



Revista Electrónica de Psicología Iztacala



Universidad Nacional Autónoma de México

Vol. 25 No. 3

Septiembre de 2022

MYALGIC ENCEPHALOMYELITIS/CHRONIC FATIGUE SYNDROME (ME/CFS) SYMPTOMS IN UNDERGRADUATE AND GRADUATE STUDENTS IN MEXICO

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ABSTRACT

Health professionals face illnesses for which is necessary to build instruments that allow diagnosis and develop treatments. One of these is Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). Bathia et al. (2020), state that the use of inconsistent ME and CFS case definitions has the potential to mask important population differences in access to specialist care and culturally-specific disease stigmatization. In addition, the lack agreement on a unified case definition leads to challenges in precisely describing the impairment and symptomatic presentation of the condition, and that given the afore mentioned issues with sampling heterogeneity; thus, there is a need to compare ME/CFS functional impairment and symptomatology in different countries using a consistent case definition. In Mexico, different efforts have been carried to study this Syndrome. However, prevalence data are not consistent. The goal for this study is to know relationship among frequency and severity with major symptoms for ME/CFS. Participants, undergraduate and graduate students (N=81), agreed to participate. Data will be based on a short version of the CFS Questionnaire from De Paul University, already validated for Mexican population, by Redcap

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platform. This questionnaire, containing 14 items and two variables of interest (frequency and severity, containing five response indicators for each item), will be published by Facebook and the main virtual media of the University we belong. Translation has been made. Preliminary results show interesting relations between age and insomnia (Factor R 0.319); weight and severity of fatigue (Factor R 0.394); frequency of pain and fatigue (Value "P" Kruskal Wallis: 0.045), correlations with factor scholar background; frequency of fatigue with minimal exercise (Value "P" Kruskal Wallis: 0.014; $p = 0.05$), among others. These preliminary results are promising in terms of people far away from Mexico City, can answer this questionnaire online, so we can have more accurate data concerning to prevalence of ME/CFS in this country.

Keywords: ME/CFS symptoms, Graduate, undergraduate students, Prevalence in Mexico.

ENCEFALOMIELITIS MIÁLGICA/SÍNDROME DE FATIGA CRÓNICA (EM/SFC) EN ESTUDIANTES DE PREGRADO Y POSGRADO EN MÉXICO

Resumen

Los profesionales de la salud se enfrentan a enfermedades para las cuales es necesario construir instrumentos que permitan diagnosticar y desarrollar tratamientos. Uno de ellos es la Encefalomielitis Miálgica/Síndrome de Fatiga Crónica (EM/SFC). Bathía et al. (2020), afirman que el uso de definiciones de casos de EM / SFC inconsistentes tiene el potencial de enmascarar importantes diferencias de población en el acceso a la atención especializada y la estigmatización de enfermedades culturalmente específicas. Además, la falta de acuerdo sobre una definición de caso unificada genera desafíos para describir con precisión el deterioro y la presentación sintomática de la afección, y dados los problemas antes mencionados, con la heterogeneidad del muestreo; por lo tanto, existe la necesidad de comparar el deterioro funcional y la sintomatología de EM/SFC en diferentes países usando una definición de caso consistente. En México se han realizado diferentes esfuerzos para estudiar este Síndrome. Sin embargo, los datos de prevalencia no son consistentes. El objetivo de este estudio es conocer la relación entre la frecuencia y la gravedad con los principales síntomas del EM/SFC. Los participantes, estudiantes de pregrado y posgrado (N=81), aceptaron participar. Los datos se basarán en una versión corta del CFS Questionnaire de la Universidad De Paul, ya validado para población mexicana, mediante la plataforma Redcap. Este cuestionario, que contiene 14 ítems y dos variables de interés (frecuencia y gravedad, conteniendo cinco indicadores de respuesta para cada ítem), será publicado por Facebook y los principales medios virtuales de la Universidad a la que pertenecemos. Se ha realizado la traducción. Los resultados preliminares muestran relaciones interesantes entre la edad y el insomnio (Factor R 0,319); peso y severidad de la fatiga (Factor R 0.394); frecuencia de dolor

y fatiga (Valor "P" Kruskal Wallis: 0,045), correlaciones con antecedentes escolares; frecuencia de fatiga con ejercicio mínimo (Valor "P" Kruskal Wallis: 0,014; $p = 0,05$), entre otros. Estos resultados preliminares son prometedores en términos de que las personas que se encuentran lejos de la Ciudad de México pueden responder este cuestionario en línea, por lo que podemos tener datos más precisos sobre la prevalencia de EM/SFC en este país.

Today, health professionals are faced with diseases for which is necessary to build instruments that allow diagnosing them and developing treatments. One of these is Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS), which is a complex condition of unknown etiology, characterized by presence of severe and debilitating physical and mental fatigue that persists for six or more months (Coffin, Jason, Jiménez, Bejar †, Bejar, Cedillo, Miralrio & Álvarez, 2011).

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a debilitating illness characterized by post-exertional malaise (PEM), sleep dysfunction, and cognitive impairment (Fukuda, K. et al., 1994; Institute of Medicine, 2015); however, individuals with this illness present with significant symptom heterogeneity.

Individuals with ME/CFS, routinely display differences in symptomatology, as well as illness course, onset, duration, and functional disability. Given such diversity, previous work has attempted to identify symptom-based ME/CFS subtypes. However, results have been inconsistent.

Approximately 20 different case definitions have been developed for ME/CFS (Bruberg, et al. 2014), each requiring a different number, type, frequency, severity, and duration of various symptoms.

The diagnostic process also varies by clinician; many report uncertainties about how to apply ME/CFS case definitions (Knight, S., et al., 2014), and there is variability in how physicians apply each case definition (McManimen, S.L., Jason, L.A., Williams, Y.J., 2015).

Lack of diagnostic clarity has led to debates about whether ME/CFS represents several illnesses with some symptom overlap, or whether ME/CFS subtypes exist (Jason, L. A., et al., 2005; Keer, J., et al., 2008; Maes, M., Twisk, FNM., Johnson, C., 2012).

In a study conducted by Hickie et al. (1995), latent class analysis (LCA) was applied to patient sample from New South Wales who met the Australian clinical criteria of ME/CFS (Lloyd, A.R., et al., 1990). The patients completed a 40-item self-report questionnaire designed by Lloyd et al. [14] that included both 'typical' and 'atypical' symptoms of the illness, as well as a battery of measures that identified functional impairment, illness course and behavior, and psychiatric morbidity. A two-class solution was selected due to its stronger fit statistics.

The larger class was characterized by less frequent and severe symptoms (both 'typical' and 'atypical'), a higher proportion of males, shorter illness duration, less disability, less severe illness course, and lower current psychiatric morbidity. The smaller class, by contrast, reported nearly all symptoms at a higher frequency and severity. A subsequent international, eight-center study largely replicated these results using latent profile analysis (Wilson, A. et al., 2001). These results suggest that individuals with ME/CFS vary by number of symptoms, but not type of symptoms.

Pathogenesis of CFS / ME is unknown, although several factors have been identified as triggers and factors of perpetuation, which seem to contribute to the emergence and evolution of the clinical symptoms of the disease. Among the most common factors, there are viral and bacterial infections, depression / anxiety, allergy, immune disorders, rheumatic diseases, disorders neuroendocrine and neuropsychiatric, among others. (Coffin, N., Miralrio, C. et al., 2015).

Friedman (2019), states that our current understanding of ME/CFS is that it is a complex, chronic, debilitating, physical disease characterized by postexertional malaise, severe, and debilitating fatigue, cognitive problems, sleep dysfunction, pain, and immune, autonomic, neurological, endocrine, and gastrointestinal symptoms (Friedberg, Bateman, et al., 2019). The severity of symptoms varies from day-to-day within the patient and varies among patients. Severity of disease is graded from patients being mildly affected, through moderately affected, to the severely affected. The severely affected are either house or bedbound, may be unable to move, speak or tolerate light (Saffron, 2009)). Post-exertional malaise (PEM) is considered one of the key symptoms of ME/CFS and is defined as the

exacerbation of the patient's symptoms following minimal physical or mental activity, occurring hours, days, or weeks after the triggering activity, and lasting for disproportionately long lengths of time (days, weeks, or months).

Huber, Sunquist and Jason (2018), mention that Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a debilitating illness characterized by post-exertional malaise (PEM), sleep dysfunction, and cognitive impairment (Fukuda, Strauss, Hickie, et al., 1994; Institute of Medicine, 2015; Jason, Corradi & Torres-Harding, 2005), however, individuals with this illness present with significant symptom heterogeneity.

Individuals with ME/CFS have shown variation in symptomatology, etiology, psychiatric comorbidity, functional disability, illness duration, and physiological abnormalities (Jason, Corradi & Torres Harding, 2005). Such diversity can interfere with the replication of findings across studies, as well as identifying a potential biomarker for the illness.

Friedman also declares (2019), that the goals of ME/CFS researchers, healthcare providers, and patients are the same as the goals of others confronting different chronic, debilitating disease: the availability of palliative if not curative treatment, an understanding of the etiology of the disease, development of therapeutic agents specific for the disease, and the development of a vaccine or some other preventative measures. The IOM report (1) concludes that progress in these areas has been disappointingly slow. That opinion is supported by comparing the progress made in the research, treatment and prevention of ME/CFS.

Bhatia, Olczyk, Jason, Alegre, Fuentes-Llanos y Castro (2020), report a cross-cultural study, Myalgic encephalomyelitis (ME) and chronic fatigue syndrome (CFS) are debilitating chronic, multi-systemic conditions of unknown origin, which are estimated to affect up to 24 million people worldwide (Johnston et al., 2013).

These authors also state that with multiple case definitions, there exists an inherent potential for heterogeneity across research samples, which may limit researchers' ability to replicate findings related to potential illness etiologies and presentation. Cross-cultural studies serve as exemplars highlighting the challenges associated with assessing symptomatic differences when using variant case definitions. In an

international study of individuals with CFS referred to clinics in Germany, the US, and the UK, researchers reported no significant differences in impairment between the samples (Hardt et al., 2001). However, the authors noted that each sample was derived from operationalizing different case definitions, prompting speculation if the lack of observed symptomatic differences were an artifact of the case definitions. A similar study consisting of participants from clinics in Australia, the US, and the UK also reported no significant differences in impairment with the use of varying case definitions (Wilson et al., 2001).

This cross-cultural study among American and Spanish population, suggests critical differences in the impairment levels experienced between the samples at tertiary care settings. It is possible that contextual features of Spanish healthcare and policy as they could pertain to adults with ME and CFS could help explain the impairment differences that were observed in this cross-cultural comparison. Disability and employment status significantly differed between countries. The findings suggest that rather than accessing disability benefits, individuals in Spain with adverse health impairment may not be able to work and are unemployed, or are able to work, though presumably at a reduced capacity as they manage their illness.

In Mexico, ME/CFS symptoms are mostly confused with another condition, as Fibromyalgia. Prevalence of ME /CFS is not clear, since there are a number of false positives diagnosed patients. Physicians tell patients that everything is normal, and they do not find any cause for this malaise.

Thus, the present study displays results of a pilot study, in which the goal is to know how some symptoms are found in a sample of Mexican patients diagnosed with a ME/CFS condition.

Method.

Participants

A convenience sample of adults self-identifying as having ME/CFS was obtained. Eligible participants (N= 81), were at least 18 years old, capable of reading and writing Spanish, and had a current, self-reported diagnosis of ME/CFS. Participants were able to complete the study measures electronically.

Measures

All participants completed the DePaul Symptom Questionnaire (DSQ), (Jason, LA, et al., 2010), validated for Mexican population, consisting on a 54-item self-report measure of ME/CFS symptomatology, demographics, and medical, occupational, and social history. Participants are asked to rate each symptom's frequency over the past six months on a 5-point Likert-type scale, with 0 = none of the time, 1 = a little of the time, 2 = about half the time, 3 = most of the time, and 4 = all of the time. Additionally, participants rate each symptom's severity over the past six months on a 5-point Likert-type scale, with 0 = symptom not present, 1 = mild, 2 = moderate, 3 = severe, and 4 = very severe. The Mexican version of DSQ has demonstrated adequate test-retest reliability of Cronbach alpha= 0.959, as well as good construct, convergent, and discriminant validity. (Coffin, N., et al., 2011). The Mexican version of DSQ is publicly available in the shared library of the Research Electronic Data Capture (REDCap) [25], hosted at Facultad de Estudios Superiores Iztacala, Universidad Nacional Autónoma de México, <https://is.gd/fatigacalidadvida>

Moral and Ethics

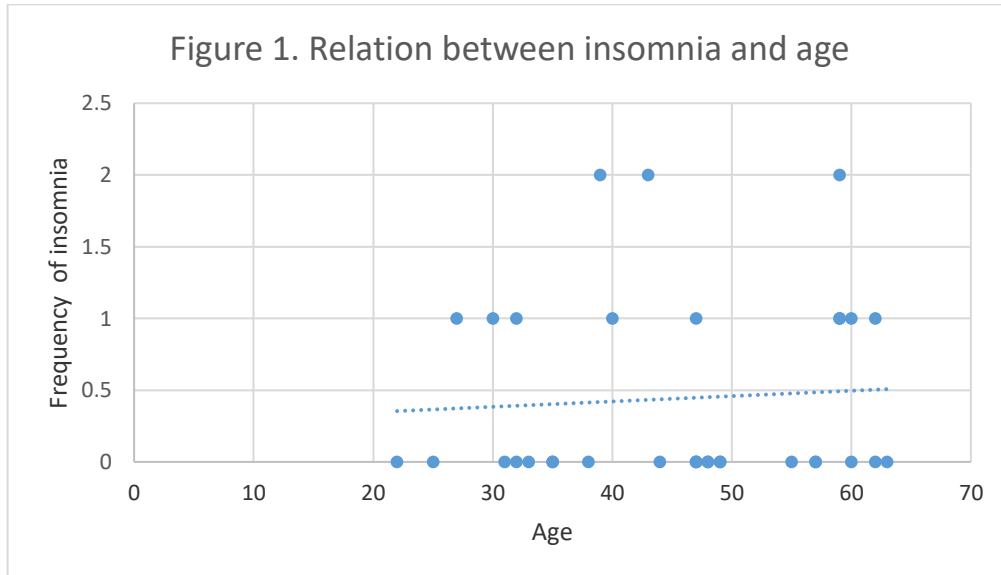
Participants were considered eligible for the present study if they were at least 18 years old and had completed a written *informed consent* process included in the questionnaire. Participants completed the study measures electronically, volunteer and anonymously.

Results.

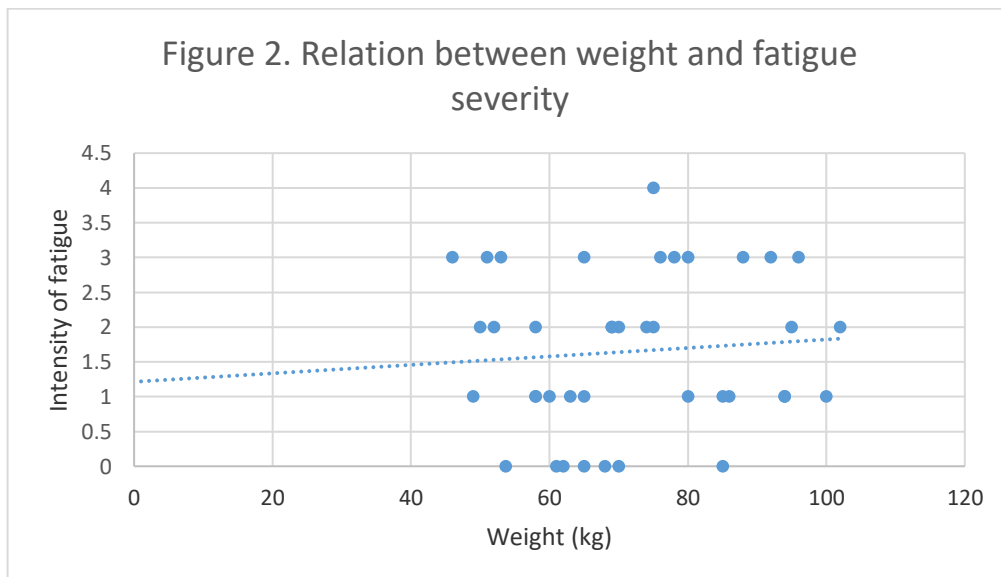
The next results show the relation among several variables, considered as important in a ME/CFS condition. There are presented relations between: biological age and frequency of insomnia; body weight and intensity of fatigue; fatigue and pain after carrying out some activity; tiredness and performance of minimal exercise; school grades regarding fatigue, when minimal exercise is carried out; degree of pain and fatigue, after a day of non-strenuous activities; and frequency of tiredness when performing a minimal exercise.

As we can see in Figure 1, there is a moderate correlation between the frequency of insomnia and age, ($r = -.319, p < .05$), from which it can be stated that the older the

age, the higher the frequency of insomnia, although it should be specified that this joint variation is fairly proportional to a minimum.

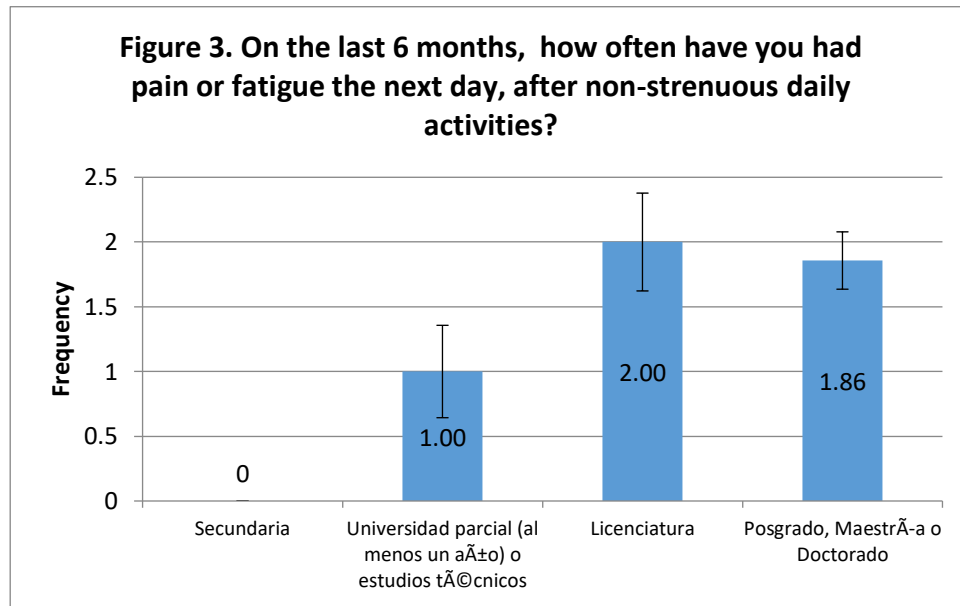


In the case of the relationship between the intensity of fatigue and age, there is a moderate correlation between the frequency of insomnia and age, ($r = -.319, p < .01$), from which it can be stated that the older the older the frequency of insomnia, although it should be noted that this joint variation is moderately proportional to a minimum. We can see this in the scatter diagram shown in Figure 2.

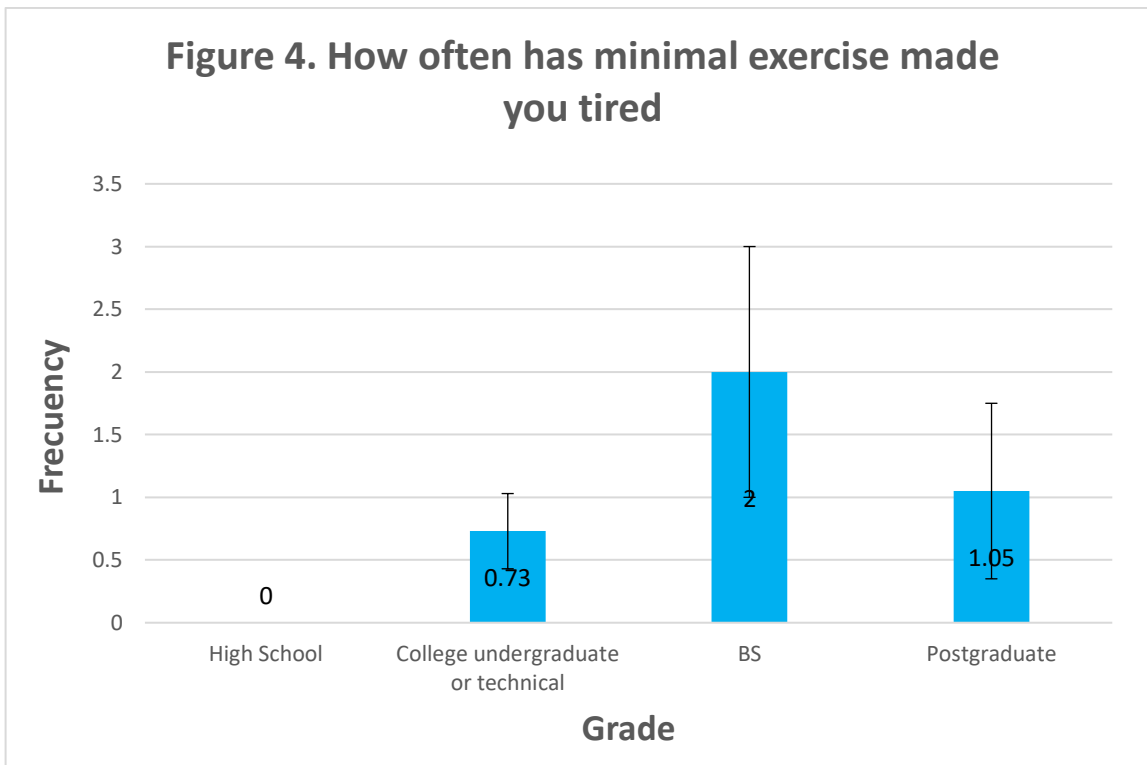


In Figure 3, we can observe the analysis of the experience of fatigue or tiredness experienced by different groups after carrying out their daily activities, in relation to their level of studies: Significant differences are identified among those participants

whose maximum level of studies was the bachelor's degree (BS), in comparison with those who have professional or postgraduate studies. These differences were significant between the groups with a p value $<.05$. Undergraduate students are the ones who present a higher level of fatigue after carrying out their daily activities.



Regarding the differences in the frequency with which symptoms of fatigue appear after exercising, when comparing the values observed in the students of High school, College undergraduate or technical students of Bachelor Sciences and postgraduates, significant differences were identified (Kruskall Wallis, p -value $<.05$). The highest scores were presented by the BS students, as we can see in figure 4.



Concerning to Figure 5 (below), significant differences were identified among the different educational levels in relation to the frequency in which symptoms of fatigue appear, after performing an exercise routine (Kruskall Wallis, p value $<.05$). BS students' sample are the ones who reported lower values, despite having greater variability, while graduate students present values close to the mean with less variability (see Figure 5). Although the data show significant differences among the groups, depending on the level of studies, it should also be considered that a higher academic degree also presents less physical activity, and this may be biasing to some extent the results obtained.

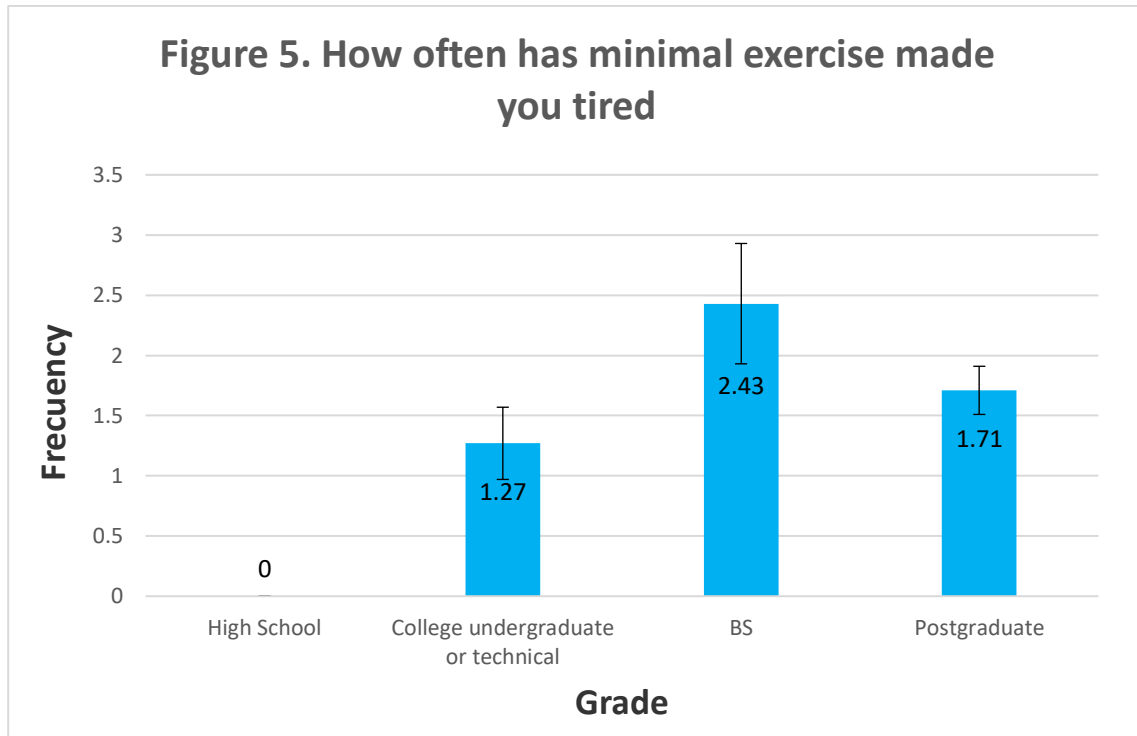
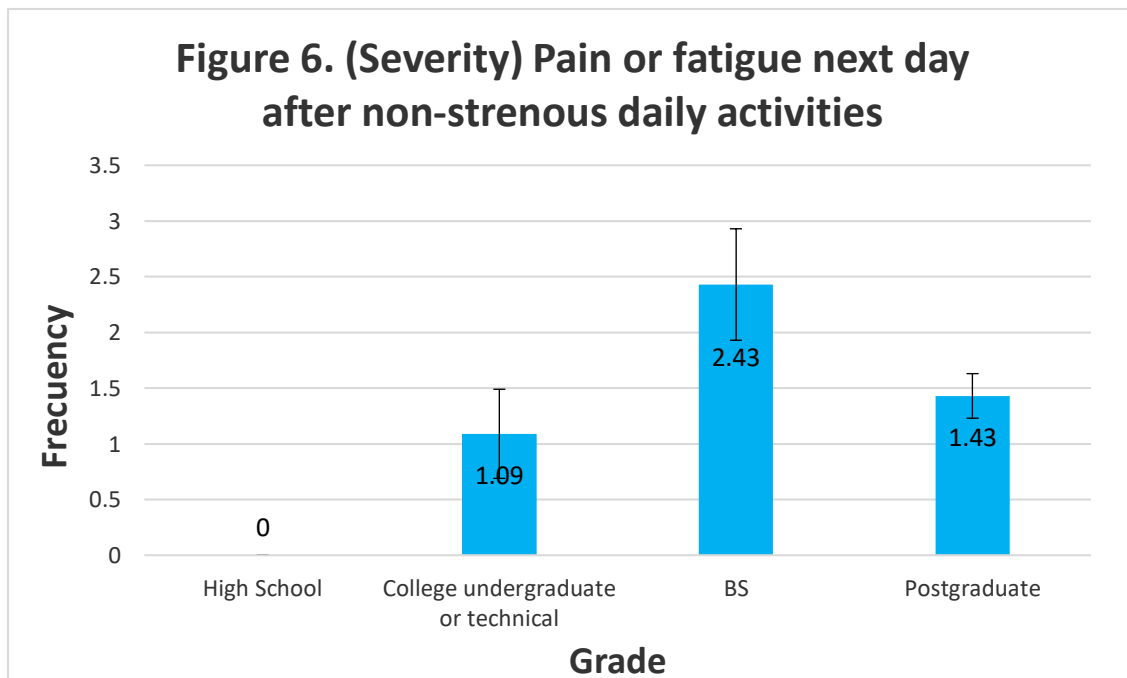


Figure 6 shows the comparison of the frequency, in which the different groups evaluated, reported symptoms of fatigue and pain 24 hours after they performed strenuous activities. Significant differences are identified between the four groups (Kruskall Wallis, p value $<.05$). The BS students' group were the ones who presented the highest values, while the High School students did not report symptoms.



When contrasting the frequency with which each of the evaluated groups presented symptoms of fatigue and pain, after having performed a minimum of exercise, significant differences are identified among the four groups (Kruskall Wallis, p value $<.05$). As can be seen in Figure 7, BS students are the ones who most frequently reported signs of fatigue, compared to the rest of the groups, and at the same time, it is the group with the greatest variability; the undergraduate / university, technician, and postgraduate groups presented more homogeneous values.

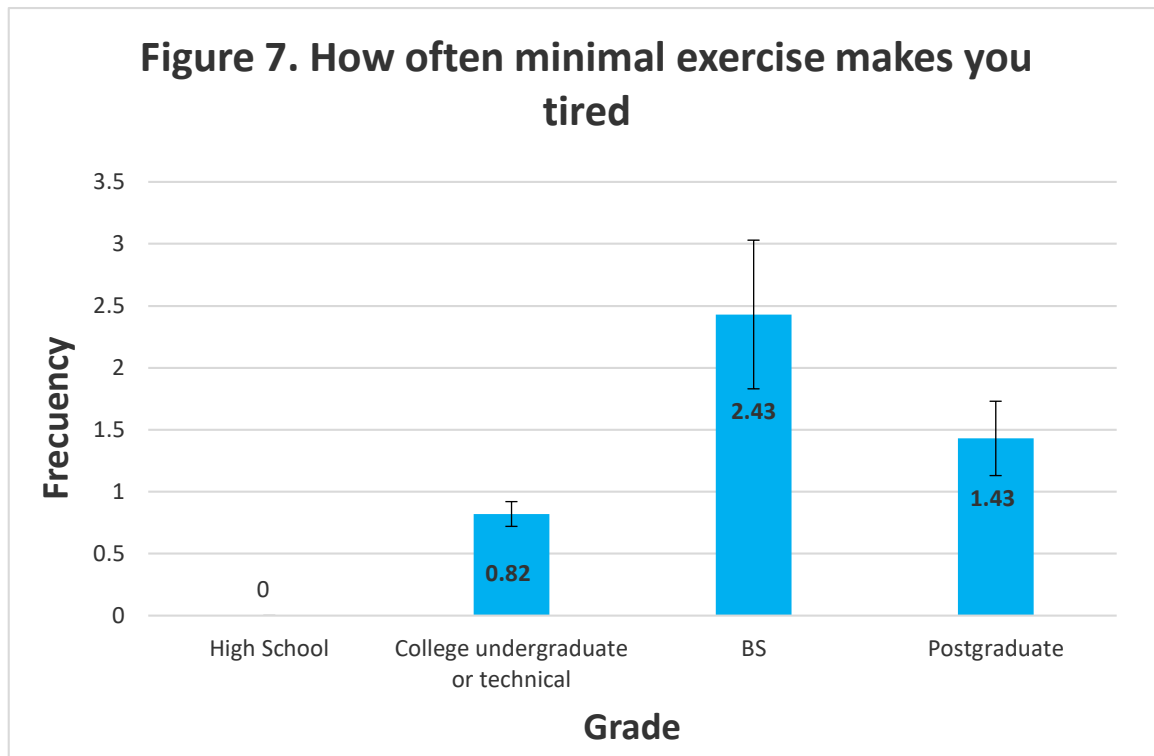
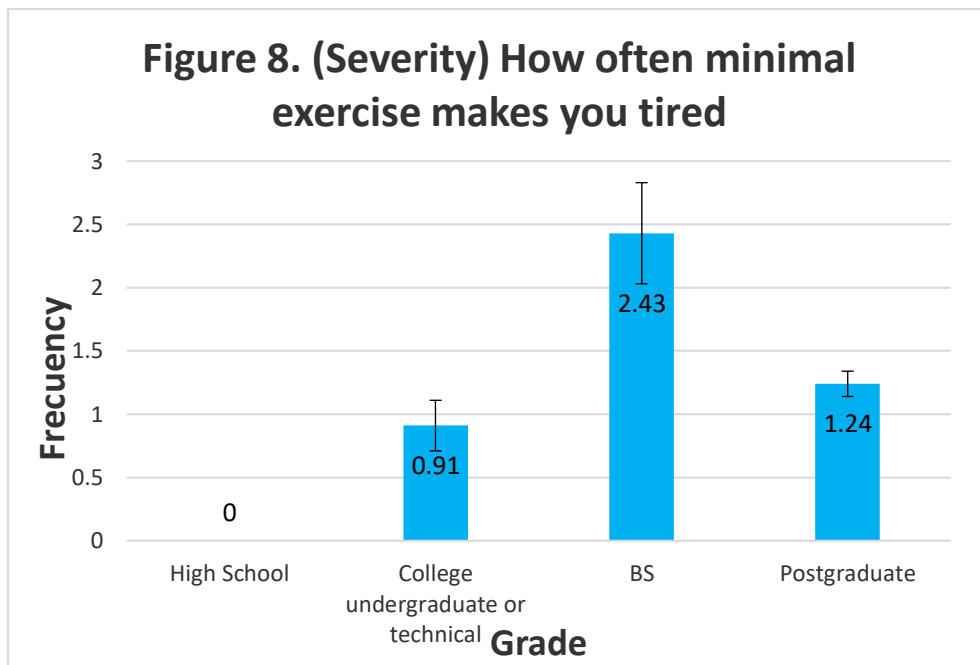
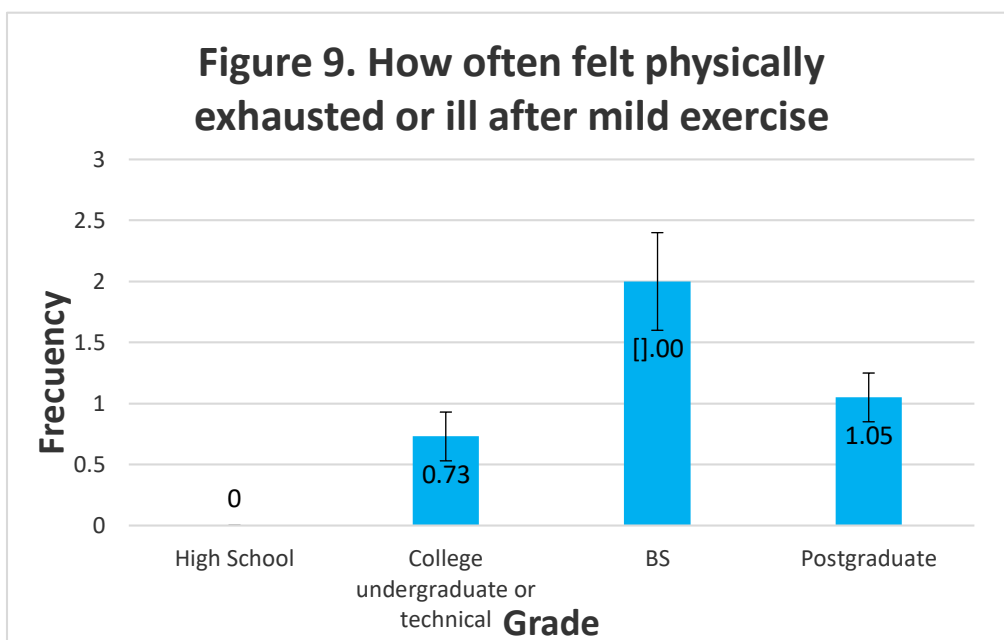


Figure 8 shows the frequency with which exhaustion is experienced after doing minimal exercise in recent months. After analyzing the average scores of each of the groups, significant differences were again identified (Kruskall Wallis, p value $<.05$). As in the previous analyzes, it was the BS students' group who reported the highest values and with greater variability.



Finally, when comparing the four groups (see Figure 9), according to physical state after doing moderate exercise, we again found significant differences (Kruskall Wallis, p value $<.05$) in the presence of symptoms of tiredness and fatigue; once more, the group of BS students were the ones who presented higher values, and with greater variability, this is due to the heterogeneity between the members of this group.



Discussion.

In Mexico, not enough research has been developed to sustain the prevalence of CFS/ME. Diagnosis result in a confuse state for the patients, due the fact that Fibromyalgia shares some symptoms with CFS/ME. This causes patients misdiagnosed as false positives for CFS/ME condition, and vice versa.

This study states the importance and need of studying more about this condition, based on Jason, Corradi and Torres-Harding (2005), Results clearly show the correlation between fatigue and some other traits of this Syndrome, such as post exertional malaise, sleep disfunction and cognitive impairment (Fukuda, K. et al, 1994). It also shows a severity of fatigue after mild exercise (Friedman, 2019), among students of BS at Technical or Postgraduate.

Jason, Corradi and Torres-Harding (2005), This diversity across studies might be due to the different cultural challenges associated with symptomatic differences for a case definition (Bathia, et al, 2020).

As we could observe, BS students ranks, unfortunately, superior at the other degrees, in most of the symptoms. This must take our attention in this specific population.

In conclusion, although results in this study agree with previous findings, and seeing that among the study groups, BS students present greater symptoms, it is urgent to analyze more groups in cross-cultural studies, to find a more generalized case definition for CFS/ME.

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