



## Psychiatric comorbidities in a sample of Iranian children and adolescents with epilepsy

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### Abstract

**Introduction:** Epilepsy is a common disorder worldwide, commonly starting during childhood. Despite the high impact of psychiatric comorbidities in these patients, little is known about Iranian children with epilepsy.

**Methods:** This cross sectional study was carried out in the tertiary clinics of the Tabriz University of Medical Sciences, Tabriz, Iran. All of the children (aged between 6 and 18) with a diagnosis of epilepsy were enrolled in this study. A semi-structured psychiatric interview was carried out using the Farsi (Persian) version of the Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version (K-SADS-PL).

**Results:** From a total of 298 participants, 270 (90.6%) completed the process, including 120 (44.4%) girls and 150 (55.6%) boys. At least one psychiatric diagnosis was made in 222 (82.2%) patients. The most prevalent psychiatric disorders in children and adolescents with epilepsy were attention deficit/hyperactivity disorder (34.4%), major depressive disorder (MDD) (29.6%), social phobia (14.8%) and oppositional defiant disorder (ODD) (14.8%). Agoraphobia and anorexia nervosa were significantly more prevalent among girls. The following disorders were more prevalent in children aged between 13 and 18: MDD (47.5%), psychotic disorder (2.5%), social phobia (23.7%), generalized anxiety disorder (GAD) (15.3%), conduct disorder (13.6%), chronic motor tic disorder (13.6%) and substance related disorders (4.8%). Separation anxiety (15.1%) and enuresis (1.5%), on the other hand, were more prevalent among younger children. A logistic regression model showed that psychiatric disorders in parents or siblings could independently predict at least one psychiatric comorbidity in children with epilepsy.

**Conclusion:** Iranian children with epilepsy face a high burden of psychiatric and behavioral comorbidities compared to same aged general population that should be considered for comprehensive care.

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### Introduction

Epilepsy is a common and chronic disorder with a prevalence of 1.8%-3.9%<sup>1-3</sup> in different populations, including over 30 million children.<sup>4</sup> An increased incidence of psychiatric disorders has been noticed in patients with epilepsy compared with the general population.<sup>4</sup> Epilepsy starting during childhood is a challenging condition for families, thus, psychiatric comorbidities

could have essential clinical and therapeutic implications.<sup>5</sup> Studies clearly indicate that such children have a lower health related quality of life and higher medication side effects compared with patients with epilepsy without psychiatric comorbidity.<sup>6,7</sup>

Prevalence studies performed on the association between epilepsy and psychiatric disorders have found that epilepsy can precede, co-occur with or follow the

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diagnosis of a psychiatric disorder.<sup>8</sup> Studies have been conducted on the risk of mental health disorders in these patients from different regions. A cohort of patients with epilepsy for a mean follow-up duration of 35 years showed that the lifetime prevalence of psychiatric disorders was higher in these patients compared with the general population (23% vs. 7%), especially in patients with childhood-onset epilepsy.<sup>9</sup> These included depressive disorders,<sup>10,11</sup> anxiety disorders,<sup>12,13</sup> psychotic disorders<sup>14</sup> and attention deficit/hyperactive disorder (ADHD).<sup>15,16</sup>

A population based study also indicated that rate of psychiatric disorders is twofold higher in these patients compared to general population.<sup>17</sup> Epilepsy is associated with decreased health-related quality of life and adaptive abilities in children<sup>18</sup> as well as a higher prevalence of suicidal ideation and attempts.<sup>19,20</sup> Thus, the clinical evaluation for comorbidities with psychiatric disorders in children and adolescents with epilepsy is of great importance. Available literature indicates that there is a growing interest in determining the optimal diagnosis and choice of treatment based on the proper identification of coexisting psychiatric and behavioral disorders to achieve the best outcome.

There are a few reports on psychiatric disorders in patients with epilepsy in Iran, although they are restricted to the adult population<sup>3,21,22</sup> and comparable with the results from a US adult population.<sup>19</sup> These reports indicate a significant impact of epilepsy on different aspects of life and also a high psychiatric comorbidity.<sup>21,22</sup> No reports were found regarding a similar situation with children and adolescents. The current study aimed to identify lifetime prevalence of psychiatric disorders in children and adolescents with epilepsy within an Iranian population, using a face-to-face psychiatric interview with both the parents and the child. The second aim was to find factors related to the presence of a psychiatric condition in these children. As specific contributing factors are not available yet, the

demographics of children were recorded to evaluate possible relation to presence of a psychiatric disorder. The hypothesis was that Iranian children and adolescents with epilepsy have a high rate of psychiatric comorbidity.

### Methods

This cross-sectional study was done in the tertiary clinics of Tabriz University of Medical Sciences, Tabriz, Iran, and the procedure was approved by the review board prior to implementation of the study. The regional ethical committee also approved the procedure and a comprehensive explanation of the aim of the study was given to the parents or caregivers of the participants and all gave written consent. Children of parents who refused to participate received the standard care. The results of the psychiatric evaluation were provided to the parents along with education on the detected disorder and the available treatments.

All the children (aged between 6 and 18) with the diagnosis of epilepsy, regardless of the seizure type, were enrolled in the study over a period of one year (September 2013 to September 2014). The diagnosis of epilepsy in children was established by a board certified child neurologist. Patients with serious sensory impairment (uncorrectable with a sensory substitution aid,  $n = 2$ ), intellectual disability ( $IQ < 70$ ,  $n = 5$ ) or confirmed complicated syndromic diagnosis (e.g. Down's syndrome, cerebral palsy,  $n = 4$ ) were excluded.

The diagnosis of epilepsy was made after obtaining an inclusive history, a thorough physical examination, evaluation of blood chemicals, neuro-imaging and electroencephalography. Patients and their caregivers were both referred to a child and adolescent psychiatrist for further clinical evaluation. Children were interviewed as soon as the diagnosis of epilepsy was established, regardless of their degree of seizure control. An anti-epileptic medication was initiated following the psychiatric interview.

Established psychiatric disorders in parents were derived from their medical

records. Academic failure of children was defined as a significant drop in scores, lasting for at least two semesters.

A semi-structured psychiatric interview with both parents and child was conducted using the Farsi (Persian) version of the Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version (K-SADS-PL)<sup>23</sup> for detecting psychiatric conditions in children. The K-SADS-PL is based on criteria defined by the Diagnostic and Statistical Manual for Mental disorders, 4<sup>th</sup>-edition (DSM-IV). Psychiatric diagnosis was made for each participant if she/he fulfilled the diagnostic criteria at any time.

The sample size was estimated to be 256 according to Cochran's rule for sampling and considering the Z value = 1.96 (for 95% confidence level) and 0.5 as the estimated percentage. Allowing for 5% dropouts, 270 patients were required as a minimum. The prevalence of behavioral and emotional problems fulfilling the criteria for lifetime diagnosis was measured. Patients with more than one psychiatric diagnosis were considered in comparison for each of the diagnoses.

The SPSS for Windows (version 17, SPSS Inc., Chicago, IL, USA) was used for the analysis. Data are given in mean (standard deviation) or number (percentage, giving the frequency), where appropriate. The normality of distribution of scores was tested by the Q-Q plots and Kolmogorov-Smirnov test. An independent-sample t-test was used to compare the mean age of the samples. A chi-square test was used to test the differences between groups with categorical variables (place of residence, history of epilepsy in parents or siblings, academic failure, age category, family history of psychiatric disorder and psychiatric hospitalization). Logistic and linear regression analyses were then performed for binary and continuous dependent variables (as described above), respectively, to identify variables with a predictive value for having a psychiatric comorbidity. For all the statistical tests, differences and correlations were considered to be statistically significant at  $P < 0.05$ .

## Results

From a total of 298 participants, 270 (90.6%) completed the process, including 120 (44.4%) girls and 150 (55.6%) boys. Their mean age was  $11.4 \pm 3.6$  years. Most of children were from the urban area (60.4%). Established epilepsy was positive in 15.2% of mothers, 13.3% of fathers and 23.7% of siblings. At least one psychiatric disorder was already established in 45.6% of mothers, 38.6% of fathers and 45.6% of siblings. Mean age of mothers and fathers was  $37.8 \pm 8.3$  and  $42.0 \pm 8.4$  years, respectively.

**Epilepsy:** Types of seizure (frequencies) were as follows: generalized tonic-clonic (50.4%), complex-partial (14.1%), generalized atonic (11.9%), generalized tonic (4.1%), unilateral clonic (2.2%), simple partial (11.9%), absent (1.9%), unilateral tonic (1.1%) and myoclonic seizure (0.7%). The mean duration of symptoms was  $5.7 \pm 4.6$  months. More than half (65.6%) had been admitted to hospital for evaluations.

**Psychiatric comorbidity:** At least one psychiatric disorder was diagnosed in 222 (82.2%) patients. As described in table 1, the most prevalent psychiatric disorders in children and adolescents with epilepsy were ADHD (34.4%), major depressive disorder (MDD) (29.6%), social phobia (14.8%) and oppositional defiant disorder (ODD) (13.7%).

**Characteristics of patients with psychiatric comorbidity:** There were a few differences observed between girls and boys. Agoraphobia and anorexia nervosa were significantly more prevalent among the girls compared with the boys with epilepsy (Table 1). The difference in prevalence of other disorders was not significant. Results are described in table 1.

Children with enuresis were younger than children without. In contrast, the mean age of children with MDD, psychotic disorder, post-traumatic stress disorder (PTSD), bipolar mood disorder (BMD), obsessive compulsive disorder (OCD), panic disorder, social phobia, generalized anxiety disorder (GAD), chronic motor tic disorder, conduct disorder and substance related disorder was higher than children without these diagnoses. Results are described in table 2.

**Table 1.** Prevalence of psychiatric disorders in children and adolescents with epilepsy: gender difference

Psychiatric disorders	Total (n = 270)	Girls (n = 120)	Boys (n = 150)	$\chi^2$	P*
Mood disorders [n (%)]					
MDD	80 (29.6)	43 (35.8)	37 (24.7)	3.98	0.060
BMD	4 (1.5)	1 (0.8)	3 (2.0)	0.62	0.630
Psychotic disorders [n (%)]	13 (4.8)	4 (3.3)	9 (6.0)	1.03	0.390
Anxiety disorders [n (%)]					
Panic disorder	12 (4.4)	6 (5.0)	6 (4.0)	0.15	0.770
Separation anxiety	31 (11.5)	18 (15.0)	13 (8.7)	2.63	0.120
Social phobia	40 (14.8)	20 (16.7)	20 (13.3)	0.58	0.490
Agoraphobia	28 (10.4)	20 (16.7)	8 (5.3)	9.21	0.004
PTSD	23 (8.5)	12 (10.0)	11 (7.3)	0.60	0.510
GAD	26 (9.6)	15 (12.5)	11 (7.3)	2.04	0.210
OCD	10 (3.7)	6 (5.0)	4 (2.7)	1.01	0.340
Disorders beginning during childhood [n (%)]					
ADHD	93 (34.4)	35 (29.2)	58 (38.7)	2.66	0.120
Enuresis	4 (1.5)	1 (0.8)	3 (2.0)	0.62	0.630
Nocturnal enuresis	13 (4.8)	5 (4.2)	8 (5.3)	0.19	0.770
ODD	37 (13.7)	13 (10.8)	24 (16.0)	1.50	0.280
Conduct disorder	19 (7.0)	7 (5.8)	12 (8.0)	0.47	0.630
Chronic motor tic disorder	27 (10.0)	9 (7.5)	18 (12.0)	1.50	0.300
Chronic vocal tic disorder	19 (7.0)	8 (6.7)	11 (7.3)	0.04	> 0.999
Eating disorders [n (%)]					
Anorexia nervosa	4 (1.5)	4 (3.3)	0 (0)	5.07	0.030
Bulimia nervosa	4 (1.5)	3 (2.5)	1 (0.7)	1.53	0.320
Substance related disorders [n (%)]					
Nicotine	7 (2.6)	1 (0.1)	6 (4.0)	2.64	0.130
Alcohol	2 (0.7)	0 (0.0)	2 (1.3)	1.61	0.500
Amphetamine	2 (0.7)	0 (0.0)	2 (1.3)	1.61	0.500
Sedative-hypnotic	2 (0.7)	1 (0.1)	1 (0.7)	0.02	> 0.999
Cannabis	0 (0)	0 (0)	0 (0)	-	-

ADHD: Attention deficit/hyperactive disorder; ODD: Oppositional defiant disorder; MDD: Bipolar mood disorder; MDD: Major depressive disorder; OCD: Obsessive compulsive disorder; GAD: Generalized anxiety disorder; PTSD: Post-traumatic stress disorder

\*The alpha level of significance was set to 0.05 in all comparisons

In another view, children were divided into two age groups:  $\leq 12$  and 13- to 18-years old. The following disorders were more prevalent in children aged between 13-18: MDD (47.5%), psychotic disorder (2.5%), social phobia (23.7%), GAD (15.3%), conduct disorder (13.6%), chronic motor tic disorder (13.6%) and substance related disorders. Separation anxiety (15.1%) and enuresis (7.2%), on the other hand, were more prevalent among children younger than 12.

A chi-square test showed that having a comorbid psychiatric disorder was not related to the location of the residence of the children (rural vs. urban) or positive history of epilepsy in the parents or siblings (non-significant findings). A history of

academic failure ( $P < 0.001$ ), older age ( $P < 0.001$ ), history of a psychiatric disorder in siblings or parents (each  $P < 0.001$ ) and history of psychiatric hospitalization ( $P = 0.001$ ) were associated with the higher number of cases of psychiatric comorbidity.

As scores were normally distributed, suitable predictors were selected from the variables for inclusion in the regression models after a series of univariate analyses. A logistic regression model showed that among the factors mentioned above, psychiatric disorder in the mother ( $P = 0.004$ ), father ( $P = 0.042$ ) or siblings ( $P = 0.001$ ) could independently predict at least one psychiatric comorbidity in children with epilepsy. Results are described in table 3.

**Table 2.** Mean age and standard deviation (SD) of children and adolescents with epilepsy regarding the comorbid psychiatric disorder

Psychiatric disorders	With psychiatric comorbidity	Without psychiatric comorbidity	P*
Mood disorders (mean ± SD)			
MDD	13.6 ± 3.2	10.5 ± 3.4	< 0.005
BMD	15.8 ± 2.5	11.3 ± 3.6	0.015
Psychotic disorders (mean ± SD)	15.1 ± 2.6	11.2 ± 3.6	< 0.005
Anxiety disorders (mean ± SD)			
Panic disorder	14.2 ± 2.4	11.2 ± 3.6	0.006
Separation anxiety	10.9 ± 3.7	11.4 ± 3.6	0.415
Social phobia	13.4 ± 3.3	11.0 ± 3.6	< 0.005
Agoraphobia	12.1 ± 3.2	11.3 ± 3.7	0.253
PTSD	13.1 ± 3.3	11.2 ± 3.6	0.020
GAD	13.7 ± 2.9	11.1 ± 3.6	0.001
OCD	14.3 ± 3.6	11.3 ± 3.6	0.009
Disorders beginning during childhood (mean ± SD)			
ADHD	11.7 ± 3.5	11.2 ± 3.7	0.361
Enuresis	7.1 ± 0.7	11.4 ± 3.6	0.019
Nocturnal enuresis	9.3 ± 2.8	11.5 ± 3.7	0.031
ODD	11.5 ± 3.8	11.4 ± 3.6	0.908
Conduct disorder	14.1 ± 3.1	11.2 ± 3.6	0.001
Chronic motor tic disorder	13.3 ± 3.7	11.2 ± 3.6	0.004
Chronic vocal tic disorder	12.3 ± 3.7	11.3 ± 3.6	0.242
Eating disorders (mean ± SD)			
Anorexia nervosa	13.5 ± 4.3	11.4 ± 3.6	0.239
Bulimia nervosa	14.0 ± 4.7	11.3 ± 3.6	0.150
Substance related disorders (mean ± SD)			
Nicotine	15.9 ± 1.6	11.3 ± 3.6	0.001
Alcohol	17.1 ± 0.0	11.3 ± 3.6	0.028
Amphetamine	16.6 ± 0.8	11.3 ± 3.6	0.045
Sedative-hypnotic	16.5 ± 0.7	11.3 ± 3.6	0.046
Cannabis	-	-	-

ADHD: Attention deficit/hyperactive disorder; ODD: Oppositional defiant disorder; BMD: Bipolar mood disorder; MDD: Major depressive disorder; OCD: Obsessive compulsive disorder; GAD: Generalized anxiety disorder; PTSD: Post-traumatic stress disorder

\*The alpha level of significance was set to 0.05 in all comparisons

The lifetime prevalence of any psychiatric disorder was 100% in patients with complex partial seizure, 87.5% in simple partial seizure, 81.3% in generalized atonic, 80.0% in absence

and 75.6% in patients with generalized tonic-clonic seizure. This rate was significantly higher in children with complex partial seizure ( $\chi^2= 12.72$ ,  $P = 0.042$ ).

**Table 3.** Impact of child and family characteristics on having at least one psychiatric comorbidity in children and adolescents with epilepsy

Child and family characteristics	OD (95% CI)	P*
Male gender	0.543 (0.194-1.515)	0.243
Age	1.184 (0.603-2.325)	0.616
Academic failure	2.144 (0.735-6.256)	0.163
Place of residence	1.417 (0.435-4.426)	0.549
Educational level of father	0.723 (0.411-2.269)	0.258
Educational level of mother	1.210 (0.709-2.065)	0.484
Psychiatric disorder in father	4.417 (1.053-18.538)	0.042
Psychiatric disorder in mother	20.596 (2.559-165.801)	0.004
Psychiatric disorder in siblings	8.149 (2.382-27.875)	0.001
Epilepsy in father	0.775 (0.163-3.682)	0.748
Epilepsy in mother	1.726 (0.372-8.008)	0.486
Epilepsy in siblings	0.613 (0.208-1.808)	0.375

OD: Odds ratio; CI: Confidence interval

\*The level of significance was set to 0.05 in all comparisons

However, no difference was observed between the types of seizure with respect to a six-month prevalence of any psychiatric disorder.

### Discussion

This study evaluated a large sample of Iranian children and adolescents with epilepsy and showed that 82.2% of these patients had received at least one psychiatric diagnosis, in which ADHD, MDD, social phobia and ODD were the most prevalent. A positive family history for a psychiatric disorder (in parents or siblings) could independently predict a psychiatric comorbidity in children with epilepsy. These findings indicate the vital need for clinical intervention.

Despite the broad physical and psychosocial impacts of childhood-onset epilepsy, little is known regarding the psychiatric conditions of Iranian children with epilepsy. A well-designed study has recently estimated psychiatric disorders in general population of children.<sup>21</sup> According to our results, the prevalence of almost all psychiatric disorders was higher in youth with childhood-onset epilepsy compared with results of this study. Previously, the overall prevalence of any psychiatric disorders in Iranian children (6-11 years old) was reported 17.9%, using the same method of interview as we employed in our study.<sup>24</sup> This population-based study have also reported a prevalence of 4.5% for MDD, 1.8% for BMD, 0.6% for psychosis, 0.6% for panic disorder, 5.9% for separation anxiety, 0.3% for substance related disorders, 7.3% for ODD, 8.6% for ADHD and 1.1% for PTSD,<sup>24</sup> which were lower than our study. However, age and gender distributions of these comorbid conditions are comparable to children without epilepsy. For example, enuresis was found to be more common in younger children, while MDD was more common in the older age group of children, and anorexia nervosa was more common among the girls. So there was no remarkable difference with our normal population (except for the higher rate), and raising

awareness and attracting more attention will result in a better diagnosis of children who need psychiatric interventions. Moreover, the high rate of psychiatric disorders in children with epilepsy has clinical and research significance. This well-known pattern may be explained by the shared pathophysiological mechanisms, genetic, psychosocial and iatrogenic factors.<sup>11,16</sup>

Similar studies from other populations have reported a wide range of results.<sup>6,11,16</sup> Most of these studies differ in terms of sampling and method of diagnosing the psychiatric comorbidity. Lower prevalence of MDD (8.3%, but not bipolar depression that is 1.8%) and anxiety disorders (3.6%), as well as externalizing disorders (20.9%) was reported from a study evaluating patients with childhood onset epilepsy,<sup>6</sup> but another study evaluating children with new onset epilepsy reported similar results to our study regarding MDD, anxiety disorders and externalizing disorders (22.6%, 26.4% and 32.5%, respectively).<sup>24</sup> A population based study reported prevalence of depressive disorders screened by a rating scale to be 36.5%.<sup>25</sup> Regardless of the reason for the difference in the reported numbers, all of the studies agree that young people with epilepsy are at serious risk of being affected by psychiatric disorders. Early detection of psychiatric comorbidity prevents their symptoms to be confused with the adverse effect of medications. Depression calls for special consideration as it appears to be the most common psychiatric comorbidity reported by all the studies. Depression can significantly decrease the treatment adherence.<sup>23</sup> Researchers agree that early identification and treatment of depression by effective multimodal treatment approaches is an important clinical task.<sup>22</sup>

As described before, studies about psychiatric comorbidities in Iranian patients with epilepsy are limited to adult population. In a population-based study on patients aged over 15, the prevalence of comorbid psychiatric condition was more than 50.0%,<sup>3</sup> that is higher than general population.

However, the present study showed a higher rate in children with epilepsy. Remission of psychiatric disorders like ADHD, separation anxiety, enuresis or conduct disorder may explain this difference to some extent. Moreover, personality disorders and substance related disorders are not reported by the described study on adults.<sup>3</sup> An increasing stigma toward epilepsy should also be considered as a possibility that might increase the perceived stress by children.

Another important finding from the current study is that psychiatric problems among the family members (either parents or siblings) could predict psychiatric comorbidity. A review of the literature relating to similar articles<sup>4,6</sup> indicates that factors concerning the psychopathology in other family members and the parent-child relationships have a stronger influence on the children's psychopathology than the factors related to epilepsy themselves. Whereas most of the emotional problems in family members arise subsequent to epilepsy, low quality of the parent-child relationship, depression in mothers, and problems with family functioning have been proposed as important family factors.<sup>25</sup> As a result of the study design, we did not include epilepsy related factors (frequency of seizure, seizure control) in the analysis. However, these results still highlight that treatment of the psychiatric problems and psychological maladjustments within the family should be followed independently.

Complex partial seizure was found to be associated with a higher rate of psychiatric comorbidity compared with other types of epilepsy in the present study sample. A disparity between the different types of epilepsy had been noticed in prior reports indicating that some kinds of epilepsy (e.g., typical absence epilepsy) often have poorer psychosocial outcomes.<sup>26</sup> Further research especially in population-based scales is recommended to address these characteristics to answer whether this difference is related to the nature of epilepsy or influenced by the psychosocial consequences. However, our

findings indicate that children with epilepsy should be screened and treated for psychiatric problems, regardless of type of epilepsy.

This study had some limitations. This study was not population-based but gathered all the patients from university clinics and considering the large number of cases, a rational picture of the condition was probably given. Majority of the children and adolescents with epilepsy refer to university clinics in this region. Other clinics might visit milder cases, which may bias the result. So the fact that this is a tertiary care sample may also skew findings. Medical history of the family members was obtained from the participants by interview. Medical records were not available for all of them at the time of interview. This process could only reveal established conditions and limits the results. In addition, the reported correlations were not made with seizure severity, localization, number of medications, or other seizure related characteristics. Despite these limitations, the current study highlights the need for additional attention to psychiatric comorbidities in these children, as well as the need for future research directed toward preventing and limiting the comorbidities associated with epilepsy and their treatment.

Both epilepsy and psychiatric disorders still carry a stigma in Iranian culture. While the general knowledge and attitudes towards epilepsy seem to be improved in most of its aspects,<sup>27</sup> patients with epilepsy still percept a high level of stigma.<sup>28</sup> This perceived stigma have established effects on both child and their parents and should be addressed early in the process of diagnosis. The current treatment plans need to include strategies for reducing self-perception of stigma and more effort should be given to education as an essential part. The perceived stigma was not measured in this study. However according to the high prevalence of psychiatric comorbidities in this sample of patients, we believe this should be a target of further studies.

### **Conclusion**

In conclusion, children with epilepsy face a

high burden of psychiatric and behavioral comorbidities, beyond seizures. If ignored and left untreated, these comorbid conditions can potentially affect their socioeconomic status as adults, as well as their employment, educational achievement and quality of life. Comprehensive care for these patients must include recognition and an effective treatment of these chronic comorbid conditions.

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#### Authors' Contribution

Shahrokh Amiri developed the original idea and the protocol and performed diagnostic evaluation and wrote the manuscript. Meygol Taghibeigi and Mehran Aghamohammadpour contributed to developing the protocol and neurologic diagnostic evaluations. Seyed Gholamreza Noorazar substantially contributed to conception and performed the

psychiatric diagnostic evaluations. Sara Farhang participated in design of the study, and abstracted and analyzed data. All authors approved the final manuscript.

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#### Conflict of Interest

Authors have no conflict of interest.

#### Ethical Approval

The regional medical ethics committee of Tabriz University of Medical Sciences approved the procedure and a comprehensive explanation of the aim of the study was given to the parents or caregivers of the participants and all gave written consent.

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