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Chronic nausea and vomiting syndrome and impact on quality of life

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KEYWORDS
Nausea;
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Quality of life

Abstract
Introduction and aim: Chronic nausea and vomiting syndrome is a disorder of gut-brain interaction that affects the productive-age population. Our aim was to determine the association of this disorder with quality of life, workplace performance, and socioeconomic impact related to gastrointestinal health.
Methods: A cross-sectional study on a Mexican population was conducted. The patients were classified as having chronic nausea and vomiting syndrome or other disorders of gut-brain interaction. A comparative analysis of quality of life, workplace productivity, annual medical consultations, and digestive health-related expenses was carried out, applying a logistic regression model.
Results: One thousand patients were included, 79.2% of whom met the criteria for a disorder of gut-brain interaction. Of the 792 patients, 10.3% presented with chronic nausea and vomiting syndrome. Said syndrome was associated with a negative impact on usual activities (OR 4.34, 95% CI 1.90-9.30, $p \leq 0.001$), pain/discomfort (OR 2.09, 95% CI 1.31-3.33, $p \leq 0.001$), anxiety/depression (OR 2.08, 95% CI 1.30-3.40, $p \leq 0.001$), workplace presenteeism (OR 3.96, 95% CI 2.47-6.44, $p \leq 0.001$), and workplace absenteeism (OR 2.54, 95% CI 1.52-4.16, $p \leq 0.001$). There was also a higher number of annual medical consultations for digestive health ($p = 0.013$), without generating a greater annual expense due to digestive health ($p = 0.08$).

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Conclusions: Chronic nausea and vomiting syndrome produces a negative impact on quality of life, which could be secondary to its symptomatology or its association with anxiety and depression.

PALABRAS CLAVE
Náusea;
Vómito;
Síndrome de náusea y vómito crónico;
Trastornos de la interacción cerebro intestino;
Calidad de vida

Síndrome de náusea y vómitos crónicos e impacto en la calidad de vida

Resumen
Introducción: El síndrome de náusea y vómito crónico es un trastorno de la interacción cerebro intestino que afecta a la población en edad productiva. El objetivo fue determinar la asociación de este trastorno con la calidad de vida, desempeño laboral e impacto socioeconómico relacionado a la salud gastrointestinal.
Métodos: Un estudio de corte transversal en población mexicana. Los pacientes se clasificaron como síndrome de náusea y vómito crónico u otros trastornos de la interacción cerebro intestino. Se realizó un análisis comparativo de la calidad de vida, productividad laboral, consulta médica anual y gastos relacionados a salud digestiva aplicando un modelo de regresión logística.
Resultados: Se incluyeron 1000 pacientes, de los cuales 79.2% cumplían criterios de algún trastorno de la interacción cerebro intestino. De los 792 pacientes, 10.3% presentaban síndrome de náusea y vómito crónico. El síndrome de náusea y vómito crónico se asoció a un impacto negativo en las actividades usuales (OR 4.34, IC95%, 1.90-9.30, p = <0.001), Dolor/Malestar (OR 2.09, IC95%, 1.31-3.33, p = <0.001), Ansiedad/Depresión (OR 2.08, IC95%, 1.30-3.40, p = <0.001), presentismo laboral (OR 3.96, IC95%, 2.47-6.44, p = <0.001) y ausentismo laboral (OR 2.54, IC95%, 1.52-4.16, p = <0.001). También presentaron un mayor número de consultas médicas anuales por salud digestiva (p = 0.013) sin generar un mayor gasto anual por salud digestiva (p = 0.08).
Conclusiones: El síndrome de náusea y vómito crónico genera un impacto negativo en la calidad de vida, lo que podría ser secundario a su sintomatología o a su asociación con ansiedad y depresión.

Introduction and aims

Chronic nausea and vomiting syndrome (CNVS) is a rare disorder of gut-brain interaction (DGBI) that makes up part of the gastroduodenal disorders in the nausea and vomiting disorders group described by the Rome IV criteria.[1–3] Diagnosis of this entity is made in populations that present with nausea or vomiting at least once a week, with no evidence of other causes of said symptoms, and ruling out dietary disorders, induced vomiting, regurgitation, or rumination.[4] The overall prevalence of nausea and vomiting as isolated symptoms is from 9.5% and 2.7%, respectively.[5] The prevalence of functional disorders of nausea and vomiting is 2.2%, 50% of which corresponds to cyclic vomiting syndrome (CVS) and 45% to CNVS.[2,5] According to a global epidemiologic study by the Rome Foundation on more than 70,000 subjects, CNVS is estimated to affect 0.9% (0.8-1.0) of the population worldwide.[6]

CNVS has no predilection for race or sex and its prevalence progressively decreases with age. It frequently affects productive-age patients, at a mean age of 37 years.[2,3,6]

In relation to the impact on workplace productivity, in a study on 21,128 persons of working age by Camilleri et al., they found that nausea and vomiting had been the cause of absenteeism in the workplace in the three months prior to the evaluation of the patients, with a total of 6.6 and 13.1 workdays lost, respectively.[5] Despite the awareness of the impact nausea and vomiting have on quality of life as isolated symptoms, there is little evidence on the impact that CNVS has on quality of life. However, its impact on physical and mental status has been described.[3,7–10] The negative impact that CNVS has on quality of life could be secondary to the frequent overlapping with other gastrointestinal disorders, such as functional dyspepsia, which has been described to be significantly associated with this nausea and vomiting disorder (aOR 3.4, 95% CI 1.8-6.5, p < 0.0001).[2] In a significant number of patients diagnosed with a DGBI, poor quality of life may be secondary to the overlap with somatic symptom disorders, such as fibromyalgia and chronic fatigue syndrome, but regarding CNVS, an association with somatic symptom disorders has not been demonstrated.[2,3]

In addition, there is evidence of the economic impact on patients with CNVS. For example, patients with CNVS have been reported to generate a high annual requirement of healthcare-related resources, with frequent hospital admis-

sions to emergency rooms and hospitalization, resulting in total health costs of $57,140 USD in the United States. [5,11]

Regarding treatment, there is no consensus on a recommendation for managing CNVS, predisposing to the use of multiple therapeutic options with a variable therapeutic response, numerous medical opinions, and a high risk of adverse effects that can lead to elevated healthcare-related costs.[1,7,8,11] Therefore, the aim of the present study was to determine the impact of CNVS on the quality of life of those affected, including its effect on workplace performance and its socioeconomic impact.

Material and methods

Design and subjects

A cross-sectional study was conducted in seven Mexican states (Baja California, Sonora, Nuevo León, Jalisco, Morelos, Estado de México, and Mexico City) on an open population, coordinated by gastroenterologists from a tertiary care hospital in Western Mexico, within the time frame of March 1, 2021, to November 14, 2022. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist was employed. The general population was invited to voluntarily participate in the protocol registered as ''The impact of CNVS on workplace productivity and quality of life in the Mexican population'' during the established period.

Data collection and variables

The data were collected through the application of an online Internet survey on an open population. The patients were collected through cluster sampling. The sociodemographic data, including annual healthcare expenses on gastrointestinal health and workplace information, such as type of job, presenteeism, absenteeism, and workdays lost (subjectively evaluated by the poor performance or workplace absenteeism item in the questionnaire secondary to the gastrointestinal symptomatology present). Medical histories with comorbidities and current medical management were also collected, as well as gastrointestinal symptomatology related to esophageal, gastroduodenal, intestinal, and anorectal disorders, according to the Rome IV criteria, including the diagnostic criteria for CNVS.[1] The population above 18 years of age was included, excluding those with an organic disease that could explain the gastrointestinal symptomatology. Patients that met the CNVS criteria, according to the Rome IV recommendations, were selected for the comparative analysis.[1] According to the definition of CNVS, patients with possible secondary causes of nausea and vomiting were excluded, including those diagnosed with pregnancy, diabetes, thyroid disorders, migraine, and chronic kidney disease, as well as those that actively used cannabinoids, opioids, nonsteroidal anti-inflammatory drugs, anticholinergics, estrogens/progestogens, lubiprostone, GLP-1 agonists, and chemotherapy agents.

A 7-point Likert scale was applied to evaluate the severity of the gastrointestinal symptomatology of nausea and vomiting, considering a score $\geq$ 6 points as severe. Screening for anxiety and depression was carried out through the hospital anxiety and depression scale (HADS), validated in Spanish in the Mexican population. Anxiety and depression were considered to be present, when scores were $\geq$ 11 points in the sub-analyses for the two conditions.[12] The quality-of-life evaluation was carried out by applying the Spanish-validated EQ-5D descriptive system questionnaire, with its five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), without taking its quantitative score into account.[13]

Statistical analysis

An analytic, cross-sectional study was conducted, comparing patients that met the CNVS criteria with those that did not.[1] A logistic analysis, utilizing a log-linear goodness-of-fit model, was carried out, with deviation as the statistic for determining whether CNVS was independent from the categorical variables to be the variable studied. The results were expressed utilizing the odds ratio with a 95% confidence interval, and statistical significance was set at a $p \leq 0.05$. The Akaike information criterion was also employed to select the viable models with a significant association. A distribution analysis with the Kolmogorov-Smirnov test was carried out for the quantitative variables and the Levene's test was used for the equality of variances. According to the distribution of the variables (heteroscedasticity or homoscedasticity), the Mann-Whitney U test was applied, with or without standard transformation, utilizing the square root for the comparative analysis of medians and the Student's t test, with or without the Welch transformation, for the analysis of means.

Bioethical considerations

The project was registered with the local bioethics committee (register number: 113/21) and met the requirements for its approval. Protocol implementation adhered to the recommendations established in the universal declaration on bioethics and human rights on October 19, 2005, at the general conference of the UNESCO. There were no known or inherent risks for the subjects that participated in the research protocol, and their information and confidentiality were managed with extreme care. The subjects authorized their participation and signed statements of informed consent before providing information and before the data collection.

Results

One thousand subjects were included and 792 (79.2%) of them met the criteria for a DGBI (mean age of 30 $\pm$ 10 years, female sex 69.9% [n = 554]). A total of 208 subjects did not meet the criteria or presented with a comorbidity, and so were excluded from the descriptive statistical analysis. Of the 792 patients, 125 (15.7%) stated having frequent nausea and vomiting and 82 (10.3%) of them met the CNVS criteria.

Table 1 General sociodemographic characteristics.

Variable	CNVS (n = 82)	Other DGBIs (n = 710)	p
Age, median (IQR)	26 (22-31)	26 (23-33)	0.86
Sex			0.056
Female, n (%)	64 (78)	490 (69)	
Male, n (%)	18 (22)	220 (31)	
Occupation			0.12
Worker, n (%)	32 (39)	345 (48.5)	
Student, n (%)	26 (31.7)	232 (32.7)	
Student-worker, n (%)	24 (29.3)	133 (18.7)	
Decline in workplace and academic productivity			
Presenteeism, n (%)	52 (63.4)	216 (30.4)	<0.001
Absenteeism, n (%)	27 (32.9)	115 (16.2)	<0.001
Medical attention			
Medical consultation due to gastrointestinal symptoms, n (%)	60 (73.2)	386 (54.4)	0.001
Annual medical consultations, median (IQR)	1 (0-2)	[1.0](0-2)	0.013
Annual digestive health-related costs (MXN), mean (SD)	1495.1 (659.6)	983.9 (150.5)	0.080
Decline in the EQ-5D dimensions			
Mobility, n (%)	3 (3.7)	15 (2.1)	0.422
Self-care, n (%)	1 (1.2)	6 (0.8)	0.581
Usual activities, n (%)	10 (12.2)	22 (3.1)	0.001
Pain/discomfort, n (%)	38 (46.3)	207 (29.2)	0.002
Anxiety/depression, n (%)	54 (65.9)	341 (48)	0.005
Hospital Anxiety and Depression Scale			
Anxiety, n (%)	13 (15.9)	192 (27)	0.032
Depression, n (%)	3 (3.7)	39 (5.5)	0.617
Anxiety and depression, n (%)	53 (64.6)	307 (43.2)	<0.001

Demographics, quality of life, and workplace activity

Table 1 shows the demographic, quality of life, workplace, and academic data. The patients with CNVS were predominantly young women, but there was no statistically significant difference between sexes (CNVS: women, 78% vs other DGBIs: women, 69%, p = 0.056) or regarding age (CNVS: 26, 22-31 years vs other DGBIs: 26, 23-33 years; p = 0.86) between the two groups. The analysis of the variables showed a statistically significant difference, with respect to workplace and academic productivity, consultations for gastrointestinal symptomatology, annual medical consultations, and the EQ-5D descriptive system dimensions of daily activities, pain/discomfort, and anxiety/depression, as well as the diagnosis of anxiety and depression (Table 1).

Clinical characteristics

The patients with CNVS also had overlapping with other gastrointestinal disorders and symptoms, such as the typical symptoms of gastroesophageal reflux diseases (52.4%, n = 43), belching disorder (46.3%, n = 38), dysphagia (17.2%, n = 14), epigastric pain syndrome (31.7%, n = 26), postprandial distress syndrome (24.4%, n = 20), dyspepsia in the presentation of overlap syndrome (22.9%, n = 28), diarrhea-predominant irritable bowel syndrome (26.8%, n = 22), mixed irritable bowel syndrome (15.9%, n = 13), chronic functional diarrhea (19.5%, n = 16), chronic diarrhea (13.4%, n = 11), anal pain (30.5%, n = 20), and fecal incontinence (2.4%, n = 2) (Table 1).

Quality of life

The application of the logistic model produced no significant association between CNVS and the descriptive dimensions of the EQ-5D model for self-care (OR 1.45, 95% CI 0.08-8.61, p = 0.731) or mobility (OR 1.76, 95% CI 0.40-5.47, p = 0.386). However, the dimensions of usual activities (OR 4.34, 95% CI 1.90-9.30, $p \leq 0.001$), pain/discomfort (OR 2.09, 95% CI 1.31-3.33, $p \leq 0.001$), and anxiety/depression (OR 2.08, 95% CI, 1.30-3.40, $p \leq 0.001$) were independently associated with the presence of CNVS (Table 2).

Workplace productivity

Upon evaluating workplace productivity generated by CNVS, more than 50% of the patients stated it had a negative impact on work-related activities and CNVS was independently associated with presenteeism (OR 3.96, 95% CI 2.47-6.44, $p \leq 0.001$) and absenteeism (OR 2.54, IC95%, 1.52-4.16, $p \leq 0.001$) in the workplace (Table 2).

Annual medical consultations and expenses related to digestive health

Patients with CNVS were found to have sought medical attention more frequently, having a higher number of annual

Table 2 Multivariate analysis: CNVS and its association with poor quality of life.

Variable	OR	95% CI	p
Decline in workplace and academic productivity			
Presenteeism, n (%)	3.96	2.47-6.44	< 0.001
Absenteeism, n (%)	2.54	1.52-4.16	< 0.001
Decline in the EQ-5D dimensions			
Mobility, n (%)	1.76	0.40-5.47	0.386
Self-care, n (%)	1.45	0.08-8.61	0.731
Usual activities, n (%)	4.34	1.90-9.30	< 0.001
Pain/discomfort, n (%)	2.09	1.31-3.33	< 0.001
Anxiety/depression, n (%)	2.08	1.30-3.40	< 0.001
Hospital Anxiety and Depression Scale			
Anxiety, n (%)	0.50	0.27-0.94	0.291
Depression, n (%)	0.65	0.19-2.16	0.483
Anxiety and depression, n (%)	2.39	2.39-3.86	< 0.001

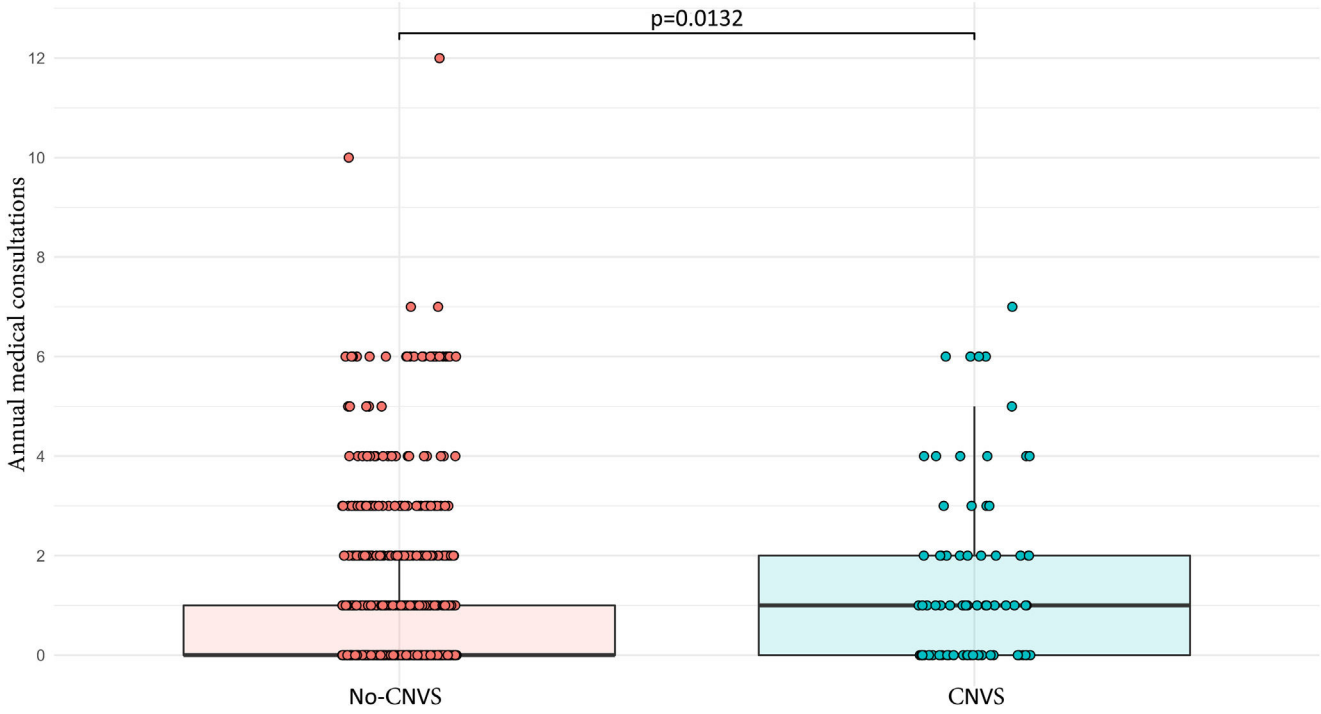

Figure 1 Comparison of annual medical consultations between patients with CNVS and other DGBIs.

medical consultations due to digestive health (CNVS: 73.2% vs other DGBIs: 54.4%, p = 0.001) (Fig. 1). Nevertheless, upon comparing digestive health-related costs per capita, the patients with CNVS had higher annual expenses but with a nonsignificant trend (CNVS: 1495.1 ± 659.6 MXN vs other DGBIs: 150.5 ± 983.9 MXN) p = 0.08 (Fig. 2).

Discussion and conclusions

CNVS is a frequent gastroduodenal disorder that affects the productive-age population, producing a negative impact on their quality of life. In our study, the prevalence of CNVS was 8.0% (95% CI 6.0-10.0), similar to the 9.0% (95% CI 8.0-10.0) reported in other studies.[6] The mean age of affected patients was 26 years (IQR 22-31), with a predominance of women (n = 64, 78%), and 68.3% were active workers.[2,3,5] As with the majority of DGBIs, CNVS tends to present as an overlap syndrome with other gastrointestinal disorders. In our population, the most prevalent overlap was with esophageal symptomatology, such as the typical symptoms of gastroesophageal reflux disease (52.4%) and belching disorders (46.3%).[14] This can be explained by the fact that initially many of those patients can be misdiagnosed with gastroesophageal reflux disease, thus delaying the accurate diagnosis. CNVS is an entity described as having a negative impact on quality of life, and in our study, we found that the descriptive dimensions of the EQ-5D model of usual activities (OR 4.34, 95% CI 1.90-9.30, p ≤ 0.001), pain/discomfort (OR 2.09, 95% CI 1.31-3.33, p ≤ 0.001), and

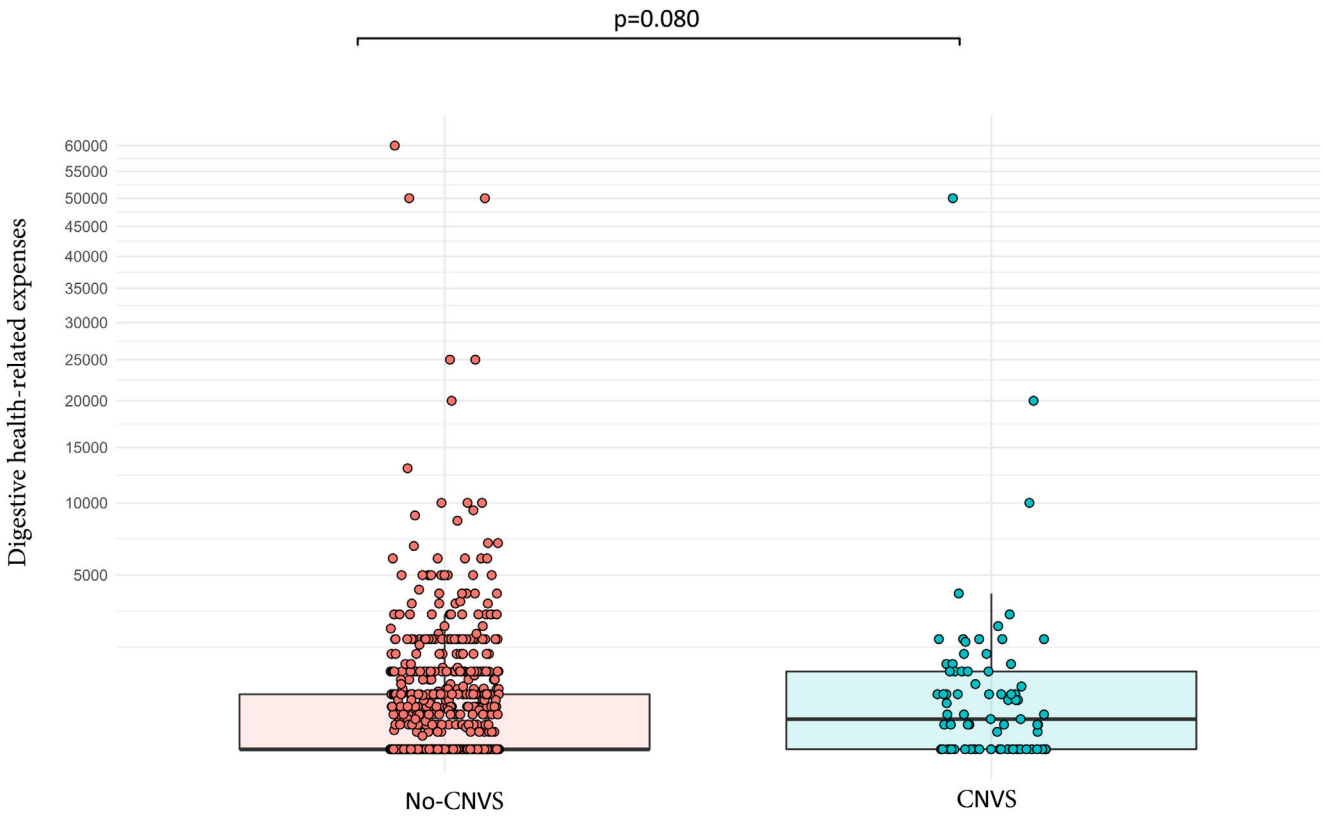

Figure 2 Comparison of annual digestive health-related expenses between patients with CNVS and other DGBIs.

anxiety/depression (OR 2.08, 95% CI 1.30-3.40, $p \leq 0.001$) were affected. Our results are similar to those described by Aziz et al.,[2] who reported that the physical (aOR 1.07, 95% CI 1.04-1.10, $p \leq 0.001$) and mental (aOR 1.04, 95% CI 1.02-1.07, $p \leq 0.001$) dimensions of the SF-36 questionnaire were significantly affected in the patients with CNVS.

DGBIs can also have a negative impact on workplace activities. For example, patients with irritable bowel syndrome and abdominal pain are known to experience a substantial negative impact on their work and daily life activities due to their symptoms.[15] Nevertheless, fewer studies on the impact of other DGBIs, and CNVS in particular, have been carried out. In our study, 63.4% and 32.9% of the patients with CNVS presented with workplace presenteeism and absenteeism, respectively. The negative impact on quality of life in patients with CNVS may be secondary to nausea and vomiting but can also be secondary to its association with anxiety and depression or its frequent overlapping with other gastrointestinal symptoms.[2,16] Another precipitating factor of the negative impact CNVS has on patient quality of life is symptom recurrence and refractory symptoms that cause the patients to seek medical attention more frequently, consequently resulting in greater healthcare-related expenses. We found that the patients with CNVS sought medical attention more frequently, which in turn produced greater annual expenses. Our findings are similar to those of Aziz et al.[2] who showed that 86.2% of the patients with CNVS sought medical attention at least once a year.

Even though our results are interesting, we must recognize certain limitations of our study, such as the feasible presence of selection bias, when using subjects that voluntarily answer an Internet survey. Furthermore, organic disease could not be verified or ruled out because the information was collected through questionnaires. Lastly, due to the fact that the participants were from seven different states of Mexico, heterogeneity was likely, and a comparative study between the different states was not conducted.

We conclude that CNVS is a frequent and underdiagnosed disorder that has a negative impact on quality of life, affecting the daily activities and workplace productivity of the patients with this condition. Said impact can be secondary to the symptoms of CNVS, but also to their association with anxiety and depression. Therefore, it is important to consider the overlapping of this disorder with other DGBIs, when evaluating these patients. Treatment should take into account the effect of CNVS on quality of life and its socioeconomic impact, as well as considering screening for the detection of psychiatric disorders, so that patients can be referred to the corresponding medical services, thus providing them with holistic disease management.

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Conflict of interest

The authors declare that there is no conflict of interest.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.rgmxen.2024.10.001.

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