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Review Article

Prevalence of Functional Neurological Disorders in Iran: A Systematic Review and Meta-Analysis

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Abstract

Background: Functional Neurological Disorder (FND) is characterized by neurological symptoms that are incompatible with known neurological diseases. This disorder can be disabling, imposing a significant burden on patients, society, and the healthcare system. There is limited data on the epidemiology of FND in Iran. This study aims to investigate the prevalence and manifestations of FND in Iran.

Methods: Electronic databases, including Embase, ISI, Google Scholar, PubMed, IranDoc, and the Scientific Information Database, were systematically searched in 2024 using keywords related to the epidemiology of FND in Iran. Additionally, other scientific reports, such as national survey reports and dissertations, were reviewed. After screening and assessing the articles, eligible studies were included in the review. A meta-analysis was conducted using the random-effects model.

Results: A total of 578 articles were screened from which 20 full-text articles were assessed. Finally, nine studies were included in the quantitative synthesis. Of these, three were conducted in psychiatric wards, four in general hospitals and non-psychiatric departments, one in a neuropsychiatric service, and one in community and school settings. The reported prevalence of FND across these studies ranged from 3.2 to 8.2%.

Conclusion: Seizures were the most common manifestation of FND. The prevalence rate of FND varied across studies depending on the study setting and methodology.

Keywords: Conversion disorder, Electronics, General hospitals, Iran, Prevalence, Psychiatric, Department, Search engine, Seizures

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Introduction

Functional Neurological Disorder (FND) is a condition in which patients experience one or more neurological symptoms such as gait problems, abnormal movements, difficulty swallowing, speech symptoms, sensory problems, falls, or seizures, among others. These symptoms are inconsistent with other identified diseases (1). Although the brain's structure appears normal in these patients, its functioning is impaired (2).

Iran's national mental health survey reported a 1.8% prevalence of unexplained Medical Symptoms (MUS) (3). Globally, the annual incidence of FND is approximately 4-12 *per* 100,000 (4,5). These symptoms escalate in clinical settings, with 5% of general hospital patients diagnosed (6), and 19% identifying FND as a primary concern (7). Additionally, 10–30% of neurological outpatients show symptoms unrelated to structural brain lesions (4,8). Despite their prevalence, FND is frequently misdiagnosed, often mistaken for conditions like multiple sclerosis (9).

Global FND epidemiology remains unclear, with variations influenced by cultural, societal, and healthcare factors. Emphasis on somatic over psychological symptoms may lead to misdiagnosis and delayed interventions. Socioeconomic and healthcare disparities further contribute to inconsistencies in prevalence and symptom patterns (10,11).

In Iran, with its strong psychiatric foundation and significant MUS prevalence, addressing FND epidemiology is essential to improving patient care. This review provides a systematic analysis of FND epidemiology in Iran, highlighting diverse prevalence rates across studies.

Given the high comorbidity with psychiatric disorders (12) and FND's long-term debilitating nature (13), psychiatric attention in diagnosis and treatment is critical. Treatments have shifted from purely psychological to integrative approaches, combining psychotherapy, drug therapy, and physiotherapy to improve symptoms and reintegrate patients into their communities (14-16).

However, the findings on a history of physical injuries in these patients (17), concurrently with structural lesions existing even before the disease, have raised the assumption that physical injuries can be a factor in triggering these symptoms (18), and it was observed that physical injuries could trigger the onset of functional symptoms (19). In addition to these findings, imaging data such as the variation in brain function during the beginning of these symptoms compared to their voluntary performance (20), or to the control group (21,22), or a drop in activity in the temporoparietal area demonstrated these patients have defects in movement agency, attention and movement control (23,24). In other words, the brain's functioning is disturbed even though no problem is found in the brain's structure.

Therefore, the psychological view was replaced by a functional standpoint, and the name of conversion disorder for these symptoms as a psychological reaction was changed to a Functional Neurological Disorder in 2013 (1).

The treatment of patients with FNDs was transformed by altering the aetiology view from a purely psychological approach to a brain disorder approach, factoring the psychological aspects leading to better communication with the patients and explaining the symptoms to them (25), and helping them manage thoughts and emotions related to the symptoms (26) and behavioural activation. Furthermore, physiotherapy was employed to rehabilitate and re-educate movement and healthy function in treating these patients, along with administering psychological treatments (27).

There was a need in Iran, a country benefitting from 80 years of modern psychiatry and a high prevalence of unexplained medical symptoms, to review the present situation to improve the quality of services for patients with FNDs. Assuming the prevalence of unexplained medical and physical symptoms disorders has been discussed in previous studies in the national surveys of psychiatric disorders, we can refer to Mohammadi *et al*'s study (28). The one-year prevalence of somatoform disorders by Sharifi *et al* was reported as 4.2% in 2011 (29). By considering theese scattered data, this study aims to review the current state of FNDs epidemiology of FND in Iran.

Materials and Methods

Both Persian and English electronic databases, including Embase, ISI, Google Scholar, PubMed, IranDoc, and SID, for original articles were

comprehensively searched investigating the epidemiology of FNDs in Iran. Additionally, other sources, such as national surveys and dissertation reports were reviewed, to ensure a thorough identification of relevant studies. The search covered all the records from 1970 to October 2021, using a combination of keywords related to FNDs, their symptoms, and Iran, including Conversion disorder, Functional neurological disorder, Hysteria and psychogenic disorders. Furthermore, to ensure a comprehensive search, various terms related to FND symptoms were combined with these primary keywords, including functional movement disorder, dysphasia, weakness, paralysis, hysterical paralysis, sensory loss, anaesthesia, dystonia, abnormal movements, tremor, spasm, epilepsy, seizure, psychogenic non-epileptic seizure, parkinsonism, numbness, paraesthesia, blurred vision, double vision, temporary blindness, hearing loss, tinnitus, non-epileptic seizures, syncopal episode, dysphonia, functional dysphonia, functional aphonia, slurred speech, functional dysphagia, chronic pain, and fatigue.

The search strategy involved combining these keywords using Boolean operators "(AND, OR)" to capture all the potentially relevant studies. Duplicates were removed, and the remaining records were screened for eligibility based on their titles, abstracts, and full texts by two researchers, and had their findings confirmed by a third researcher. Consensus was gained through group discussions. Additionally, the reference lists of included studies were screened to find additional citations. Two researchers concluded the qualitative evaluation after reviewing the article titles. The Joanna Briggs Institute Critical Appraisal Checklist for Prevalence Studies (30) was applied to assess the methodological quality studies estimating the prevalence of FND or the prevalence or patterns of one or more FND symptoms (Supplementary file). To assess publication bias, two indicators were considered: publication delay and grey literature bias (31).

For publication delay bias, it was assessed whether the speed of publication differed between studies with larger sample sizes or those with higher prevalence of FND or its symptoms. For grey literature bias, it was evaluated whether the sample size or prevalence magnitude differed between unpublished reports and published studies. Based on group consensus regarding these evaluations, no indication of publication bias was observed.

Meta-analysis

In order to provide a pooled estimate on the prevalence/frequency of FND and its symptoms and determine the extent and potential source(s) of heterogeneity between studies, meta-analysis was performed with random effects model. Heterogeneity was evaluated using the Cochran's Q test and I^2 statistics. Significant heterogeneity was declared at Q-test ($p<0.10$) and $I^2 >50\%$. Data was analyzed in Stata software (v. 14).

Results

Initially, 6324 citations were identified, including five from sources other than the searched databases. After removing the duplicates, 5690 unique citations remained. Following a detailed review of article abstracts and their relevance to the study's objectives, 57 original articles were selected for examination. Among these, nine articles met the inclusion criteria (Figure 1).

Demographic indicators related to FNDs in different studies are different since they were run in various regions of Iran, with the details presented in Table 1. These studies consisted of 1,694 patients (1,040 male and 654 female) from five different provinces of Iran. The oldest one was published in 1992 and the latest in 2019. Of the nine studies included, three were conducted within psychiatric departments (Pakrah *et al* (32), Shakeri *et al* (33), and Samimi-Ardestani *et al* (34), four were conducted in general hospitals and non-psychiatric departments (Vafaee *et al* (35) Farnam (36) Asadi Pooya *et al* 2013 (37) and 2014 (38) the latter involving patients initially diagnosed with epilepsy and subsequently referred to the respective clinic). One study was conducted in a neuropsychiatric service (39) and one was carried out within the community and school (40) settings (Table 1). Prevalence rate between these different studies varied between 3.2 to 8.2%.

The prevalence of conversion disorder symptoms varied across these studies. The studies were categorized based on whether they were conducted in general hospitals/clinics or psychiatric hospitals/

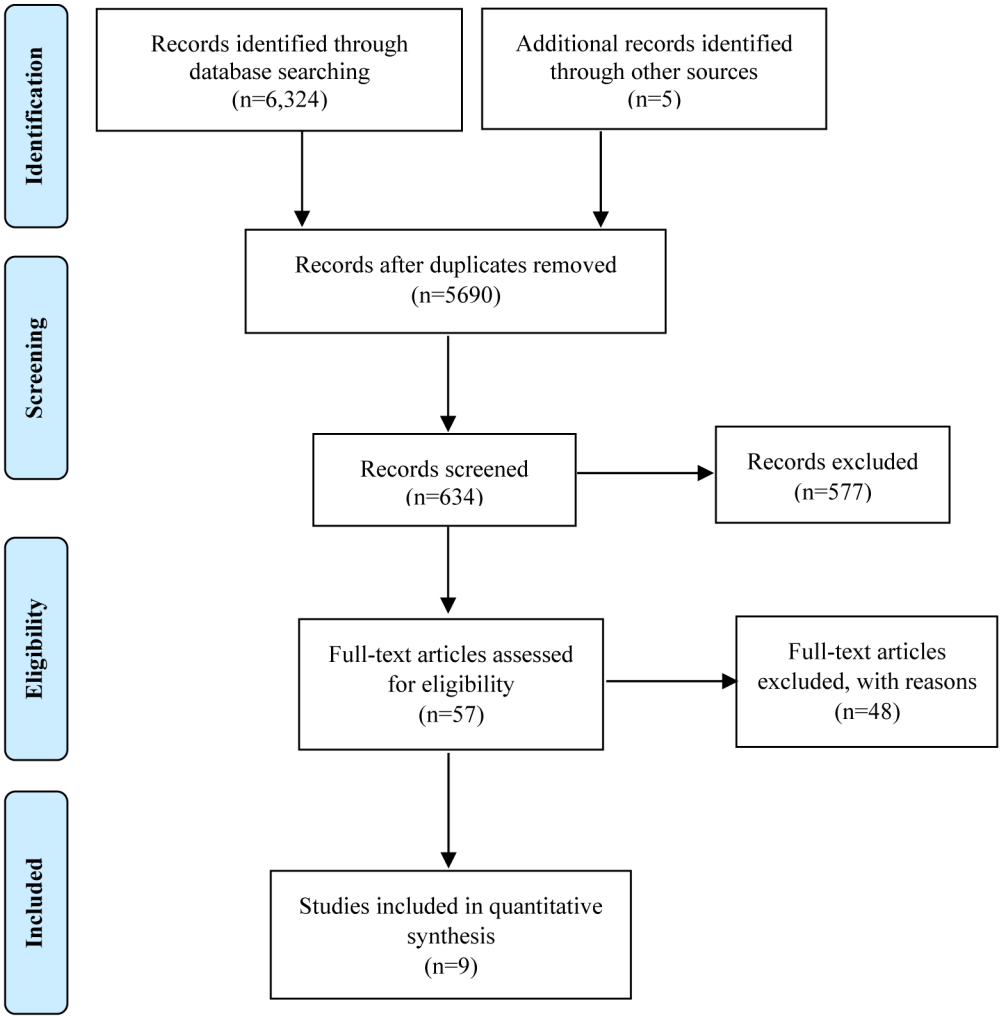

Figure 1. Summary of the study selection process.

Table 1. Prevalence of functional neurological disorder and its associated factors in Iran

Article Author and year	Study year	City	Sample Size (Male/ Female)	age range (Year)	Sample source	Sampling Method	Prevalence	Diagnostic criteria	Associated factors	Marital status			Educational level			
										Single	Married	Separated	Primary or less	Lower than diploma	Diploma	University
Yasamy *et al*, 1999 (40)	1992	A rural area in Kerman	10(0/10)	14-15	School	Census – From school children	-	-	Postvac-cination mass psychogenic illness in an iranian rural school	100%	0	0	0	100%	0	0
Pakrah, 1999 (32)	1991-1998	Kerman-shah	321(202/ 119)	N/S	Psy-chiatry hospital	Con-venience –From patients of psychiatry hospital	3.2%	-	63% female, most common age group was 20-29 y/o, primary school education	N/S	N/S	N/S	N/S	N/S	N/S	N/S

Contd. table 1.

Vafaee *et al* 2004 (35)	2004	Tabriz	100 (35/65)	5-65	Hospital/ clinic	Con-venience – From patients admitted in health services (psychiatry or general hospitals/ clinics)	-	DSM4	65% married, 89% suddenly, 38% associated with familial disputes, 65% female, 19% histrionic PD	35%	65%	0	50%	37%		13%	
Farnam *et al* 2008 (36)	2005-2006	Tabriz	42 (22/20)	19-32	Hospital	Con-secutive – From patients admitted to emergency ward	-	DSM4	Pre-valence of depression in conversion disorder was 96%	N/S	N/S	N/S	N/S	N/S	N/S	N/S	
Shakeri *et al* 2010 (33)	1996-2006	Kerman-shah	625 (409/216)	N/S	Psy-chiatry hospital	Con-venience – From patients of psychiatry hospital	-	DSM-4 TR	70.6% in 31-50 Y/O, 51.1% male, 63.3% married, 9.7% separated	27%	63.3%	9.7%	45.4%		39.2%		15.4%
Asadi-Pooya *et al* 2013 (37)	2008-2012	Shiraz	2800 persons in epilepsy clinic PNES patients: 188 (129/59)	12-71	Epilepsy clinic	Con-venience	7.9%	Video EEG monito-ring	There is no gender difference among patients with PNES	N/S	N/S	N/S	N/S	N/S	N/S	N/S	
Asadi-Pooya *et al* 2014 (38)*	2008-2013	Shiraz	3034 persons in epilepsy clinic PNES patients: 211 (141/70)	12-71	Epilepsy clinic	Con-venience	8.2%	Video EEG monito-ring	16.6 percent also had confirmed epilepsy. Family history of epilepsy reported in 33.1 %. History of physical or sexual abuse	45%	51.2%	3.8%		50.7%		25.1%	17.1%
Samimi-Ardes-trani *et al* 2020 (34)	2017	Tehran	96 (68/28)	18 -65	Emer-gency depart-ment, psy-chiatry ward	Con-secutive – From patients with FND symptoms referred to psy-chiatry ward or Emergency department	-	DSM-IV (SCID)	Frequency of bipolar spectrum disorder was 35.4% in patients with conversion disorder	30.2%	61.5%	8.3%	55.2%		31.3%		13%
Masjedi *et al* 2022 (39)	2018-2019	Tehran	101 (34/67)	>18	Psy-chiatry clinic	Con-secutive sampling	-	diag-nosis by psychi-atrist	78 % of the patients had stressor before symptom onset	55%	36%	9%	6.9%		25.8%		67.3%

* Education level was not reported in 7.1% of the patients. N/S: not specified.

Table 2. Frequency of functional neurological disorder symptoms in Iran §

FND symptom specifiers	General hospital Vafaee *et al* (35) ¥** SS:100 n (%)	Psychiatry unit Samimi-Ardestani *et al* (34) ¥ SS:96 n (%)	Psychiatry unit Pakrah (32) ¥ SS:321 n (%)	Psychiatry unit Masjedi *et al* (39) ¥ SS:101 n (%)
With weakness or paralysis	29(29%)	21(21.8%)	Was not reported	12(11.8%)
With abnormal movement	12(12%)	7(7.2%)	Was not reported	11(10.8%)
Swallowing symptoms	4(4%)	1(1.0%)	Was not reported	2(1.9%)
With speech symptom	24(24%)	11(11.4%)	Was not reported	7(6.9%)
With attacks or seizures	60(60%)	44(45.8%)	Reported as most common manifestation	44(43.5%)
Anesthesia or sensory loss	12(12%)	-	Was not reported	11(10.8%)
Special sensory symptom	-	4(4.1%)	Was not reported	14(13.8%)
With mixed symptoms	14(14%)	8(8.3%)	Was not reported	-

§: Only four studies reported the frequency of each FND symptoms. ¥: Each individual could have more than one symptom; thus, the total percentages can exceed 100%. SS: Sample size.

clinics, as illustrated in table 2. Utilizing Random-effect Meta-analysis, the prevalence was calculated as follows:

Attack/seizure (50%), Weakness/paralysis (19%), Speech symptoms (13%), Abnormal movement (11%), Anaesthesia/sensory loss (11%), Mixed symptoms (10%), Special sensory symptoms (7%), Swallowing symptoms (2%) (Table 2 and Figure 2). There was no significant variation in the frequency of FND symptoms between patients receiving care in general hospital settings and those referring to psychiatric clinics or hospitals, as was evident from the overlap in estimated 95% Confidence Intervals (CIs) as illustrated in figure 2. Frequency of weakness /paralysis, speech symptoms, and attacks/seizures showed the greatest statistical heterogeneity between studies. For the weakness/paralysis and speech symptoms, this heterogeneity was mainly caused from the estimate provided by Masjedi *et al* (38). For the attacks/seizure's subgroup, the estimate of Vafaee *et al* (30) was the source of heterogeneity.

Regarding accompanying psychiatric disorders, Farnam *et al* (36) reported that 96% of the cases were linked with depressive disorder, while 10% were associated with histrionic personality disorder in the study of Vafaee *et al* (35). In contrast, Ardestani *et al*'s study (34) revealed that 35.4% of the patients were diagnosed with bipolar disorder, and the study of Masjedi *et al* (38) recorded a prevalence of 44.4% for major depressive disorder (39) (Table 1).

The study conducted by Vafaee (35), was among patients admitted to general hospitals while the other studies were among psychiatric patients. However, no significant difference was observed between the frequency of symptoms in these groups, considering overlaps in estimated 95% CIs. Studies with zero success were removed from the meta-analysis. I2 was not computed for subgroups with less than three estimates.

Discussion

In this review, nine studies were analysed, encompassing three conducted in psychiatric hospitals, four in general hospitals, one in a neuropsychiatric service, and one in a school setting. The predominant clinical manifestation observed was psychogenic seizures. The diagnosis of FNDs necessitates a thorough neurological evaluation, which revealed seizures as the most prevalent manifestation among patients in this study.

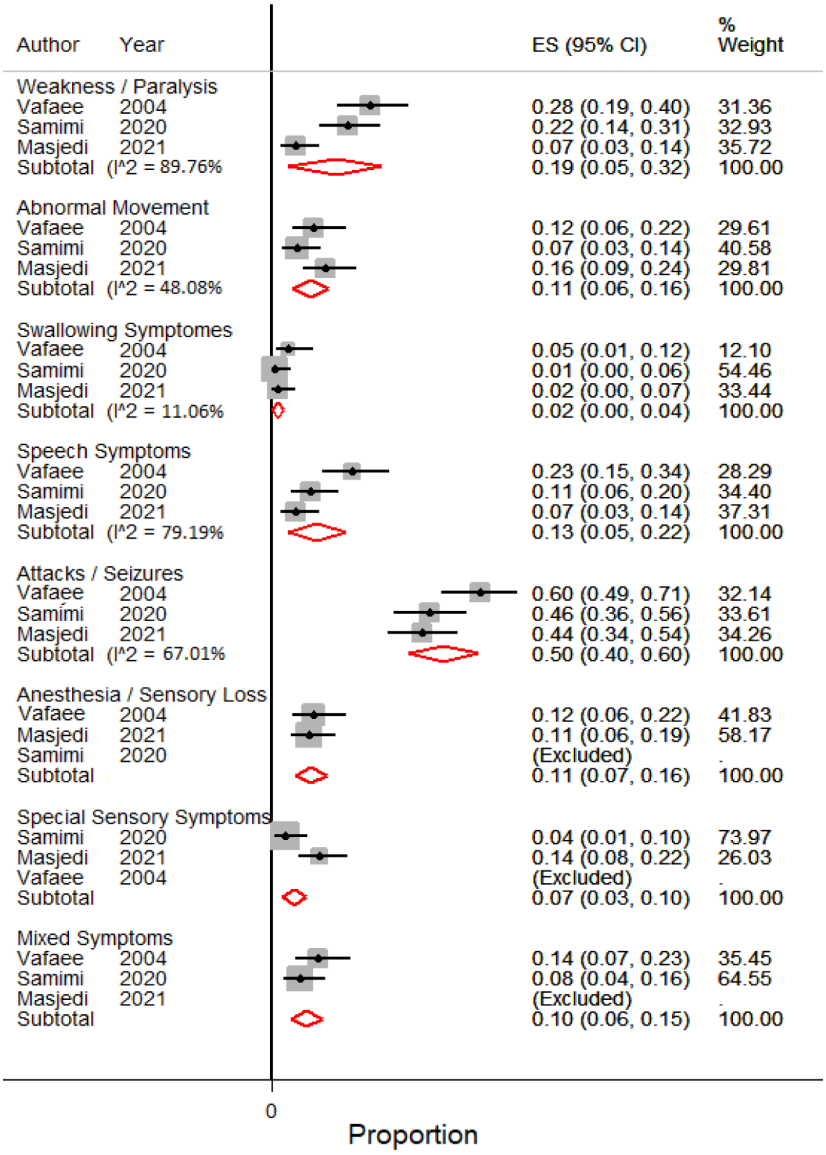

Figure 2. Frequency of FND symptoms among Iranian patients.

With the exception of one case, all the studies were conducted in outpatient clinics, indicating a higher attendance in outpatient services compared to hospitalization, consistent with findings from other studies. The observed prevalence of conversion disorder symptoms varied widely, ranging from 8% to 88%, highlighting the diverse methodologies and sample populations used across epidemiological studies on dysfunction.

The publication of studies conducted in general hospitals (four studies) compared to those in psychiatric departments (three studies) suggests that more patients are referred or present in non-psychiatric departments, underscoring the importance of recognizing their clinical manifestations in diverse healthcare settings. This hypothesis can be further confirmed by our observation that there was no significant difference in the frequency of FND symptoms between patients attending general hospitals and those referring psychiatric clinics (Figure 2). Nevertheless, adequate training and resources in non-psychiatric services can facilitate comprehensive treatment approaches.

Studies conducted in Iran have identified major depressive disorder as the most common psychiatric comorbidity among FND patients, often associated with familial conflict as a prevalent predisposing factor (39). Notably, the initial and most frequent referrals for these patients are to neurologists and, in second place, general physicians (39). Convulsions

emerged as the most common symptom across five studies, followed by paralysis in two studies. It seems convulsion manifestations are more common in other studies, such as physical or movement disorders or paralysis in Iran (41). This fact could be, of course, due to the bias of studies dealing with psychogenic seizures. In a study by Asadi-Pooya *et al* (38), possibly influenced by the focus on psychogenic seizures in certain investigations.

Consistently, more women than men were identified as suffering from nervous dysfunction in (33-35), with married individuals showing a higher prevalence in some studies, also indicative of family discord (39) as a significant stressor. Therefore, it was noted that violation of family stressors is essential and requires attention, thus if there is a need to implement interventions utilizing these patients, it can be guided by using the five-factor It is important to acknowledge the significance of addressing family stressors when dealing with patients experiencing FND. Implementing interventions based on the five-factor cognitive-behavioral models could be beneficial in treating FND.

Studies have highlighted a history of sexual abuse among a majority of patients (42), although this finding is not consistently reported across all studies, possibly reflecting challenges in assessing trauma and cultural differences. Additionally, while one study noted conversion disorder cases in a school setting, specifically post-vaccination (40), such occurrences are rare. However, occurrence of FND symptoms following COVID-19 vaccination warrant further investigation.

Only one study (38) focused on patients with neurological conditions, indicating a lack of attention to FND outside psychiatric departments. This underscores the necessity of interdisciplinary collaboration between psychiatry and neurology, emphasizing the establishment of joint neuropsychiatry units for comprehensive patient assessment and treatment.

Evaluation of patients with FND predominantly relies on psychological approaches to identify underlying factors and accompanying psychiatric disorders, with limited mention of other interventions in the reviewed studies (34,39). Notably, assessments for organic disorders revealed a 10% occurrence, similar to international findings, indicating insufficient attention to organic factors among these patients (35). Common psychiatric disorders associated with FND include mood disorders, particularly depressive disorder, which may precede or follow the onset of FND (34,35,39). Evaluating these relationships and providing timely interventions are crucial for effective patient management. Furthermore, drug abuse was found to be prevalent among FND patients (43), potentially serving as self-treatment or exacerbating somatic symptoms.

While efforts to improve diagnosis and referral services for FND patients have been initiated in certain healthcare facilities, further expansion of these services is warranted.

Conclusion

In conclusion, the current study underscored the scarcity of epidemiological research on FND in Iran, revealing a critical gap in understanding this complex condition within our population. The available studies indicated a noteworthy prevalence of various FND symptoms, with psychogenic seizures emerging as the most prevalent manifestation within the Iranian context. However, comprehensive investigations encompassing diverse populations and geographic regions across the country are imperative to fully elucidate the epidemiological landscape of FND. These endeavors are vital for informing healthcare policies, designing targeted interventions, and ultimately enhancing the quality of care for individuals affected by FND in Iran. Therefore, the authors advocate for further research initiatives aimed at unraveling the multifaceted nature of FND and its implications on public health in Iran.

Conflict of Interest

The authors declare that there is no conflict of interest in this study.

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