Research article

Mental health outcomes and risk factors among female physicians during the COVID-19 pandemic

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H I G H L I G H T S

- Prevalence for female physician depression, anxiety and sleep disturbances was 72.6%, 64.3% and 77.8% respectively.
- Previous history of mental health disorders was associated with current depression, anxiety, PTSD, and sleep quality disturbances.
- Younger age was related to depression and PTSD symptoms development.
- Being at COVID-19 frontline of attention was related to depression symptoms.

A R T I C L E   I N F O

A B S T R A C T

The fast spread of the COVID-19 pandemic brought a huge workload burden. Health care workers have become a particular risk group for developing mental health symptoms, with women being the most affected group according to preliminary data. The aim of this study was to provide information about the prevalence of depression, anxiety, sleep disturbances, and post-traumatic stress disorder symptoms in female physicians during the COVID-19 pandemic and describe risk factors associated with them. Using a cross-sectional design, we applied an online questionnaire to 303 female physicians inquiring about COVID-19 changes in their social and professional dynamics. To assess the presence of depression, anxiety, sleep disturbances, and post-traumatic stress disorder symptoms, the participants responded the 9-item Patient Health Questionnaire (PHQ-9), the 7-item Generalized Anxiety Disorder scale (GAD-7), the Pittsburgh Sleep Quality Index (PSQI), and the PTSD Checklist for DSM-5 (PCL-5). The prevalence for depression, anxiety, sleep quality disturbances and PTSD symptoms was 72.6%, 64.3%, 77.8%, and 19.4% respectively. The main risk factor associated with every outcome was having a previous history of any mental health disorder. Younger age and being at the frontline for COVID-19 attention were relevant to depression symptoms. Our results were in agreement with previous studies, confirming the need for specific age-tailored mental health interventions in female physicians, especially those with previous diagnoses of mental health disorders.

1. Introduction

On the 30th of January 2020, the World Health Organization declared the novel coronavirus SARS-COV 2 that causes COVID-19 disease, an international public health emergency. The rapid, worldwide spread of the virus introduced a huge challenge on our society, making us face unprecedented demands for adaptation. Confinement, closure of schools, and social distancing were among the most used strategies aimed to contain the pandemic.

The outbreak of COVID-19 as a major health care crisis has exerted a great impact on people's health, both mentally and physically. The rapid spread of the virus also brought a vast economic and workload burden on healthcare systems, making healthcare workers a particular risk group for experiencing mental health symptoms (Cai et al., 2020).

Previous studies have documented that epidemics like severe acute respiratory syndrome (SARS) were associated with increased mental health symptoms, demands of workload, burnout, and risk of infection

among healthcare workers in the front lines of the epidemic, as well as their families (Lu et al., 2006).

Early on studies made in Wuhan, China, focused on documenting the degree and extent of mental health outcomes among healthcare workers treating COVID-19 infected patients.

The study made by Jianbo Lai et al. reported depression in 50.4%, anxiety in 44.6%, insomnia in 34%, and distress in 71.5% of participants, with women in the frontlines of attention reporting a higher degree of severity in all measurements. The 7-ítem Generalized Anxiety Disorder scale (GAD-7) scores among women were twice as severe as men scores 4.0 vs 2.0, while both the 9-item Patient Health Questionnaire (PHQ-9) and the 7-item Insomnia Severity Index (ISI) scores were significantly higher in women compared to men 5.0 vs 3.0 (Lai et al., 2020). This finding was also supported by Rossi et al., in Italy, where they reported that women had higher odds of having stress, depression, anxiety and posttraumatic stress disorder (PTSD) symptoms during the COVID-19 pandemic (Rossi et al., 2020).

This gender difference in symptom prevalence and severity was also reported in general population studies by Nianqi Liu et al., reporting a prevalence of 7% for PTSD, with women reporting statistically significantly higher scores in the PTSD Checklist for DSM-5 (PCL-5) than male respondents (16.35 vs 12.02), also describing that they had higher re-experiencing, negative alterations in cognition, mood, and hyperarousal prevalence than males (Liu et al., 2020).

The findings in these studies underline the need to enhance our understanding about mental health in female physicians during the COVID-19 pandemic. This study aimed to provide information about factors associated with the mental health of female physicians in Mexico during the COVID-19 pandemic and to assess symptoms of depression (PHQ-9), anxiety (GAD-7), sleep disturbances (Pittsburgh Sleep Quality Index - PSQI) and posttraumatic stress disorder (PCL-5) in them.

2. Methods

2.1. Study population and sample

A web-based open invitation for female physicians to participate was made using two of the biggest and more active closed Facebook groups of female physicians in Mexico coinciding with the initial phases of the COVID-19 pandemic in the country from May 2020 to July 2020. Social media and Facebook in particular has been successfully used as a recruitment tool for health research purposes (Whitaker et al., 2017) (Shaver et al., 2019). During COVID-19 pandemic social media represented a safe way to reach out to health care workers, respecting social distancing measures (Srivastav et al., 2021) (Rossi et al., 2020).

In Mexico, according to the latest study about physician's internet habits, 93% of physicians use social media and 64% of them use Facebook on a regular basis (Asociación de internet MX, 2021). 303 female physicians with a mean age of 37.08 years participated in our study, most of them where married and had a specialty degree. The inclusion criteria to participate were a) identifying as a female and having a medical degree, b) age >18 years, and c) being a resident in Mexico during the pandemic. The exclusion criterion was an incompletely answered form.

2.2. Rating instruments

An online form was developed to include structured questions inquiring demographic information, place of residency, area of specialty, years of experience, current work status, current or past medical and mental health diagnoses, among others. They were also asked about COVID-19 related factors associated with social distancing and quarantine status, children care dynamics, current or previous COVID-19 infection, COVID-19 information exposure, and experiences of loss, discrimination and hostility towards them as healthcare workers during the pandemic.

To assess the presence and degree of depression, anxiety, sleep disturbances, and PTSD, the participants also responded to the 9-item

Patient Health Questionnaire (PHQ-9), the 7-item Generalized Anxiety Disorder scale (GAD-7), the Pittsburgh Sleep Quality Index (PSQI), and the PTSD Checklist for DSM-5 (PCL-5).

The PHQ-9 is a 9-item self-report measure that assesses the frequency of nine symptoms of depression rating them on a four-point Likert scale, ranging from 0 (not at all) to 3 (nearly every day), providing a total score range from 0 to 21. The cut-off scores used to determine the presence and severity of depression are 5–9 (mild), 10–14 (moderate), 15–21 (moderately severe), and 20–27 (severe) (Kroenke et al., 2001).

The GAD-7 is a 7-item self-report measure based on seven core anxiety symptoms that inquires the frequency of presentation within the last two weeks. It uses a four-point Likert scale ranging from 0 (not at all) to 3 (almost every day), providing a total score range from 0 to 21. The cut-off scores used to determine the presence and severity of anxiety are 5–9 (mild), 10–14 (moderate), and >15 (severe) (Spitzer et al., 2006).

The PSQI is a 19-item self-report questionnaire that measures sleep quality and disturbances within the previous month. The sum of individual items rated on a 0–3 Likert scale, creates 7 components that produce a global score with a range of 0–21, higher scores indicating worse sleep quality. The PSQI has a sensitivity of 89.6% and a specificity of 86.5% for identifying cases with sleep disorders, using a cut-point score of 5 (Buysse et al., 2008).

The PCL-5 is a 20-item self-report measure that assesses the presence and severity of PTSD symptoms and corresponds with DSM-5 criteria. It is intended to evaluate symptoms over the past month and rate the severity of each particular symptom on a five-point Likert scale ranging from 0 (not at all) to 4 (extremely). The items are summed up to provide a total severity score with a range from 0-80. The PCL-5 can determine a provisional PTSD diagnosis by summing up all 20 items and using a cut-point score of 33 points or by treating each item rated as 2 or higher as an endorsed symptom, then following the DSM-5 diagnostic rules (Blevins et al., 2015).

2.3. Data analysis

Data was analyzed using SPSS Version 20.0. Descriptive statistics was utilized to create a clear overview on the demographic characteristics of the subjects. To determine association between mental health outcomes (Depression symptoms, anxiety symptoms, sleep quality, PTSD) and relevant categorical variables we used X^2 and determined a P value of <0.05 to establish statistical significance. We used 2 × 2 contingency tables and calculated the odds ratio for each variable. Univariate analyses were conducted to associate single variables like age with mental health outcomes. A multivariate logistic regression model was conducted to ascertain the effects of previously significant variables on the likelihood of depression symptoms.

2.4. Ethical considerations

The study was approved by the Tecnologico de Monterrey School of Medicine Committee. All participants gave their informed consent to participate in the study and were given clear information about the objectives and procedures. Participants were allowed to leave the survey at any desired time, anonymity and confidentiality of information was assured. At the end of the survey, the participants received personal feedback on their results, and specific contact information for specialized mental health attention if needed. The procedures of this study complied with the Declaration of Helsinki standards regarding research on human subjects.

3. Results

The demographics and principal characteristics of the study population are shown in Table 1. A total of 303 female physicians were recruited, among which 57.1% were between the ages of 31–40, with the participants' place of residency distributed all over the country. 62% of

Table 1. Demographic and occupational characteristics during COVID-19 pandemic (n = 303).

Age	37.08 ± 7.3
Marital Status	
Single	98 (32.3%)
Married	188 (62%)
Divorced	17 (5.6%)
Educational Level	
Medical degree	97 (32%)
Medical specialty degree	184 (60.7%)
Master's degree	16 (5.3%)
PhD	6 (2%)
Previous Mental Health Diagnosis	
Yes	89 (29.3%)
No	214 (70.6%)
Children	
Yes	178 (58.9%)
No	125 (41.1%)
Children Care Support	
Yes	153 (85.9%)
No	25 (14.1%)
Isolation from Home due to Occupational Risk Infection	
Yes	150 (49.5%)
No	153 (50.4%)
Working at COVID-19 Frontline	
Yes	120 (39.6%)
No	183 (60.3%)
Main Source of Current Information and News for COVID-19	
Internet	185 (61%)
Social Media	93 (30.6%)
Television	17 (5%)
Radio	02 (0.6%)
Other	06 (1.9%)
Daily Exposure Time to Information Related to COVID-19	
Less than 1 h	77 (25.4%)
1–2 h	133 (43.8%)
2–3 h	39 (12.87%)
3–4 h	35 (11.5%)
5–10 h	16 (5.2%)
More than 10 h	03 (0.9%)
Discrimination Against for Being Identified as a Health Care Worker During the Pandemic	
Yes	92 (30.3%)
No	211 (69.6%)
Verbal Aggression While Attending COVID-19 or Being Identified as a Health Care Worker During the Pandemic	
Yes	46 (15.18%)
No	257 (84.8%)
Physical Aggression While Attending COVID-19 or Being Identified as a Health Care Worker During the Pandemic	
Yes	12 (3.9%)
No	291 (96%)

them were married and 60.7% reported having a medical specialty degree, being family medicine (18.1%), pediatrics (13.5%), and anesthesiology (6.6%) the most common fields. Some of them also had a master's degree (5.3%) and some other a PhD (2%).

Most participants reported having children, being 2 (29.6%), the most frequent quantity. 35.9% were supported in childcare by their partners, 24.7% by their parents (children's grandparents), and 14.1% reported no support.

Regarding changes in work, living, and COVID-19 pandemic information dynamics, the participants reported that 46.8% reduced their

exposure in their daily practice by modifying their workdays or schedules, while 43.8% maintained their regular work schedule. 49.5% reported having to isolate themselves from home due to higher occupational risk of infection, and 33.3% reported having a family member within their household with a higher risk of mortality from COVID-19. 39.6% reported working at COVID-19 designated care facilities, while 60.3% were not working at said facilities.

Participants reported that their main source of current information and news regarding COVID-19 was the internet (61%), social media (30.6%), and television (5%). Academic medical data for COVID-19 was acquired mostly through scientific articles (50.4%), medical groups or societies (23.7%), and through official training provided by their hospital or workplace (20.7%). Daily exposure time to information related to COVID-19 was between 1-2 h for 43.8% of participants.

Inquiring about other risk factors derived from being a healthcare provider, 30.3% reported being discriminated against when identifying themselves as healthcare personnel during the pandemic, 15.1% suffered verbal aggression while treating patients or for identifying themselves as healthcare personnel, and 3.9% were exposed to physical aggression within the same context.

With respect to mental health symptoms outcomes, 28.7% reported increased alcohol consumption and 8.5% tobacco consumption. Table 2 provides more detail on the found diagnoses. The total prevalence for depression symptoms was 72.6%, while 64.3% reported having anxiety symptoms, 77.8% disturbances on sleep quality, and 19.4% post-traumatic stress disorder positive symptoms. The mean score for PHQ-9 was 9.36 (SD 5.94), 7.73 (SD 5.41) for GAD-7, 10.21 (SD 4.19) for PSQI, and 17.45 (SD 16.60) for PCL-5.

We explored the association of specific factors with experiencing depression, anxiety, poorer sleep quality, and PTSD. A statistically significant ($P < 0.001$) relationship between the presence of previous diagnoses of mental disorders with the presence of current symptoms of sleep disturbances, depression, anxiety, and PTSD was obtained. Sleep quality disturbances were the most prevalent symptoms however, they were the least related to specific risk factors, only related to a previous history of mental health diagnosis. In contrast, having symptoms of depression was found to be related to having children ($P < 0.001$), not having children care support ($P < 0.001$), being a COVID-19 frontline

Table 2. Mental health outcomes.

Depression (PHQ-9)	*N* (%)
None	83 (27.3%)
Mild	**99 (32.6%)**
Moderate	66 (21.7%)
Moderate to severe	36 (11.8%)
Severe	19 (6.2%)
Generalized Anxiety Disorder (GAD-7)	
None	**108 (35.6%)**
Mild	99 (32.6%)
Moderate	65 (21.4%)
Severe	32 (10.5%)
Sleep Quality Disturbance (PSQI)	
Present	**236 (77.8%)**
Absent	67 (22.1%)
Posttraumatic Stress Disorder (PCL-5)	
Present	59 (19.4%)
Absent	**244 (80.5%)**
Increase in Alcohol Consumption	
Present	87 (37.5%)
Absent	**145 (62.5%)**
Increase in Tobacco Consumption	
Present	26 (19.8%)
Absent	**105 (80.2%)**

Table 3. Variables related to mental health outcomes.

	Depression				Anxiety				PTSD				Sleep Quality			
	X^2	P	OR	95% CI	X^2	P	OR	95% CI	X^2	P	OR	95% CI	X^2	P	OR	95% CI
Having children	80.276	.000	**1.87**	1.633–2.149	.124	.725	1.08	.676–1.755	.239	.625	.867	.488–1.538	.013	.908	.968	.552–1.696
Children Care Support	25.411	.000	**2.18**	1.839–2.597	2.22	.136	1.90	.809–4.468	.824	.364	1.78	.502–6.373	1.96	.161	1.929	.761–4.892
Personal Loss	5.485	.019	.541	.323–.908	2.96	.085	.653	.401–1.062	3.13	.077	.563	.297–1.069	1.83	.175	1.516	.828–2.776
Previous mental health diagnosis	34.215	.000	.851	.512–1.415	31.4	.000	.907	.565–1.457	27.2	.000	.893	.501–1.591	21.4	.000	.957	.549–1.670
Discrimination for Being Identified as a Health Care Worker	6.076	.014	.516	.304–.877	.700	.403	.806	.486–1.337	.433	.510	1.22	.669–2.244	.192	.661	1.146	.623–2.109
Verbal or Physical Aggression	15.589	.000	.317	.176–.570	.456	.500	.820	.460–1.461	.165	.004	**1.15**	.578–2.305	.002	.968	.986	.496–1.958
Increased Tobacco Consumption	8.254	.004	.280	.114–.688	.909	.340	1.56	.622–3.912	1.19	.274	1.80	.621–5.214	1.23	.267	1.904	.602–6.023
Increased Alcohol Consumption	.641	.423	1.28	.698–2.35	5.60	.018	**2.03**	1.125–3.685	1.18	.275	.673	.330–1.37	2.81	.093	1.786	.902–3.53
Working at COVID-19 Frontline	11.957	.001	.408	.244–.683	.299	.585	.875	.542–1.41	.610	.435	1.25	.707–2.23	.150	.698	1.12	.634–1.97

health care worker (P = 0.001), being exposed to personal loss (P = 0.019), verbal or physical abuse during the pandemic (P < 0.001) and to being discriminated against for identifying themselves as a healthcare worker (P = 0.014). Increased tobacco and alcohol consumption were found to be related to depression (P = 0.004) and anxiety symptoms (P = 0.018) respectively. Table 3 describes statistically significant relationships found for each outcome. Univariate analysis and logistic regression found that age was negatively associated with PTSD and depression symptoms (B = -.053, Wald's statistic = 5.576, p = 0.018, OR = 0.949, 95% Cl .908-.991).

As we obtained at least eight statistically significant related variables to depression symptoms, we performed a multivariate logistic regression to ascertain the effects of those previously significant variables on the likelihood of symptoms. The logistic regression model was statistically significant, $x^2(4)$ = 35.852, p < 0.001. Of the eight predictor variables only two were determined to be statistically significant: Age and working at COVID-19 frontline, as shown in Table 4.

4. Discussion

This study enrolled 303 female physicians in Mexico during the initial phase of COVID-19, Most participants were specialists, aged between 31 to 40 years, married, and actively maintained their regular work dynamic, which revealed a high prevalence of mental health symptoms among them. Overall, 77.8% of all participants reported symptoms of sleep disturbances, 72.6% symptoms of depression, 64.3% symptoms of anxiety, and 19.4% reported symptoms of PTSD. These prevalence rates were higher than those reported in the study made by Jianbo Lai et al. at the beginning of the pandemic in Wuhan, which reported a 50.4%, 44.6%, and 34% of depression, anxiety, and insomnia, respectively; and the one made in Italy by Rossi et al., reporting 24.73% symptoms of depression, 19.80% symptoms of anxiety, and 8.27% of insomnia, where the prevalence of PTSD symptoms was higher in this last study (49.38%) compared to our results (19.4%).

These differences could be explained by several factors, mainly that a higher prevalence of mental health disorders has been observed in the female gender as seen in previous reports, but also cultural and psychosocial factors, perception of governmental or institutional support, the evolution of the infection in terms of morbimortality in each country, the timing of assessment for the disorder, among others (Chatterjee et al., 2020). A study made in Colombia by Monterrosa-Castro et al. also reported that compared to male participants, female participants had twice the presence of anxiety symptoms, whereas feeling protected by the state or employer, being satisfied with their job, and trusting governmental measures and information were associated with a lower presence of anxiety (Monterrosa-Castro et al., 2020). Another study made in Iran by Saeideh Motahedi et al. also found higher levels of anxiety in their female participants, including not only clinical, but administrative and cleaning staff (Motahedi et al., 2021).

Balancing family demands has been previously identified by Shanafelt et al. as a common stressor and risk factor for burnout and emotional exhaustion for all physicians (Shanafelt et al., 2020). One of the specific interests of our study was to inquire about the changes in living and work dynamic and their influence on mental health for female physicians. 58.7% of the participants reported having children, with a majority of them ranging between 3 to 11 years old. This is of particular importance due to the specific care needs related to children in preschool and grade school, and the need for adaptation due to the closure of school and daycare facilities. Most of the respondents reported being supported with respect to childcare by their spouses or partners, grandparents being the next most common type of support. Also, most responded that they always or almost always managed to spend exclusive time with their children. Meanwhile, 8.2% of the respondents reported not having any type of support on childcare, and 13.1% reported almost never or never getting exclusive time with their children. We found a statistically significant relationship between having children, the absence of care support and the

Table 4. Logistic regression predicting likelihood of depression based on relevant variables.

Variable	B	SE	Wald	df	p	Odds Ratio	95% CI for Odds Ratio Lower	Upper
Age	.234	.091	6.572	1	**.010**	.791	.662	.946
Having children	.152	.394	.149	1	.699	1.164	.538	2.520
Personal Loss	.145	.776	.035	1	.852	1.156	.253	5.295
Discrimination Against for Being Identified as a Health Care Worker	.672	.759	.783	1	.376	1.958	.442	8.672
Verbal or Physical Aggression	1.522	.877	3.012	1	.083	4.583	.821	25.572
Increased Tobacco Consumption	.371	.783	.225	1	.635	1.450	.312	6.726
Working at COVID-19 Frontline	1.595	.736	4.696	1	**.030**	4.928	1.165	20.856
Previous mental health diagnosis	.467	.691	.457	1	.499	1.596	.412	6.182

presence of depression symptoms. This could be related to the presence of more stress and overload in women already being subjected to increased workloads (Almeida et al., 2020) and represents another area that calls for fast adaptation by women, independently of their position as frontliners, second line workers, or academia (Minello, 2020).

A statistically significant relationship was found between the presence of previous diagnoses of mental disorders and the presence of current symptoms of sleep disturbances, depression, anxiety, and PTSD. These findings coincide with those reported by Hao et al. which suggested that people with psychiatric disorders were at a higher risk of displaying more symptoms of PTSD, depression, anxiety, stress and insomnia, worries about physical health, anger and irritability, and suicidal ideation as compared to healthy controls (Hao et al., 2020).

Being exposed to verbal or physical abuse during quarantine was related to presenting symptoms of depression and PTSD. This is a factor of great importance considering increased incidences of gender violence during the COVID-19 pandemic have been reported. According to the Organization for Economic Co-operation and Development, femicide rates in Latin America are among the highest in the world, and the region has seen a dramatic rise in reports of domestic violence since the beginning of the pandemic (Data OECD, 2020.) (Nations U, 2020). Being discriminated against for identifying as a healthcare worker was found to be related to the presence of symptoms of depression. These findings, concur with previous findings of stigma and discrimination related to the management of other infectious diseases within the context of the population's urge to avoid diseases and the development of negative attitudes towards healthcare workers as collateral damage (Duan et al., 2020). It would be desirable to establish a continuity in the assessment of these factors due to their possible relationship not only with the presence of symptoms of depression and anxiety in health personnel, but also symptom severity and a delay to seek help in order to avoid even more stigmatization. Campo-Arias et al. developed a scale to evaluate the presence of some factors associated to stigma and discrimination that could provide a tool for obtaining more information on the subject and to develop a proper intervention for it (Campo-Arias et al., 2021).

After analyzing statistically significant variables for depression symptoms through a logistic regression model, the two factors that remained relevant for impact in depression symptoms were age and being at COVID-19 frontline of attention.

Younger age was associated with symptoms of PTSD and depression, but not with other outcomes. This coincide with Varma et al. study, were younger adults had worst scores regarding depression, stress and anxiety symptoms in comparison with older adults that had lower ratings, finding that within younger adults, loneliness was associated with poorer depression outcomes while older adults demonstrated more resilience than other age groups (Varma et al., 2021). This could represent possible risk and protective factors against psychological distress mediated by age and merits further study.

The finding of the impact of being a frontline health care worker during COVID-19 pandemic has also been reported by several studies during COVID-19 pandemic like Lai et al. and Xing et al., were high prevalence of depression among the frontline health care workers during

COVID-19 pandemic in China was also related to age and worries about falling ill with COVID-19, insufficient protective equipment, and disinfection measures sufficiency (Xing et al., 2020), outlining the importance to identify both risk and protective factors in our population.

4.1. Limitations and future directions

There are some limitations to this study. First, although our study provides clear descriptive information about participants revealing the presence of mental health symptoms, given the study's cross-sectional design and temporality of development (early in the pandemic for Mexico) the obtained data could represent only a preliminary sample of mental health issues in female physicians and leaves a need to further develop more research to drawn stronger conclusions about causality and associated factors. Second, the use of Facebook groups could represent a selection bias, limiting the possibility to reach physicians that are not present in social media. Third, the convenience sample conduction could have resulted in a more robust participation of women concerned about their mental health, influencing the high rates of mental health symptoms reported. Finally, as the focus of the study was to provide information about women's mental health status and associated factors, no male physician data was recollected. There is a need for future studies inclusive of diverse population, with different time lapses and follow up of the symptoms 'evolution, also adding an exploration on protective factors like resilience to get more information and further refine age-tailored interventions.

5. Conclusions

To our knowledge, this is the first published report on mental health outcomes and risk factors among female physicians in Mexico during the COVID-19 pandemic. Our results were in line according to previous studies made in China and Italy, confirming the need for further follow up and implementation of specific, age-tailored mental health interventions in female physicians, especially those with previous diagnoses of any mental health disorder and in the frontline row of COVID-19 attention. As the pandemic continues to unfold, female physicians are still under the burden of increased workload and a need for adaptation in their social and family dynamics, which can condition both acute and chronic mental health symptoms. The development of a gender specific and age tailored approach for interventions and support is needed to comprehensively protect women wellbeing.

Declarations

Author contribution statement

Barbara Garza Ornelas: Performed the experiments; Wrote the paper.

Julieta Rodríguez-de-Ita: Conceived and designed the experiments; Performed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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