

# Neuropsychiatric symptoms of post-COVID-19 condition in Mexican healthcare personnel

## Síntomas neuropsiquiátricos post-COVID-19 en trabajadores de salud mexicanos

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### Abstract

**Objective:** The aim of the present study was to identify anxiety and depression in health personnel who suffered COVID-19, and to associate them with blood inflammatory markers.

**Materials and methods:** The design of this study was descriptive and cross-sectional. We evaluated 51 healthcare workers who survived COVID-19 disease with Hamilton scales for anxiety and depression, also we calculated inflammatory markers (systemic immune-inflammation index, SII; monocyte lymphocyte ratio, MLR; platelet lymphocyte ratio, PLR; and neutrophil lymphocyte ratio, NLR) using blood venous samples. This study was carried out from August 2021 to December 2022. Statistical analysis was performed using SPSS v. 26.

**Results:** Our study included 51 healthcare personnel, females (n=29) and males (n=22). The mean age was 40.54 ± 11.00 years. The most frequent acute symptoms for COVID-19 presented were dysgeusia (n=20), anosmia (n=18), and headache (n=17). The most common comorbidities were overweight (n=24), obesity (n=22), and hypertension (n=11). According to the Hamilton Rating Scale for Anxiety (HARS) and Hamilton Rating Scale for Depression Rating (HRSD) we identify anxiety and depression in 72.5% (n=37) and 51% (n=26) within the health personnel, respectively.

**Conclusions:** In our study, we observed a high frequency of anxiety and depression in healthcare workers with post COVID-19 condition. However, we did not observe an association between inflammatory markers (NLR, PLR, MLR, and SII) with anxiety and depression in health personnel post-COVID-19. We suggest follow-up assessments in healthcare personnel with post-COVID-19 condition, to evaluate if mixed emotional disorders persist.

**Keywords:** Anxiety; Depression; Mental disorders; Inflammation; COVID-19.

**Objetivo:** Identificar ansiedad y depresión en el personal de salud que padeció COVID-19, y asociarlos con niveles de marcadores inflamatorios en sangre.

**Materiales y métodos:** El estudio fue descriptivo y transversal. Evaluamos a 51 trabajadores del área de la salud con antecedente de COVID-19, se aplicó las escalas de ansiedad y depresión de Hamilton, y calculamos marcadores inflamatorios (índice de inmunidad/inflamación sistémica, índice monocito/linfocito, índice plaqueta/linfocito, índice neutrófilo/linfocito) obtenidas de muestras de sangre venosa. El estudio se realizó durante el periodo de agosto del 2021 a diciembre del 2022. El análisis estadístico fue realizado en SPSS v. 26.

**Resultados:** Nuestro estudio incluyó a 51 personas del área de salud, 29 mujeres y 22 hombres. La edad media fue 40.54 ± 11.00 años. Los síntomas agudos más frecuentes que presentaron los trabajadores fueron disgeusia (n=20), anosmia (n=18), y cefalea (n=17). Las comorbilidades más frecuentes fueron: sobrepeso (n= 24), obesidad (n=22), e hipertensión (n=11). Aplicando la Escala de Ansiedad de Hamilton y la Escala de Depresión de Hamilton, identificamos ansiedad y depresión en el personal de salud en 72.5% (n=37) y 51% (n=26), respectivamente.

**Conclusiones:** En nuestro estudio observamos una alta frecuencia de ansiedad y depresión post COVID-19 en el personal de salud. No observamos asociación entre ansiedad, depresión y marcadores inflamatorios hematológicos en los trabajadores de salud en población mexicana que padeció COVID-19. Sugerimos realizar evaluaciones de seguimiento en el personal de salud en condición post COVID-19 para demostrar la persistencia de trastornos mixtos de las emociones.

**Palabras clave:** Ansiedad; Depresión; Trastornos mentales; Inflamación; COVID-19.

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## Introduction

Recently, authors reported a relationship of the pandemic worldwide with mood disorders, they estimated that 53 million people suffer major depressive disorder, and 76 million people have anxiety disorder<sup>1</sup>. Moreover, other studies indicated that psychiatric sequelae in post-COVID-19 conditions were an increased prevalence of anxiety (45%), and depression (47%) symptoms including lack of motivation, anhedonia, fatigue, irritability, sleep disturbance, and cognitive impairment<sup>2,3</sup>. Taquet *et al.*, (2021) reported that post-COVID-19 subjects had twice the risk of anxiety and depression within 90 days after COVID-19. Besides, they observed that symptoms of moderate-severe stress, anxiety, and depression persist after 4 weeks<sup>4</sup>. Chevinsky *et al.*, (2021) reported anxiety after 30-60 days post-COVID-19<sup>5</sup>. According to Takao *et al.*, a study observed psychiatric sequelae (such as concentration difficulty, cognitive dysfunction, amnesia, depression, fatigue, and anxiety) within the next year in 52.7% of patients who suffered acute COVID-19<sup>6,7</sup>. In addition, 31% out of 325 patients who recovered from COVID-19, and evaluated with the PHQ-9 scale, showed symptoms of depression: 87.8% of them had mild depression, 8.1% moderate depression, and 4% severe depression<sup>8</sup>. Thus, prolonged symptoms and neuropsychiatric state (anxious, depressive symptoms, and sleep disorders) are known as post-acute COVID-19 syndrome (PACS)<sup>9,10</sup>. According to NICE guidelines defined post COVID-19 syndrome as persistent neurological, respiratory, and cardiovascular symptoms beyond 12 weeks or months of the onset of acute COVID-19<sup>11,12,13</sup>. Some studies suggest the neuropsychiatric sequelae in post-COVID-19 syndrome may be related to the disruption of immune and inflammatory response triggering a cytokines storm, damage of the blood-brain barrier, neurotransmission dysregulation, and organ dysfunction (SNC, lung, liver, and kidney)<sup>13,14</sup>. In that sense, several studies showed hematological inflammatory markers including SII (systemic immune inflammation index), PLR (platelet lymphocyte ratio), MLR (monocyte lymphocyte ratio), and neutrophil-lymphocyte ratio (NLR) to be associated with psychiatric disorders in post COVID-19 condition<sup>15,16</sup>. Therefore, Mazza *et al.*, (2021) evaluated SII and demonstrated depressive and cognitive impairment symptoms at 3-months follow-up after SARS-Cov2 infection, changes in levels of SII in these patients may reveal depression severity<sup>15,17</sup>. Besides, recent studies indicate that inflammatory markers are reliable predictors of the severity and mortality risk of COVID-19<sup>18,19</sup>, and values of systemic inflammation indexes have a predictive power with the severity of COVID-19 in the Mexican population<sup>20</sup>. The aim of the present study was to identify anxiety and depression in health personnel who suffered COVID-19, and to associate them with blood inflammatory markers.

## Materials and Methods

This study was descriptive and cross-sectional, with a convenience sampling. We recruited 51 healthcare personnel (physicians, nurses, chemist, and pharmacists) with post-COVID-19 condition from the “Mental Health Regional High Specialty Hospital” in Tabasco, Mexico; the data collection period was from October to December 2021. We included health personnel who suffered COVID-19 regardless the vaccination status, aging from 18-60 years old, and previous diagnosis of SARS-CoV-2 with a positive PCR test. The patients were diagnosed from March 2020 to October 2021, the range of post-COVID months were 1-20 months. We excluded healthcare workers with acute COVID-19 infection and positive PCR to SARS-CoV-2 at the recruitment. Health personnel with a previous anxiety and/or depression diagnosis were excluded from the study. All healthcare personnel were invited to voluntary participation and non-financial remuneration. All subjects signed an informed consent. This study was approved by the ethics committee of the Mental Health Regional High Specialty Hospital (HRAESM/DG/UEI/467/2021), and we followed the Official Mexican Standard NOM-012-SSA3-2012 guidelines, and Helsinki’s Declaration of Ethical principles.

This study includes evaluation of medical history, sociodemographic data, anthropometric measures, symptoms of acute COVID-19, and Hamilton Rating Scale for Depression Rating (HRSD) and Hamilton Rating Scale for Anxiety (HARS). We collected sociodemographic (age, gender, occupation, education, marital status, socioeconomic status) and clinical features with a structural questionnaire containing the medical history (comorbidities) of healthcare personnel with post-COVID-19 condition. After the interview, we measured weight and height to establish body mass index, obesity, and overweight diagnostics. BMI was calculated according to the Centers for Diseases Control and Prevention (CDC) (weight in kilograms divided by the square of height in meters;  $\text{kg}/\text{m}^2$ )<sup>21</sup>. We collected 4mL blood venous samples from a single EDTA tube to determinate the inflammatory markers. The white blood cells count (WBC,  $10^3$  cells/mL), mean corpuscular volume (MCV, fL), red cell distribution width (RDW, %), neutrophil, lymphocyte, platelet, and monocyte count were determined with CELL-DYN Ruby (Abbott). We used these data for SII, NLR, PLR, MLR determination. We calculated these hematological inflammatory indexes with formulas as follows: SII index = (platelets count  $\times$  neutrophils count)/lymphocytes count; PLR = platelets count/lymphocytes count; MLR = monocytes count/lymphocytes count; NLR = neutrophils count/lymphocytes count. We classified the inflammatory markers values in tertiles.

Hamilton Rating Scale for Depression (HRSD) is a validated asses in Spanish (Cronbach's alpha of 0.92), which evaluate the severity of depressive symptoms such as no depression (0-6) and scores indicate mild depression (7-17), moderate (18-24) and severe (>24) depression. Furthermore, include somatic symptoms, vegetative, cognitive and anxiety symptoms. Hamilton Rating Scale for Anxiety (HARS) is a validated version with permitted to assess the severity of anxiety symptoms (Cronbach's alpha of 0.89.); mild anxiety (6-17); moderate anxiety (18-24); severe anxiety (25-30) and very severe anxiety (31-56). It consists of 14 items, evaluating psychological and somatic symptoms, which include anxious mood, tension, fears, insomnia, cognition, depressed mood, somatic and autonomic symptoms.

We described numerical variables as mean  $\pm$  standard deviation (SD) for variables with normal distribution; otherwise, we employed median and interquartile range (IQR). The categorical variables are expressed as frequency and percentages (%). We performed Shapiro-Wilks test to assess normality in our sample. We used the Chi-squared test for categorical variables; for numerical data, we made ANOVA or Kruskal Wallis tests. P-value <0.05 was considered significant in all analyses. Chi-squared test, Kruskal Wallis test, and ANOVA test were made with SPSS v. 26. Word cloud of symptoms was made with word cloud package for R studio v.4.2.

## Results

### Sociodemographic and clinical characteristics in health personnel post-COVID-19

This study included 51 health personnel (29 female and 22 male). The mean age was  $40.55 \pm 11.00$  years. We evaluated variables such as schooling ( $16.32 \pm 4.07$  years), weight ( $80.37 \pm 14.74$  Kg), and Body Mass Index ( $30.80 \pm 5.65$ ). In addition, we found that (92.15%  $n=47$ ) of the participants with mild COVID-19 symptoms required home treatment in social isolation, and only one healthcare worker was hospitalized (Table 1).

### Anxiety and depression in health personnel post-COVID-19

According to the Hamilton Rating Scale for Anxiety (HARS), we detected anxiety (72.5%,  $n=37$ ) in healthcare personnel; when the results were stratified by categories, we found mild anxiety (54.9%,  $n=20$ ), moderate anxiety (9.8%,  $n=5$ ) severe anxiety (2%,  $n=1$ ), and very severe anxiety (3.9%,  $n=2$ ). Besides, considering the Hamilton Rating Scale for Depression Rating (HRSD), we detected depression in (51%,  $n=26$ ) healthcare workers. Similarly, when stratified by categories, we observed mild depression (41.2%,  $n=21$ ),

moderate depression (7.8%,  $n=4$ ), and severe depression (2%,  $n=1$ ). We observed a predominance of anxiety (54%,  $n=20$ ) and depression (65%,  $n=17$ ) in female health personnel in comparison with male health personnel with anxiety (46%,  $n=17$ ) and depression (35%,  $n=9$ ) (Table 1).

### Inflammatory markers in health personnel post-COVID-19

In table 1 we described the mean/median value for hematological inflammatory markers and the highest and lowest ratio of SII (9.52 - 1.21), NLR (3.20 - 0.59), PLR (216.40 - 29.09), and MLR (1.14 - 0.08) indexes of post-COVID-19 condition in healthcare workers. We found no significant differences when we performed the variance analysis for the biochemical parameters and inflammatory markers.

**Table 1.** Psychiatric assessment, Inflammatory markers in post-COVID-19 Mexican health personnel.

Variables	Value
Age (years) (M $\pm$ SD)	40.55 $\pm$ 11.00
Schooling (years) (M $\pm$ SD)	16.32 $\pm$ 4.07
Weight (kilograms) (M $\pm$ SD)	80.37 $\pm$ 14.74
Body Mass Index (M $\pm$ SD)	30.80 $\pm$ 5.65
<b>Psychiatric assessment (n=51)</b>	<b>n (%)</b>
<b>Anxiety, n (%)</b>	37 (72.5)
mild anxiety	20 (54.9%)
moderate anxiety	5 (9.8%)
severe anxiety	1 (2%)
very severe anxiety	2 (3.9%)
<b>Depression, n (%)</b>	26 (51)
mild depression	21 (41.2%)
moderate depression	4 (7.8%)
severe depression	1 (2%)
<b>Inflammatory markers</b>	<b>M <math>\pm</math> SD, Median (IQR)</b>
SII, Median (IQR)	430294 (288358 - 514052)
NLR, Median (IQR)	1.51 (1.22 - 2.02)
PLR, (M $\pm$ SD)	122 $\pm$ 42.64
MLR, Median (IQR)	0.22 (0.17 - 0.26)

Source: Authors' own elaboration from the study survey

M: mean; SD: standard deviation; SII: Systemic immune-inflammation index; NLR: neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio; MLR: monocyte-lymphocyte ratio

On the other hand, related to COVID-19 symptoms we found that dysgeusia (80.39%,  $n=20$ ) was the most frequent acute symptom, other symptoms that the health personnel presented were anosmia (76.47%,  $n=18$ ), and headache (70.58%,  $n=17$ ) (Figure1). The most common comorbidities include overweight (47.05%,  $n=24$ ), obesity (43.13%,  $n=22$ ), and hypertension 21.56%.

**Figure 1.** Acute symptoms of COVID-19 in Mexican health personnel.



Source: Authors own elaboration using R studio.

**Anxiety, depression, and inflammatory markers of post-COVID-19 condition in healthcare personnel**

The hematological inflammatory indexes were divided into the following tertiles values: SII ( $<3.16 \times 10^3$ ,  $3.16-4.74 \times 10^3$  and  $>4.743 \times 10^3$ ), NLR ( $<1.35$ ,  $1.35-1.73$  and  $>1.73$ ), PLR ( $<103.9$ ,  $103.9-134.8$  and  $>134.8$ ) and MLR ( $<1860$ ,  $0.186-0.248$  and  $>0.2487$ ); each tertile included 17 subjects (Supplementary table 1 – 4). In the present study we did not observe an association between depression, anxiety, and inflammatory markers in health personnel post-COVID-19 (Table 2).

Abbreviations:  $\chi^2$ , Chi-square test; SII, Systemic immune-inflammation index; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; MLR, monocyte-lymphocyte ratio;  $p \leq 0.05$

**Table 2.** Inflammatory ratios with depression, anxiety, comorbidities, pharmacotherapy, and symptoms in post-COVID-19 Mexican health personnel

Variables	$\chi^2$ , p			
	Tertiles			
	SII	NLR	PLR	MLR
<b>Depression</b>				
Mild depression	4.98, 0.28	6.13, 0.18	1.13, 0.88	2.53, 0.63
Moderate depression	4.30, 0.36	5.80, 0.21	2.52, 0.64	2.67, 0.61
Severe depression	1.04, 0.59	1.04, 0.59	1.05, 0.59	1.04, 0.59
<b>Anxiety</b>				
Mild anxiety	3.85, 0.42	2.39, 0.66	0.76, 0.94	2.06, 0.72
Moderate anxiety	2.72, 0.60	2.72, 0.60	2.40, 0.66	1.78, 0.77
Severe anxiety	3.12, 0.53	3.12, 0.53	2.95, 0.56	3.00, 0.55
Very severe anxiety	1.04, 0.59	1.04, 0.59	1.05, 0.59	1.04, 0.59
<b>Comorbidities</b>				
Alcoholism	2.31, 0.31	2.31, 0.31	1.32, 0.51	<b>6.29, 0.04</b>
Hypertension	<b>9.96, &lt;0.01</b>	4.40, 0.11	3.70, 0.15	4.40, 0.11
Overweight	1.41, 0.49	0.47, 0.79	<b>6.13, 0.04</b>	5.55, 0.06
<b>Pharmacotherapy</b>				
Hydroxychloroquine	2.14, 0.34	0, 0.1	0, 1.0	<b>6.35, 0.04</b>
<b>Symptoms</b>				
Sudden onset	5.20, 0.07	<b>10.23, &lt;0.01</b>	1.17, 0.55	1.17, 0.55
Rhinorrhea	4.43, 0.10	<b>10.61, &lt;0.01</b>	3.0, 0.22	2.53, 0.28
Abdominal pain	2.07, 0.35	<b>7.41, 0.02</b>	2.07, 0.35	4.74, 0.09
Arthralgia	4.39, 0.11	<b>5.80, &lt;0.05</b>	2.98, 0.22	1.09, 0.57

Source: Authors' own elaboration from the study survey

Abbreviations:  $\chi^2$ , Chi-square test; SII, Systemic immune-inflammation index; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; MLR, monocyte-lymphocyte ratio;  $p \leq 0.05$



Supplementary **Table 3.** PLR with depression, anxiety, and clinical features in post-COVID-19 Mexican health personnel.

Variables	PLR tertiles			X <sup>2</sup> , p
	Low <103.9; n=17	Medium 103.9-134.8; n=17	High >134.8; n=17	
<b>Depression</b>				
Normal	10 (58.8%)	8 (47.1%)	7 (41.2%)	3.35, 0.764
Mild depression	6 (35.3%)	7 (41.2%)	8 (47.1%)	
Moderate depression	1 (5.9%)	1 (5.9%)	2 (11.8%)	
Severe depression	0 (0%)	1 (5.9%)	0 (0%)	
<b>Anxiety</b>				
Normal	5 (29.4%)	3 (17.6%)	6 (35.3%)	4.88, 0.770
Mild anxiety	10 (58.8%)	11 (64.7%)	8 (47.1%)	
Moderate anxiety	2 (11.8%)	1 (5.9%)	2 (11.8%)	
Severe anxiety	0 (0%)	1 (5.9%)	0 (0%)	
Very severe anxiety	0 (0%)	1 (5.9%)	1 (5.9%)	
<b>Comorbidities</b>				
Alcoholism	3 (17.6%)	3 (17.6%)	1 (5.9%)	1.33, 0.516
Hypertension	1 (5.9%)	5 (29.4%)	5 (29.4%)	3.71, 0.157
Overweight	7 (41.2%)	5 (29.4%)	12 (70.6%)	<b>6.14, 0.046</b>
<b>Pharmacotherapy</b>				
Hydroxychloroquine	1 (5.9%)	1 (5.9%)	1 (5.9%)	0.00, 1.000
<b>Symptoms</b>				
Sudden onset	5 (29.4%)	6 (35.3%)	8 (47.1%)	1.17, 0.556
Rhinorrhea	5 (29.4%)	8 (47.1%)	10 (58.8%)	3.01, 0.222
Abdominal pain	1 (5.9%)	4 (23.5%)	3 (17.6%)	2.08, 0.354
Arthralgia	9 (52.9%)	11 (64.7%)	6 (35.3%)	2.98, 0.225

Source: Authors' own elaboration from the study survey

Abbreviations: x2, Chi-square test; PLR, platelet-lymphocyte ratio; p ≤ 0.05

We found SII ( $>4.743 \times 10^3$ ) associated with hypertension ( $p=0.007$ ) (Table 2, Supplementary table 1). According to assessments, the COVID-19 symptoms associated with high NLR were sudden onset ( $p=0.006$ ), rhinorrhea ( $p=0.005$ ), abdominal pain ( $p=0.025$ ), and arthralgia ( $p=0.048$ ) (Table 2, Supplementary table 2). PLR was associated with a comorbidity (overweight;  $p=0.046$ ) (Table 2, Supplementary table 3). In addition, MLR ( $>0.25$ ) showed an association with alcoholism ( $p=0.043$ ). Regarding pharmacotherapy, hydroxychloroquine presented an association with medium MLR levels ( $p=0.041$ ) (Table 2, Supplementary table 4). Notably, we observed differences between post-COVID months, PLR and SII. Higher levels of PLR were associated ( $p=0.026$ ) with fewer months after COVID infection ( $8.47 \pm 6.67$ ,  $11.94 \pm 5.84$ ,  $14.00 \pm 4.80$  for high, medium, and low levels; respectively). Likewise, SII had associations ( $p=0.031$ ) with post-COVID months ( $9.47 \pm 7.04$ ,  $10.35 \pm 6.11$ ,  $14.59 \pm 3.92$  for high, medium, and low levels; respectively). Nonetheless, we did not observe association between post-COVID months and NLR ( $p=0.092$ ) and MLR ( $p=0.507$ ).

## Discussion

In this study we observed a high frequency of anxiety and depression in healthcare workers with post COVID-19 condition. However, no association between hematological inflammatory markers and depression, anxiety was found. Recent literature reports the presence of anxiety, depression, posttraumatic stress symptoms and sleep disturbance after acute SARS-COV2. During the COVID-19 pandemic, general population and healthcare personnel has presented a higher risk of anxiety and mood disorders<sup>22</sup>. However, after acute infection the cases reported with depression were 44%, and 15% after 3 or more months after infection<sup>23</sup>.

In recently publication, no-association between anxiety, depression, and hematological inflammatory markers was reported. The authors suggest that psychological factors should be taken into consideration and analyzed while determining associations between hematological inflammatory indexes and psychiatric disorders; this

Supplementary **Table 4.** MLR with depression, anxiety, and clinical features in post-COVID-19 Mexican health personnel

Variables	MLR tertiles			X <sup>2</sup> , p
	Low <0.186; n=17	Medium 0.186-0.249; n=17	High >0.249; n=17	
<b>Depression</b>				
Normal	8 (47.1%)	9 (52.9%)	8 (47.1%)	3.44, 0.752
Mild depression	8 (47.1%)	5 (29.4%)	8 (47.1%)	
Moderate depression	1 (5.9%)	2 (11.8%)	1 (5.9%)	
Severe depression	0 (0%)	1 (5.9%)	0 (0%)	
<b>Anxiety</b>				
Normal	3 (17.6%)	6 (35.3%)	5 (29.4%)	5.67 0.684
Mild anxiety	10 (58.8%)	9 (52.9%)	10 (58.8%)	
Moderate anxiety	3 (17.6%)	1 (5.9%)	1 (5.9%)	
Severe anxiety	0 (0%)	1 (5.9%)	0 (0%)	
Very severe anxiety	1 (5.9%)	0 (0%)	1 (5.9%)	
<b>Comorbidities</b>				
Alcoholism	2 (11.8%)	5 (29.4%)	0 (0%)	<b>6.29, 0.043</b>
Hypertension	1 (5.9%)	4 (23.5%)	6 (35.3%)	
Overweight	6 (35.3%)	6 (35.3%)	12 (70.6%)	
<b>Pharmacotherapy</b>				
Hydroxychloroquine	0 (0%)	3 (17.6%)	0 (0%)	<b>6.38, 0.041</b>
<b>Symptoms</b>				
Sudden onset	6 (35.3%)	5 (29.4%)	8 (47.1%)	1.17, 0.556
Rhinorrhea	5 (29.4%)	9 (52.9%)	9 (52.9%)	
Abdominal pain	0 (0%)	4 (23.5%)	4 (23.5%)	
Arthralgia	10 (58.8%)	9 (52.9%)	7 (41.2%)	

Source: Authors' own elaboration from the study survey

Abbreviations: x2, Chi-square test; MLR, monocyte-lymphocyte ratio; p ≤ 0.05

inflammation may represent the severity of the condition, this indirectly affects depression and anxiety.<sup>(24)</sup><sup>24</sup> Our main finding was the presence of mild anxiety (54.9%) and mild depression (41.2%), suggesting that due to the severity of these symptoms the lack of association with inflammation markers was found. In accordance with Swami, *et al* (2022), the authors reported no-association of inflammatory biomarkers with depression, anxiety and stress scores in the subjects post-COVID-19 condition<sup>24</sup>.

In contrast to our results, existing data have shown that hematologic inflammatory markers are associated with psychiatric symptoms, these studies were performed with baseline data of hematological inflammatory markers. Besides, changes in SII influence the depressive symptoms<sup>17</sup>. Existing data reported depressive and anxiety symptoms post-COVID-19<sup>25,26</sup>. However, there is a wide variation of depression and anxiety data between studies (5.8%<sup>4</sup>, 37%<sup>27</sup>, and 91.2%<sup>25</sup>). Li *et al.*, (2022) demonstrated higher scores of anxiety and depression symptoms in females<sup>28</sup>. In that respect, we observed in our population the presence of

anxiety (72.5%) and depression (51%). Current guidelines suggest that the frequency of sequelae is higher in women than in men. Besides, a study reported that non-hospitalized patients who attended a neuro-COVID-19 clinic: 70% of patients were women with neurological symptoms with more than 6 weeks after COVID-19. Similarly, another study reported depressive symptoms between 11% and 28% 3 months after acute infection<sup>29</sup>. Existing reports suggest that people affected by COVID-19 with mild symptoms, medical care at home, and without direct medical observation, could have implications for mental health in the post-COVID-19 condition<sup>30</sup>. Besides, Damiano *et al.*, (2022) suggest that all post-COVID-19 patients require psychiatric screening regardless of COVID severity<sup>9</sup>.

The mechanism that relates psychiatric disorders after acute COVID-19 infection is the immune-inflammatory system disruption. Furthermore, pandemic related psychological stressor (social isolation), previous psychiatric history, and persistent psychological distress throughout the acute SARS-COV2 infection could influence the risk of mixed emotional

disorders in post-COVID-19 condition<sup>31</sup>. Moreover, neuroinflammation could be mechanism to explore in healthcare personnel in post-COVID-19 condition. We found inflammatory maker associations with PLR and SII; these results point that PLR and SII could be used as novel inflammatory biomarkers to predict the severity of disease in obese and overweight healthcare personnel post-COVID-19 condition. We observed an association of inflammatory markers with some comorbidities (SII with hypertension; PLR, and MLR with overweight). The literature proves the positively correlation between SII and PLR with mortality in COVID-19<sup>32,33</sup>. Besides, higher levels of SII were reported in hospitalized patients with COVID-19, and PLR with higher values in obese and morbid obese people<sup>34</sup>. According to this, the Mexican population is well characterized by overweight and obesity.

We acknowledge the limitations in our study, we included a small sample of healthcare personnel with post-COVID-19 condition, it represents a non-probabilistic sample. Besides, only one subject required hospitalization, and we have no data available regarding the hematological baseline markers to evaluate inflammatory differences. We considered that healthcare personnel suffered high stress levels during the pandemic, this factor could lead to unknown or undiagnosed psychiatric condition. Not only we could not gather information of occupational stress throughout the pandemic, but also it could represent a bias of mixed emotional disorders not associated with COVID-19. Finally, we did not perform a multivariate logistic regression to discard confounders. We suggest a larger sample and comparisons between non-hospitalized and hospitalized healthcare personnel, as well as a multivariate analysis to demonstrate associations or correlations between hematological markers and neuropsychiatric symptoms.

## Conclusion

In our study, we observed anxiety and depression in post-COVID-19 condition. In addition, anxiety was more frequent in female healthcare personnel. However, we did not observe an association between inflammatory markers (NLR, PLR, MLR, and SII) with anxiety and depression in health personnel post-COVID-19. The need for further research into the management of post-COVID-19 condition in healthcare professionals and the general population has been suggested by several researchers. These require the implementation of timely identification of affected people, physical rehabilitation, and mental health support services, for the well-being of the population with the effects of COVID-19. We suggest follow-up assessments in healthcare personnel with post-COVID-19 condition, to evaluate if anxiety and depression symptoms persist.

## Conflict of interest

The authors have no conflict of interest to declare.

## Ethical consideration

This study was approved by the ethics committee of the Mental Health Regional High Specialty Hospital (HRAESM/DG/UEI/467/2021), and we followed the Official Mexican Standard NOM-012-SSA3-2012 guidelines, and Helsinki's Declaration of Ethical principles.

## Contributions of the authors

Conceptualization: J.J.M.M., M.V.S.; Data curation: C,Y.A.G., R.E.S.R., G.A.N.R.; Formal analysis: G.A.N.R., J.J.M.M.; Acquisition Financing: M.V.S.; Investigation: C,Y.A.G., D.R.R., R.E.S.R.; Methodology: G.A.N.R., J.J.M.M.; Project administration: M.V.S.; Resources: M.V.S.; Software: G.A.N.R., J.J.M.M.; Supervision: J.J.M.M., M.V.S.; Validation: J.J.M.M., M.V.S.; Visualization: D.R.R., G.A.N.R.; Editorial – Original draft: C,Y.A.G., R.E.S.R.; Writing: review and editing: D.R.R., G.A.N.R., J.J.M.M., M.V.S.

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