control group being 26 (32.1%), the arterial hypertension group being 9 (52.9%), obesity group 11 (57.9%), diabetes mellitus group 3 (37.5%) and 8 (6.4%) are smokers, with control group 2 (2.5%), arterial hypertension 3 (17.6%), obesity group 2 (10.5%), and diabetes mellitus group 1 (12.5%). Of the total number of variables, 56 participants, representing 44.8%, do not practice post-COVID physical activity, with the control group being 36 (43.2%), hypertensive 4 (23.5%), obese 11 (57.9%) and diabetics 5 (62.5%), 51 (40.8%) participants practice physical activity >150 min/week, with control group 35 (43.2%), hypertensive 9 (53%), obese 6 (31, 6%, and diabetics 1 (12.5%) and 18 (14.4%) <150 min/week, with control group 10 (12.3%), hypertensive 4 (23.5%), obese 2 (10.5%), and diabetics 2 (25%) as can be seen in Table 2.

Table 2. Habits and addictions of the groups studied.

Variables	CG (n=81)	SAHG (n=17)	OBSG (n=19)	DMG (n=8)	Total/mean (n=125)
Alcoholic	26 (32,1%)	9 (52,9%)	11 (57,9%)	3 (37,5%)	49 (39,2%)
Smoker	2 (2,5%)	3 (17,6%)	2 (10,5%)	1 (12,5%)	8 (6,4%)
No physical activity	36 (44,5%)	4 (23,5%)	11 (57,9%)	5 (62,5%)	56 (44,8%)
>150 min/Without	35 (43,2%)	9 (53%)	6 (31,6%)	1 (12,5%)	51 (40,8%)
<150 min/Without	10 (12,3%)	4 (23,5%)	2 (10,5%)	2 (25%)	18 (14,4%)

Notes*: CG = Control Group; OBSG = Obesity Group; SAHG = Arterial Hypertension Group; DMG = Diabetes Mellitus Group.

In table 3, you can see the number of participants in each group who had reinfection, in addition to the total number of participants in all variables who had reinfection, 33 (26.4%).

Table 3- Reinfection of the groups studied

Variables	GC (n=81)	SAHG (n=17)	OBSG (n=19)	DMG (n=8)	Total (n=125)
Reinfection (sd)	22 (27,2%)	7 (41,2%)	2 (10,8%)	2 (25%)	33 (26,4%)

Notes*: CG = Control Group; OG = Obesity Group; AHG = Arterial Hypertension Group; DMG = Diabetes Mellitus Group; sd = Standard Deviation.

Comparing the anxiety variable, there was a significant difference between the groups ($p=0.0024$). In the pairwise comparison, the difference was between the DM group and the SAH group in relation to the control group ($p<0.05$). Comparing the depression variable, there was a significant difference between the groups ($p=0.0068$). In the pairwise comparison, the difference was between the DM group, the SAH group and the obesity group in relation to the control group ($p<0.05$) (figure 1).

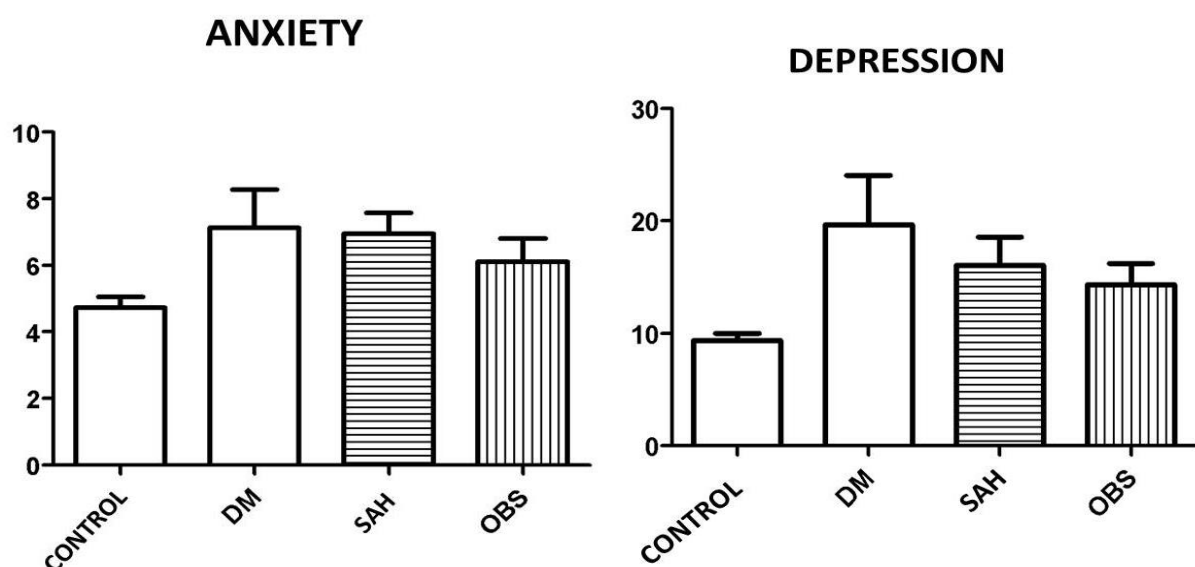


Figure 1. Assessment of anxiety and depression in patients with COVID-19 and comorbidities

Statistical test used: Kruskal-Wallis with Dunn's post test.

Notes*: DM= Diabetes Mellitus Group; SAH= Arterial Hypertension Group; OBS= Obesity Group

DISCUSSION

Anxiety and depression are significant mental health problems that affect many people around the world, and these conditions can be triggered by a variety of factors. One of the diseases that has gained prominence in recent years due to its ability to affect mental health is COVID-19. Infection with the SARS-CoV-2 coronavirus may have had significant implications for mental health, especially in patients with post-COVID-19 comorbidities. Therefore, this study aimed to investigate the relationship between COVID-19 and anxiety and depression rates in obese, diabetic and hypertensive patients diagnosed prior to SARS-CoV-2. COVID-19 has affected the population's mental health in several ways due to a combination of factors related to the disease itself, the control measures implemented, and lifestyle changes associated with the pandemic. Many people experienced fear of contracting the disease due to the exponential increase in the death rate at the height of the pandemic. Social isolation, excessive information, and concerns about health and changes in daily routine have caused psychological discomfort in the population. Asmundson; Taylor, (2020)⁽⁸⁾; and Carvalho et al. (2020)⁽⁹⁾ pointed out that the fear of contracting COVID-19, as it spreads quickly and its nature and course were still little known, could affect the psychological well-being of many people.

Several risk factors are associated with COVID 19 and its worsening. Studies show that people with previous comorbidities increase the chance of infection and there is a greater probability of death from the disease compared to people who have no pre-existing conditions^(10,11). The most relevant comorbidities are: arterial hypertension, cardiovascular diseases, diabetes and respiratory illnesses, which were considered risk factors for fatality, as these diseases share characteristics with infectious diseases, such as the pro-inflammatory state, attenuation of the innate component of the immune response and low immune function, by affecting macrophages and lymphocyte function, which can make individuals more prone to disease complications⁽¹²⁾.

Therefore, our study demonstrated that patients with diabetes and hypertension were the groups that suffered most from anxiety and depression ($p < 0.05$). This finding can be justified because these individuals are more susceptible to contracting the disease due to damage to the immune system and genetic conditions that cause fear and stress in these individuals⁽¹³⁾. A study carried out by Souza et al. (2021)⁽¹⁴⁾ investigated the frequency and causes associated with signs and symptoms of psychological disorders, such as anxiety and depression in diabetic patients during the COVID-19 pandemic. An increase in signs of anxiety and depression was observed, which is associated with the pathophysiology of metabolic syndrome.

Outside of the pandemic environment, diabetics already suffer from the pressure of having to strictly follow a treatment and diet to control glycemic levels in the body⁽¹⁵⁾. Furthermore, signs of anxiety and depression occur three times more often when compared to healthy individuals, which is justified by the impairment of brain function caused by the metabolic disorder⁽¹⁶⁾. The production of hormones and substances important for good brain function and humoral balance is deregulated in diabetes, a drop in the levels of insulin-like growth factor (IGF) in the brain is a favorable factor that contributes to episodes of depression. On the other hand, higher levels of cortisol are pre-

sent in patients with diabetes, as hyperglycemia favors a greater release of this hormone by the hypothalamic-pituitary-adrenal axis⁽¹⁷⁾.

Added to these pathophysiological factors, there is also a change in focus on the health care of individuals during the pandemic. As it is a new disease that has decimated the lives of many, COVID-19 gained attention to the detriment of other diseases already known and studied⁽¹⁸⁾. This led to a collapse in healthcare systems, a lack of medicines, especially for diabetics, which reveals a decline in the care provided to these people. Furthermore, psychological support for patients with diabetes decreased significantly during the pandemic⁽¹⁹⁾.

Therefore, due to the physiological, emotional and behavioral changes caused by diabetes, which already predisposes to anxiety and depression, together with the fear and anxiety that the COVID-19 pandemic brings, especially to people with comorbidities, and neglect in treatment and monitoring diabetic patients during the pandemic period, are determining factors for increased anxiety and depression.

In relation to patients with hypertension, in the present research it was possible to observe that the levels of anxiety and depression increased in relation to the control group and presented higher rates than those with obesity, this finding is in line with the literature. Several studies demonstrate that throughout the pandemic period there was an increase in blood pressure in patients who were already hypertensive. The study by Nagai et al.^(20,21) speculates that the central autonomic network comprising the periaqueductal gray matter, parabrachial nucleus, nucleus of the solitary tract, ventrolateral nucleus, hypothalamus, amygdala and insular cortex are responsible for regulating the cardiovascular system and that the networks of these regions are necessary to regulate the central automatic system in response to emotional stress, that is, the anxiety generated by the pandemic leads to a deregulation of the autonomic cortical pathways, resulting in an increase in sympathetic activity that leads to an increase in catecholamines and cortisol by the pituitary-adrenal axis resulting in increased blood pressure. Although the exact mechanism is unknown, periods of anxiety disorders caused by natural disasters such as earthquakes and pandemics trigger the adrenergic system. This sympathetic excitation causes an increase in heart rate and a decrease in the diameter of blood vessels and consequently results in an increase in blood pressure⁽²²⁾.

For these patients, in addition to facing a global health and social crisis, they had to deal with the constant fear of contamination and of developing the most serious form of the disease, considering that just as arterial hypertension causes several systemic changes in organisms, the progression of Covid-19 can cause cardiovascular complications. In addition, anxiety is directly associated with greater risks of cardiovascular incidents during the Covid-19 pandemic⁽²³⁾. It is important to highlight that the older the patients are, the more vulnerable they are to developing the most critical form of Covid-19, as well as the more likely they are to develop large variations in blood pressure along with stress and depression, as uncontrolled hypertension ($> 140 \times 90$ mmHg) is more significant in those who have anxiety than those who do not have anxiety, according to the study by Zhang et al.⁽²³⁾ In this group, the increase in BP is also more common due to stress, since the axis response hypothalamic-pituitary-adrenal increases with aging⁽²²⁾. In this way, it can be seen how the increase in the level of anxiety due to the pandemic and

consequently Covid-19 compared to the pre-pandemic period, interfering with people's quality of life in different aspects, such as fear, insomnia, unemployment, isolation and consequently lack of emotional support. In this sense, hypertension is a comorbidity that is directly affected by mental problems such as anxiety and depression.

Obesity is defined when the body mass index is above 30kg/m², the increase in fat cells causes functional and structural changes in the body. Excess subcutaneous fat around the chest and abdomen restricts lung expansion during the respiratory cycle⁽²⁴⁾, thereby reducing vital respiratory capacity, thus obesity significantly interferes with the respiratory condition of individuals, which contributes to the development of the severe form of covid-19, thus increasing the morbidity and mortality of patients. Obese people commonly present other conditions that are associated with the worsening of Covid-19, such as hyperglycemia, diabetes mellitus, dyslipidemia, hypertension, etc., which further worsens the prognosis of these patients. Furthermore, obesity interferes with the immune system, since visceral fat produces pro-inflammatory cytokines that are increased by viral activity that generates the cytokine storm⁽²⁴⁾, in addition to the fact that adipose cells are a reservoir for SARS-Cov-2 since it has the receptor for the enzyme present in the virus, ACE-2 (angiotensin-converting enzyme). ACE-2 gene expression is higher in visceral and subcutaneous adipose tissues than in lung tissue of the human body, an important target tissue affected by SARS-CoV-2. This suggests a mechanism by which excess adiposity can lead to greater severity of infection in patients with Covid-19 according to the study by Al-Benna⁽²⁵⁾. The deregulated immune response is multifactorial in obesity and the disorder of immune cell metabolism is an important factor. Therefore, this comorbidity negatively affects the treatment and prevention of Covid-19 as immune cell dysfunction reduces the effect of vaccination against Covid-19. SARS-CoV-2⁽²⁴⁾.

As all the changes that obesity can cause physically in the mental issue is no different, in the study by Frankli, Janet et al.⁽²⁶⁾ 20.7% said they developed severe depression and 19.5% symptoms of anxiety. The quarantine changed many habits, including food, fast food and processed foods, which saw an increase in consumption and, on the other hand, physical activity, as reported in several studies, was more difficult to maintain, including what was observed in this study, in which among participants, the majority of obese people do not practice physical activity. It was also possible to observe in the study by Frankli, Janet et al.⁽²⁶⁾ that 61.3% of people had weight gain.

It is important to remember that there is a complex relationship between psychological state, eating habits, physical activity and sleep quality. In this context, the study by Yazici et al.⁽²⁷⁾, obese people can be affected by stress and present emotional eating patterns, in this sense we can observe an increase in anxiety and depression compared to the control group in the current research that can be related to the facts already mentioned above, in addition to fear and emotional stress, however, this group in relation to hypertensive patients and those with diabetes mellitus has a lower rate of anxiety and depression values, this factor can be considered as people with obesity can be more cautious in relation to eating and exercise habits as they have already been involved in a risk group and developed certain lifestyle behaviors⁽²⁷⁾.

CONCLUSION

The COVID-19 pandemic has exacerbated mental health challenges for people with comorbidities. The study highlights the need for special attention to these risk groups considering that both levels of anxiety and depression showed an increase in relation to the control group, including psychological monitoring and ongoing care. Therefore, more research is needed on the relationship between the psychological effects resulting from post-Covid in people with diabetes, hypertension and obesity, considering that this condition continues to be present and has permanent complications as in cases of prolonged COVID. This would provide more information to meet collective health demands in a more targeted and effective way for this population with preventive measures and more specific treatment.

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