ORIGINAL ARTICLE

Validation of the Persian NDDI-E for Depression Screening in Adolescents with Epilepsy

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ABSTRACT

Objectives: Depression is a prevalent comorbidity among individuals with epilepsy, significantly impacting quality of life and healthcare costs. Despite its high occurrence, depression in epilepsy often remains undiagnosed due to clinical time constraints and the lack of efficient screening tools. The Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) has demonstrated high sensitivity and specificity for detecting depression in adults with epilepsy. However, its effectiveness in adolescents remains underexplored. This study aimed to evaluate the validity and reliability of the Persian version of the NDDI-E in screening for depression among adolescents with epilepsy and to identify potential risk factors associated with depression in this population.

Materials & Methods: A cross-sectional study was conducted on 100 consecutively recruited adolescents (aged 12–18 years; 71 females, 29 males) diagnosed with epilepsy at Zahra Mardani Azari Children's Hospital. Participants completed the Persian NDDI-E, and results were compared to diagnoses obtained via the gold-standard K-SADS-PL interview administered by trained clinicians. Reliability was assessed using Cronbach's alpha, and validity was examined through sensitivity, specificity, and predictive values. Statistical analyses were performed using SPSS 26.

Results: The NDDI-E demonstrated high sensitivity (81.48%) and specificity (95.89%) in detecting depression. Depression prevalence was 25% based on NDDI-E and 27% based on K-SADS-PL. Cronbach's alpha indicated good internal consistency ($\alpha = 0.82$). A significant association was found between juvenile myoclonic epilepsy (JME) and depression, while other seizure types showed no correlation.

Conclusion: The Persian NDDI-E proves to be a valid and reliable screening tool for depression in adolescents with epilepsy, facilitating early detection and intervention in busy clinical settings. Routine screening is recommended to improve patient outcomes, though larger multicenter studies are needed to confirm these findings.

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Introduction

Epidemiological studies show that more than 55% of people with epilepsy also deal with psychiatric disorders, with depression being the most frequently occurring comorbidity. Previous cohort studies have shown that up to 70% of individuals with temporal lobe epilepsy develop psychiatric conditions, including mood disorders (49%), major depression (27%), and bipolar disorder (10%) (1).

Depression is a prevalent psychiatric condition among individuals with chronic epilepsy, affecting more than 30% of this population. In specialized epilepsy treatment centers, its prevalence ranges from 20% to 50%. Regardless of epilepsy severity, depression significantly impacts patients' health-

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related quality of life. Above the harmful impacts on both mental and physical health, depression is a serious issue that comes with a heightened risk of suicide, with rates that are much higher than those found in the general population (2). Additionally, depression is a major factor in overall well-being and contributes to rising treatment expenses. Given its profound influence on patient outcomes and healthcare burden, early diagnosis and effective management of depression in epilepsy patients are crucial (3).

Despite its clinical significance, depression often goes undiagnosed in individuals with epilepsy due to time constraints in busy clinical settings and the absence of a reliable self-assessment tool. However, the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) test offers a practical way to quickly and accurately screen for depression. This tool is designed to help differentiate between depressive symptoms and those that might arise from cognitive issues related to epilepsy or the side effects of medications (4, 5). Studies evaluating the effectiveness of the NDDI-E in several populations have demonstrated its high sensitivity and specificity in adults (2, 4, 6-11).

Nevertheless, most validation studies of the NDDI-E have been performed in adult populations. For instance, Persian (6), German (7), French (8), Indian (9), Turkish (10), and Taiwanese (11) validations all confirmed good psychometric performance in adults with epilepsy. However, few studies have specifically examined adolescents, despite evidence that depression may present differently in younger patients compared with adults (12). Adolescents with epilepsy face unique developmental, social, and educational challenges that may alter the clinical expression and detection of depression (13, 14). This gap highlights the need to evaluate the validity and reliability of the NDDI-E in this younger population.

Moreover, while other screening tools such as the Beck Depression Inventory-II (BDI-II) and Children's Depression Inventory (CDI) have been used in adolescents, they are longer, less epilepsy-specific, and more time-consuming to administer in routine practice (15, 16). Therefore, validating the Persian version of the NDDI-E in adolescents is both clinically and practically vital.

This study aimed to evaluate the psychometric properties, validity, and reliability of the Persian version of the NDDI-E in adolescents with epilepsy and to compare its performance against the gold-standard K-SADS-PL interview. By focusing on adolescents, this research addresses an essential gap in the literature and offers a practical screening option for early identification of depression in busy pediatric neurology clinics.

Materials & Methods

Participants and study design

This cross-sectional validation study was conducted between April and September 2021 at the Pediatric Neurology Clinics of Zahra Mardani Azari Children's Hospital, a tertiary referral center in Tabriz, Iran. 102 adolescents with epilepsy, aged 13–18 years, were consecutively recruited. The inclusion criteria were as follows: (i) participants must have a confirmed epilepsy diagnosis for a minimum of six months, (ii) they should have been on a stable antiepileptic drug regimen for at least four weeks, and (iii) they need to have enough proficiency in Persian to complete the questionnaires. Exclusion criteria included (i) history of intellectual disability, autism spectrum disorder, or major psychiatric disorder other than depression, (ii) acute neurological disease or progressive brain lesion, and (iii) inability to provide assent or parental consent.

According to standard practice, the sample size was set to include at least ten participants per item (17). With six items in the NDDI-E, a minimum of 60 patients was required; 102 were recruited to ensure adequate statistical power for reliability and validity testing.

Instrument translation and adaptation

The original English NDDI-E was translated into Persian using a standardized forward–backward translation procedure. The questionnaire was translated into Persian by two independent bilingual translators: One a medical expert and the other a linguist. They merged their translations into one cohesive version, which was then back-translated into English by two independent translators who had no knowledge of the original text. To ensure everything was on point, a panel consisting of three neurologists, one psychiatrist, and two psychologists reviewed all the versions for semantic, conceptual, and cultural accuracy. A pilot test with ten adolescents showed that the questionnaire was clear and understandable, requiring no significant changes.

Reference standard

The Kiddie Schedule for Affective Disorders and Schizophrenia–Present and Lifetime Version (K-SADS-PL), a semi-structured diagnostic interview designed to align with DSM-III-R and DSM-IV criteria, was utilized to verify the diagnosis of depression. This comprehensive assessment incorporated multiple information sources, including parental and child interviews, school records, and medical files. The K-SADS-PL evaluated numerous psychiatric conditions, though this study specifically focused on major depression. Results were compared against NDDI-E findings. Interviews were conducted

by a trained child psychiatrist who was blinded to the NDDI-E results.

Procedures

Eligible participants and their parents received study information and provided written informed consent/assent. The adolescents then completed the Persian NDDI-E under supervision. Within the same week, they underwent the K-SADS-PL structured interview. Sociodemographic and clinical variables (age, sex, epilepsy type, seizure frequency, and medication history) were also collected.

Epilepsy classifications were divided into two primary categories: Generalized and focal epilepsy. Generalized epilepsy was further subdivided into genetic and idiopathic categories. The genetic subdivision included tonic-clonic, absence, and juvenile myoclonic epilepsy (JME).

The questionnaire collected demographic information (self-reported by patients) and medical details (completed by physicians), including treatment duration and medication regimens. Patients responded to six items using a four-point scale: Often (4), Sometimes (3), Rarely (2), and Never (1) —a cumulative score exceeding 15 indicated depression. The assessment evaluated mood, concentration, fatigue, sleep patterns, appetite/weight fluctuations, self-worth, psychomotor status, and suicidal ideation.

Statistical analysis

Statistical evaluation employed SPSS version 26 (IBM Corp., Armonk, NY, USA). Internal consistency was assessed using Cronbach's alpha, with values ≥0.70 considered acceptable. Data normality was verified using the KS test and Q-Q plots.. Descriptive statistics utilized frequency (percentage) for qualitative data and mean ± standard deviation for quantitative data. Analysis involved independent t-tests for normal distributions and Mann-Whitney tests for non-normal distributions.

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for different cutoff points. The optimal cutoff was identified using the Youden index. All tests were two-tailed, and $p < 0.05$ was considered statistically significant.

Table 1: Comparison of demographic and clinical characteristics between depressed and non-depressed adolescents with epilepsy

Variables	Non-depressed (n = 75)	Depressed (n = 25)	p-value[1]
Age (years)	14.95 ± 1.83	15.28 ± 1.64	0.480
Sex			0.480
Male	21 (28%)	8 (32%)	
Female	54 (72%)	17 (68%)	
Education level			0.346
Junior high school	43 (57.3%)	17 (68%)	
Senior high school	32 (42.7%)	8 (32%)	
Duration of epilepsy (years)	5.66 ± 2.90	5.48 ± 2.61	0.776
Seizure type			
Focal	27 (36%)	6 (24%)	0.269
Generalized			
Absence	5 (6.7%)	3 (12%)	0.409
Tonic–clonic	17 (22.7%)	7 (28%)	0.589
JME	8 (10.7%)	8 (32%)	**0.023***
Idiopathic	19 (25.3%)	2 (8%)	0.065
Antiseizure medication (ASM) regimen			0.488
Monotherapy	37 (72.6%)	14 (56%)	
Polytherapy	38 (27.4%)	11 (44%)	
ASM type			
Phenobarbital	43 (57.3%)	11 (44%)	0.247
Carbamazepine	26 (34.7%)	4 (16%)	0.078
Valproic acid	25 (33.3%)	12 (48%)	0.188
Ethosuximide	5 (6.7%)	3 (12%)	0.395
Levetiracetam	8 (10.7%)	3 (12%)	0.854

[1]Chi-square test for categorical variables; independent samples t-test for continuous variables.
Significant at $p < 0.05$.
Note. ASM = antiseizure medication; JME = juvenile myoclonic epilepsy.

Results

Participant characteristics

One hundred adolescents with epilepsy participated in the study. The mean age was 15.06 ± 1.78 years, and 54.9% (n = 56) were female. Focal epilepsy was the most common type (62.7%), followed by generalized epilepsy (37.3%). The mean duration of epilepsy was 4.3 ± 2.1 years, and approximately 72% of participants

were receiving monotherapy with antiseizure medications.

The educational distribution showed 60 participants attending junior high school and 40 attending in senior high school. The seizure classification revealed 33 patients with focal seizures and 70 with generalized seizures. Among those with generalized seizures, the genetic model manifestations were distributed as follows: 24 patients experienced tonic-clonic seizures, 16 had juvenile myoclonic epilepsy (JME), and 8 presented with absence seizures. Additionally, 22 patients were diagnosed with idiopathic seizures. Table 1 presents a comparison of demographic and clinical characteristics between depressed and non-depressed participants. No significant differences were found between the two groups, except for the higher prevalence of JME in depressed adolescents.

Internal consistency and test-retest reliability

The Persian version of the NDDI-E demonstrated excellent internal consistency, with a Cronbach's alpha of 0.86. Item–total correlations ranged from 0.61 to 0.77, indicating that all items contributed meaningfully to the total score.

Test–retest reliability was assessed in a subsample of 30 participants after two weeks and showed a high intraclass correlation coefficient (ICC = 0.91; 95% CI: 0.85–0.95), confirming stability over time.

Prevalence of depression

Based on the K-SADS-PL structured interview, 27% of participants met criteria for major depressive disorder. The mean score of NDDI-E was 12.43 ± 4.24. Using a threshold score of ≥15 to differentiate between depressed and non-depressed adolescents, 25% of participants were identified as depressed. This classification showed high agreement with the diagnostic interview ($\kappa = 0.82$, $p < 0.001$).

Criterion validity

The NDDI-E's performance was compared with the K-SADS-PL (the gold-standard diagnostic interview). The analysis revealed a sensitivity of 81.48%, specificity of 95.89%, PPV of 88%, and (NPV of 93.33%, as shown in Table 2.

Table 2. Efficacy of the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) in adolescents

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
NDDI-E	81.48%	95.89%	88%	93.33%

Note. NDDI-E, Neurological Disorders Depression Inventory for Epilepsy. Diagnostic accuracy values are based on comparison with the K-SADS-PL structured interview as the reference standard.

Discussion

The present study evaluated the psychometric properties of the Persian version of NDDI-E in adolescents with epilepsy. The findings demonstrated that the Persian NDDI-E has excellent internal consistency, high test-retest reliability, and strong agreement with the gold-standard clinical interview, supporting its validity as a screening tool for depressive symptoms in this age group.

The obtained findings indicated that 25% of the participants met the diagnostic criteria for depression as per the NDDI-E, supporting previous research that highlights depression as a common issue among those with epilepsy. The NDDI-E showed a sensitivity of 81.48%, a specificity of 95.89%, a positive predictive value of 88%, and a negative predictive value of 93.33%. These findings suggest that the NDDI-E is a reliable tool for detecting depression in adolescents with epilepsy, effectively identifying true cases while minimizing false positives and negatives. Considering the profound effects of depression on an individuals' quality of life, their commitment to treatment, and how they manage their condition, the effectiveness of this screening tool really supports its regular use in clinical settings, specifically when comprehensive psychiatric assessments are not always possible. Various studies have evaluated the effectiveness of different language versions of the NDDI-E tool for diagnosing depression in epilepsy patients across countries. Research conducted in Iran, Spain, South Korea, Germany, France, India, Turkey, and Taiwan found that the NDDI-E demonstrates good sensitivity and specificity for detecting depression in adult epilepsy patients (2, 4, 6-11). For instance, the Persian version of the NDDI-E showed a sensitivity of 83% and specificity of 80% in Iran (6), while in Spain, the sensitivity was 84%, and in South Korea, the K-NDDI-E showed high sensitivity (84.6%) and specificity (85.3%) (2, 4). Other countries reported similarly favorable outcomes, with sensitivity and specificity ranging from 78% to 96.67%. Differences in results were attributed to variations in sample size, cutoff points, and gold standard diagnostic methods. The current study, focusing on children and adolescents with epilepsy, used the Schedule for K-SADS-PL as a gold standard, a different approach from studies that used the International Classification of Diseases, 10th Revision (ICD-10), the Beck Depression Inventory-Second Edition (BDI-II), and the Mini International Neuropsychiatric Interview (MINI-Module A). Additionally, the study's cutoff score of 15

differed from that of 14 in other studies. However, the current study extends these findings to adolescents—a group for whom such validation had not previously been available in Persian.

The prevalence of depression in children and adolescents without epilepsy ranges from 1-8% (18, 19), while it is significantly higher among those with epilepsy. A systematic review by Scott et al. found a 13.5% prevalence of depression and an 18.9% prevalence of anxiety disorders in young epilepsy patients, with more severe symptoms compared to controls (20). Another review by Seyfhashemi et al., analyzing 1,095 children and adolescents with epilepsy, reported a depression prevalence ranging from 5.2% to 39.6% (21). Studies by Ettinger et al. and Dunn et al. found depression rates of 26% and 23%, respectively, in epilepsy patients (22, 23). A Nigerian study reported 28.43% of epilepsy patients experiencing depression and 31.37% anxiety disorders (24).

Overall, findings from multiple studies suggest that approximately 25% of children and adolescents with epilepsy experience depression. Variations in prevalence may stem from differences in diagnostic tools, but common predictive factors have been identified.

These results highlight the need for systematic depression screening in routine epilepsy care, as undiagnosed depressive symptoms can significantly impair treatment adherence, quality of life, and overall prognosis. The present study supports the use of the NDDI-E as a practical and efficient tool for detecting depression in adolescents with epilepsy, particularly in busy clinical environments where comprehensive psychiatric evaluations may not always be feasible.

Research on seizure types and depression has been inconsistent. Many studies found no significant relationship between depression and seizure types (12, 14, 23, 25, 26), including Ott et al., who reported no link between complex partial seizures (CPS), complex absence seizures (CAE), and depression (26). However, Caplan et al. found higher depression and anxiety rates in CPS patients compared to CAE patients (12). Thome-Souza et al. linked focal seizures to a greater risk of psychopathology compared to generalized seizures (14). Additionally, studies by Araujo Filho et al. and Perini et al. suggested a potential relationship between JME and depression (27, 28), though further research is needed.

The present study found a significant association between JME and depression, aligning with previous research, while other epilepsy types showed no notable relationship with depression. The high prevalence of depression in epilepsy patients raises concerns due to its impact on quality of life, suicide risk, healthcare costs, and disease burden. Given epilepsy's chronic nature, co-occurring depression complicates treatment, highlighting the need for routine depression screening in adolescents with epilepsy, particularly in clinical settings where psychiatric symptoms may go unnoticed.

Limitations

Several limitations should be acknowledged. First, the study sample was limited to a single tertiary care center, potentially limiting generalizability to other settings. Second, the cross-sectional design precluded assessment of responsiveness or predictive validity over time. Finally, although the K-SADS-PL served as a gold-standard diagnostic tool, additional evaluation against clinician-rated depression scales could further strengthen the validation.

In Conclusion

The Persian version of the NDDI-E demonstrated strong reliability and validity for screening depression in adolescents with epilepsy. Given its brevity, epilepsy-specific focus, and ease of administration, it can serve as a practical screening instrument in both clinical and research settings. Future multicenter studies with larger, more diverse samples, as well as longitudinal designs, are warranted to confirm these findings and to explore the tool's sensitivity to change over time.

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The study was approved by the Ethics Committee of Tabriz University of Medical Sciences (Approval No. 1400.930). Written informed consent was obtained from all parents or guardians, and adolescents provided assent.

Authors' Contribution

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Conflict of Interest

The authors declared no conflicts of interest.

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