Validation of the Indian version of Neurological Disorders Depression Inventory for Epilepsy (NDDI-E)

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ABSTRACT

Purpose: The Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) is an efficient tool for rapid detection of depression, an important comorbid condition in persons with epilepsy (PWE). Since social and cultural differences can potentially affect the cutoff score of NDDI-E, in this study, the reliability and validity of the Indian version of the NDDI-E in PWE was determined.

Method: After ethical clearance, 217 PWE above 18 years of age, on antiepileptic drugs (AEDs), attending neurology outpatient department (OPD) of All India Institute of Medical Sciences (AIIMS), New Delhi, India, were evaluated for depression using the NDDI-E (Indian version) and Mini International Neuropsychiatric Interview (MINI-Module A, version 6.0.0) as reference standard. Informed consent was taken before recruitment. Receiver operating characteristic (ROC) analysis and Cronbach's α, a measure of the internal consistency and reliability, were carried out to validate cutoff and questionnaire, respectively.

Results: Of the 217 PWE (112 males/105 females), mean age of 28.6 ± 9.4 years, with generalized (69.1%) or focal seizures (30.9%), 41.5% and 10.6% were diagnosed with depression using MINI and NDDI-E Indian version (at cutoff > 15), respectively. However, at a cutoff score of > 11, the Indian version of NDDI-E had a sensitivity of 96.67%, a specificity of 84.25%, a positive predictive value of 81.31%, and a negative predictive value of 97.27%. ROC analysis showed an area under the curve (AUC) of 0.9547 (confidence interval (CI) 95% = 0.929–0.979; standard error (SE): 0.0127). With the Indian version of NDDI-E, the Cronbach's α value was 0.877.

Conclusion: A periodic assessment of PWE using a quickly administrable and reliable tool for screening depression is highly desirable given the high incidence. In the Indian population with a cutoff of > 11, NDDI-E is a reliable and valid instrument to screen depression in PWE.

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1. Introduction

Persons with epilepsy (PWE) have an increased risk for cognitive, behavioral, and psychosocial disorders [1] particularly major depression, anxiety disorder, schizophrenia, and substance abuse [2]. Of these, depression is one of the most frequent comorbid conditions among PWE [3]. While the prevalence of depression in PWE ranges from 20% to 55% [4], prevalence of suicide in epilepsy is reported at 5–10%, and suicidal ideation is as high as 36.7% [2]. Epilepsy and depression are interlinked and lead to an increased risk of suicidal ideation and suicide. Researchers have reported a threefold increase in the diagnosis of depression and a fourfold increase in suicide rate among PWE compared with the general population [5]. The suicidality with epilepsy

(suicidal thoughts and attempts) accounts for >10% of deaths among PWE compared with 1.4% in general population [5,6].

In spite of high prevalence, issues related to depression and suicidality in PWE are inadequately addressed. This is probably due to paucity of time and limited resources. However, in view of the relationship between seizure control and depression [3,7], early identification and appropriate management of depression can potentially improve seizure control as well as epilepsy-related mortality and morbidity [8].

Worldwide, many different scales have been employed for detecting depression namely, Mini International Neuropsychiatric Interview (MINI), the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (SCID), the Composite International Diagnostic Interview (CIDI), and the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) [9]. Among these, NDDI-E has been developed and validated against gold standard tests like SCID and MINI as an epilepsy-specific screening tool [10,11]. However, in view

of social, cultural, and language differences across geographical locations, it has been felt that NDDI-E needs further region specific validation and though Gilliam et al. [10], in their original study, suggested a cutoff >15, the cutoff may need to be adjusted.

To the best of our knowledge, until date, NDDI-E has been validated in 13 languages: Arabic, Chinese, Danish, French, English, German, Greek, Italian, Japanese, Korean, Portuguese, Spanish, and Serbian [9, 12,13]. However, until date, no such validation study has been carried out in India. In this study, we validated the Indian version (Hindi translated) of the NDDI-E in PWE using MINI as reference standard.

2. Methods

2.1. Participants

After the Institute Ethics Committee approval of study protocol, case record form (CRF), and informed consent documents, PWE attending neurology outpatient department (OPD) at All India Institute of Medical Sciences (AIIMS), New Delhi, India were screened for eligibility as per the inclusion and exclusion criteria. The inclusion criteria were the following: age ≥18 years; and requiring treatment with one or more antiepileptic drugs (AEDs). Exclusion criteria were the following: PWE not willing to give written informed consent; and those with comorbid medical conditions, i.e., history of preexisting heart disease, diabetes, hypertension, alcohol/drug dependence, infectious blood diseases, mental retardation, dementia, and psychosis.

2.2. Experimental protocol

After providing written informed consent, patient details, treatment details, and lab parameters relevant to the study were recorded in the study-specific CRF. The screening tools were administered by a healthcare professional trained for the same, and the responses were recorded. Data analysis was carried out by an observer naive to study objective.

2.3. Neuropsychiatric evaluation

Screening tools used for the detection of depression in PWE were NDDI-E and MINI.

2.3.1. NDDI-E
The NDDI-E is a 6-item questionnaire developed by Frank G Gilliam. All items are scored from 1 (never) to 4 (always or often) (refer to Table 2) [10].

2.3.1.1. Translation of the NDDI-E. The original English version was translated into Hindi language by a professional interpreter at Hindi section, AIIMS, New Delhi, India, and the translated version was translated back into English by another professional interpreter. The translated version was validated by a third independent English and Hindi fluent individual. The questionnaire was piloted in 10 volunteers to identify any difference before administering to PWE.

2.3.1.2. Validation of the Indian version of NDDI-E. Different cutoffs were applied to screen PWE positive for depression, and receiver operating characteristics (ROC) were calculated in order to determine sensitivity and specificity of the Indian version of NDDI-E at different cutoff points. Cronbach's coefficient α was computed to measure the posttranslation internal consistency of the six items of NDDI-E.

2.3.2. MINI (version 6.0.0)
The MINI is an internationally validated structured interview used as gold standard for validation of depression screening tools [12,14]. Permission for use of the paper version of the MINI (version 6.0.0) was duly obtained.

2.3.3. Statistical analysis
Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) software, version 23. A significance level of $p < 0.05$ (two-tailed) was adopted. Descriptive statistics of the categorical (frequencies and percentage) and continuous variables (mean and standard deviation) were calculated. The sensitivity, specificity, positive and negative predictive values, likelihood ratio positive and negative, and area under the curve (AUC) for the ROC curve with its 95% confidence intervals (CIs) were calculated. Cronbach's coefficient α if an item is deleted, and corrected item–total correlation was computed to measure the internal consistency of the six items of NDDI-E.

3. Results

3.1. Clinical and demographic features

Two hundred and seventeen participants with epilepsy were enrolled in the study and underwent neuropsychiatric evaluation. The age of the participants ranged from 18 to 63 years, with a mean age of 28.6 ± 9.4 years. One hundred and fifty PWE (69.1%) had a diagnosis of generalized seizures, and 67 PWE (30.9%) had focal seizures. Among these PWE, 59% were on monotherapy, and the rest of the participants were on polytherapy. The most frequently used AEDs in monotherapy were levetiracetam (45.3%), valproate (21.9%), and carbamazepine (20.3%). Other AEDs being used were phenytoin (7%), clobazam (3.1%), clonazepam (0.8%), oxcarbazepine (0.8%), and lamotrigine (0.8%). While 55.8% of PWE (49.6% monotherapy, 50.4% polytherapy) had a seizure episode within the last 2 years, 44.2% (70.8% monotherapy, 29.2% polytherapy) were seizure-free ≥2 years (Table 1).

3.2. Neuropsychiatric evaluation

Participants had a psychiatric interview with a healthcare professional trained for the same and were evaluated using the MINI and NDDI-E to assess depressive symptoms and suicide risk. The Indian version of the NDDI-E was quickly administered, well received, and understood by all PWE. A variable percentage of PWE screened positive for depression using MINI and NDDI-E Indian version (at cutoff >15) 41.5% and 10.6%, respectively.

3.3. Determination of cutoff for NDDI-E

The frequency of responses of each item of the NDDI-E Indian version is given in Table 2. On applying different cutoffs from >10 to >15, the percent screened positive for depression ranged from 10.6% to 49.3% (Table 3).

3.4. Validation of cutoff for NDDI-E using MINI as reference standard

The ROC analysis revealed that at a cutoff score of >11, the Indian version of NDDI-E had a sensitivity of 96.67%, a specificity of 84.25%, positive and negative predictive values of 81.31% and 97.27%, respectively, and an AUC of 0.9547 (CI 95% = 0.929–0.979; standard error (SE): 0.0127) (Fig. 1, Table 4). The Cronbach's α value for the Indian

Table 1
Characteristics of the study sample.

No. of persons with epilepsy (PWE) enrolled		217
Males		112 (51.6%)
Females		105 (48.4%)
Median age (range in years)		26 (18–63)
Seizure type	Generalized seizures	150 (69.1%)
	Focal seizures	67 (30.9%)
Drug therapy	Monotherapy	128 (59%)
	Polytherapy	89 (41%)

Table 2

Indian version of NDDI-E, adapted from Gilliam et al. [10] and frequency response of each item of the NDDI-E.

Item	Always or Often हमेशा या अधिकांशत: (4)	Sometimes कभी-कभी (3)	Rarely मुश्किल से/ विरले ही (2)	Never कभी नहीं (1)
Everything is a struggle मुझे हर कार्य करने में कठिनाई होती है।	0	31 (14.3%)	130 (59.9%)	56 (25.8%)
Nothing I do is right जो कुछ भी मैं करता/करती हूं वह सही नहीं हो पाता है	2 (0.9%)	25 (11.5)	100 (46.1%)	90 (41.5%)
Feel guilty अपराध बोध का अनुभव होता है	5 (2.3%)	46 (21.2%)	52 (24%)	114 (52.5%)
I'd be better off dead मेरा मर जाना ही ठीक होता।	3 (1.4%)	7 (3.2%)	8 (3.7%)	199 (91.7%)
Frustrated क्या आप हताश महसूस करते हैं	3 (1.4%)	60 (27.6%)	73 (33.6%)	81 (37.3%)
Difficulty finding pleasure आनंद का अनुभव नहीं होता।	22 (10.1%)	81 (37.3%)	91 (41.9%)	23 (10.6%)

version of NDDI-E, a measure of internal consistency and reliability, was 0.877 and ranged from 0.834 to 0.894 after items were removed (Table 5). All NDDI-E items were significantly and positively associated with the total NDDI-E score, and none of them significantly increased α if it was deleted.
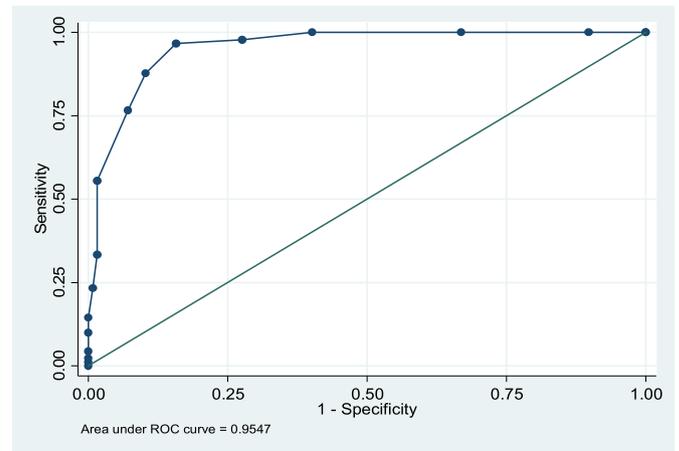
4. Discussion

Depression is a common comorbidity of epilepsy, significantly impacting health-related quality of life, it may also decrease treatment adherence and increase the risk of suicide. The diagnosis and treatment of depression in PWE often seems to be overlooked and has not been adequately addressed worldwide. In a Canadian study, 70% of PWE who had depression were not receiving treatment for it [15]. In different studies in PWE, the prevalence of depression has been reported from 20% to 55% [4,16,17]. This depression can potentially affect seizure control and quality of life in PWE, hence, the need for assessment and treatment.

A number of methods are available to detect depression or depressive symptoms, such as psychiatric or psychological assessments, structured or semistructured interviews, and self-report screening tools, which have been tried in PWE [12]. A good screening method for the diagnosis of major depressive episode must be practical and reliable, exhibiting an adequate balance between sensitivity and specificity to avoid false positive or negative results. A specificity of at least 75% is suggested as desirable for any tool [14,18]. It is important to use a recognized reference or gold standard (e.g., the SCID or the MINI) when assessing the diagnostic accuracy of other screening tools (e.g., the NDDI-E, Hamilton Depression Rating Scale (HAM-D), Patient Health Questionnaire-9 (PHQ9)).

The NDDI-E is a short, convenient, and reliable screening tool used specifically for PWE and is proposed to nullify the impact of AED side effects and common cognitive deficits in PWE, while screening for depression. Friedman et al. demonstrated a 10-fold increase in detection of

Fig. 1. Receiver operator characteristic curve of the Indian version of the NDDI-E.

depression in a seizure clinic after introduction of screening with NDDI-E [19,20].

It is, therefore, not surprising that NDDI-E is the most frequently used tool for depression in PWE. Since cultural differences in the expression of depression are important and well-recognized [21], a difference in social and cultural aspects may lead to over- or underestimation of the depression rate in population. The NDDI-E was originally designed in English, and now, it has been translated from English into Portuguese, Italian, Spanish, Japanese, German, Korean, Greek, Arabic, French, Chinese, and Danish for use [7,13,22–33], hence, the need for validation studies for different language versions of NDDI-E [9]. Apart from this, a score of more than 15 in NDDI-E was proposed to have a specificity of 90% and sensitivity of 81% for a diagnosis of major depression in the original work [10], but for the translated versions, varying cutoff points have been used [21]. For instance, cutoff in Korean version of NDDI-E is ≥11, Chinese version is ≥12, Danish version is ≥13 [13], Italian version is ≥13 [31], Serbian version is ≥14 [33], German version is ≥14 [7]. In most cases, it is lower than that of the original version, i.e., >15 [10].

The reason proposed for wide variation in the cutoff scores of NDDI-E is the language in different geographical areas and the cross-cultural differences, for example, in some cultures, grief or suffering is openly expressed while in other cultures, such emotions are concealed. Although NDDI-E has not been validated in India or in any Indian language [34], one study suggested cutoff of ≥14 to assess depression in PWE [35]. In the present study, using the original cutoff (>15), only 10.6% of PWE were screened positive for depression while with MINI, this percentage was 41.5%. This clearly suggests the need to validate the Indian version as well as the cutoff score of NDDI-E. It was found that the internal consistency and validity of the Indian version was well within the desired range as assessed by Cronbach's α values, but the cutoff of >15 proposed originally was found to be high for the Indian setup. It was seen that at a cutoff score of >11, the Indian version of NDDI-E had the sensitivity, specificity, positive predictive value, and negative predictive value in

Table 3

PWE with depression status as per MINI and NDDI-E at different cutoffs.

Scales		Depression (%)	Without depression (%)
MINI		90 (41.5)	127 (58.5)
NDDI-E	>10	107 (49.3)	110 (50.7)
	>11	92 (42.4)	125 (57.6)
	>12	78 (36)	139 (64)
	>13	52 (24)	165 (76)
	>14	32 (14.7)	185 (85.3)
	>15	23 (10.6)	194 (89.4)

Table 4

ROC and diagnostic efficiency statistics of the Indian version of the NDDI-E for the diagnosis of depression in PWE, based on the MINI.

Cut-point	Sensitivity	Specificity	PPV	NPV	AUC	CI 95%	SE
>10	97.78	72.44					
>11	**96.67**	**84.25**	**81.31**	**97.27**	**0.9547**	**0.929–0.979**	**0.0127**
>12	87.78	89.76					
>13	76.67	92.91					
>14	55.56	98.43					
>15	33.3	98.43					
>16	23.33	99.21					

AUC: area under curve; SE: standard error; PPV: positive predictive value; NPV: negative predictive value; SE: standard error; CI: confidence interval.

Table 5
Corrected item-total correlation and Cronbach's alpha if item deleted from the NDDI-E.

Item from NDDI-E	Corrected item-total correlation	Cronbach's alpha coefficient if item deleted
Everything is a struggle/मुझे हर कार्य करने में कठिनाई होती है।	0.676	0.858
Nothing I do is right/जो कुछ भी मैं करता/करती हूं वह सही नहीं हो पाता है	0.742	0.846
Feel guilty/अपराध बोध का अनुभव होता है	0.741	0.847
I'd be better off dead/मेरा मर जाना ही ठीक होता।	0.400	0.894
Frustrated/क्या आप हताश महसूस करते हैं	0.802	0.834
Difficulty finding pleasure/आनंद का अनुभव नहीं होता।	0.752	0.843

the acceptable range. Receiver operator characteristic analysis further validated this cutoff. This Indian version of the NDDI-E was quickly administered, well received, and understood by all PWE and can prove to be a reliable and valid instrument to screen depression in PWE.

4.1. Limitation of the study

Our study was performed in a tertiary care center in North India where majority is a Hindi-speaking population. It has to be kept in mind that this version, given the diverse linguistic character of India, may not be suitable for other parts like southern India.

5. Conclusion

Given the high prevalence of depression among PWE, routine and periodic screening of all PWE for early detection and appropriate management of depression is highly desirable. In this study, NDDI-E was found to be appropriate for use in PWE in Indian setup providing the cutoff point is > 11.

Disclosure

None of the authors have any conflict of interest to declare.

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