

# Non-Epileptic Attack Disorder, Psychiatric Co Morbidities and their Outcomes



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## Abstract

**Background:** NEAD is a common presentation in epilepsy clinics and is often misdiagnosed. This study was therefore planned to understand the prevalence of psychiatric co morbidities in patients diagnosed as NEAD and to study the outcome of both the conditions over 6 months with pharmacotherapy and supportive psychotherapy.

**Material & Method:** 71 patients of NEAD were enrolled and assessed on SCID 1 to diagnose psychiatric co morbidity with rating of severity of anxiety & depression on HDRS & HARS.

Patients were divided into Groups A & B depending on the presence or absence of existing co-morbid psychopathology respectively and were followed up over 6 months to assess outcomes. Psychiatric medication was given to Group A patients and both groups received supportive psychotherapy on follow up.

**Results:** Group A had 50 patients with psychiatric co morbidity and Group B included 21 patients. Depressive disorders were common psychopathology and follow up at 3& 6 months revealed a reduction in the total mean scores of HARS and HDRS from baseline. Outcome of NEAD at the end of 6 months revealed 100% reduction in 28% and 50% reduction in 15 – 16% of both group patients.

**Conclusions:** There are very few Indian studies on short or long term outcomes of NEAD and there is a need to create awareness among the treating physicians regarding the impact of associated psychiatric co morbidities which would affect the prognosis of NEAD.

**Key words:** Pseudoseizures, outcome, psychiatric comorbidity, NEAD

## Introduction

Research in epilepsy found a significant component of psychiatric co morbidities in patients especially diagnosed as having non-epileptic attack disorders (NEAD). As per DSM 5, “Functional Neurological Symptom Disorder” is the newer and broader term where

the features include neurological symptoms and signs affecting the motor or sensory function; that can't be explained by a neurological disease or any other medical condition. ICD 10 calls all these disorders as Dissociative disorders.<sup>1</sup>

These episodes of pseudo seizures or hysterical seizure, psychogenic seizure, non epileptic seizure or non-epileptic attack disorder (NEAD) pose diagnostic dilemmas and therapeutic uncertainties. NEAD may be defined as a sudden, disruptive change in a person's behavior, perception, thinking or feeling that is usually time limited and resembles or is mistaken for epilepsy but does not have the characteristic electrophysiological changes in the brain detectable by EEG that accompanies a true epileptic seizure.<sup>1</sup> It is frequently accompanied with co morbid psychopathology, especially depression, anxiety and somatoform disorders.<sup>2-7</sup> The prevalence of NEAD has been estimated to be greater than 10% of the epilepsy clinic population and accounts for 10-20% of tertiary referrals for refractory epilepsy.<sup>8-11</sup> Prevalence of NEAD was found to be 2.9 per 1000 population in a study in rural India<sup>9</sup> and is currently estimated as 2–50/100,000 in the general population.<sup>8</sup>

NEAD has been associated with lower socioeconomic status, lower education, rural background, lack of psychological sophistication and chaotic families.<sup>7</sup>

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However as countries develop, there may be a declining incidence seen in relation to time due to improved education and medical and psychological sophistication.<sup>12-13</sup> Treatment for NEAD includes pharmacological i.e. anti-anxiety and antidepressant therapy and psychological therapies like cognitive behavioral therapy (CBT), hypnotherapy and paradoxical therapy. However, evidence towards the efficacy of these various treatments has not been noted<sup>14</sup> and neither using CBT has caused any harm.<sup>15</sup>

There is a dearth in the Indian literature regarding NEAD, its co morbid psychopathologies and the outcomes of both the conditions as each may affect the prognosis of the other. This study was undertaken to understand the prevalence of psychiatric co morbidities in patients diagnosed as NEAD and to study the outcome of both the conditions over 6 months with pharmacotherapy and supportive psychotherapy.

### Methods & Materials

The study was conducted in the psychiatry department of a general municipal hospital after institutional ethics committee approval and written informed consent from the study participants from June 2004 to August 2005. The sample consisted of seventy-one patients. Those patients who were attending the epilepsy clinic of a tertiary general municipal hospital and were diagnosed by the neurologist as having NEAD with or without concomitant true seizures were then referred to the psychiatry outpatient department after video EEG monitoring which identified the current attacks to be non-epileptic (i.e. unaccompanied with any seizure like activity on the video EEG). The referred patients (n=89) were screened and only those who consented and satisfied the inclusion and exclusion criteria were recruited in the study. Patients in the age group 15-45 years, having no epileptiform activity on video EEG, manifesting any type of seizure semiology having mixed seizures (true and pseudo seizures) were included in the study. Two patients having pre-existing psychopathology with ongoing psychiatric treatment from private were excluded from the study. Patients with medical or surgical complications, history of cognitive decline and seizures due to sequelae of drugs / infective pathology (n=14) were excluded from the study. Three patients refused consent. The sample size thus consisted of 71 patients.

#### Tools:

##### Assessment of Psychiatric Morbidity

The Structured Clinical Interview (SCID I) for DSM IV classification proforma was used by both the investigators to collect data to diagnose psychopathology of patients with non epileptic attack disorder (Spitzer, 1995). The multi modular scale was developed to obtain

information, using a structured interview, for making the major Axis I diagnosis according to the fourth edition of the DSM (DSM IV). The scale attempts to describe what the manifestations of mental disorder are and the definition of the disorders usually consists of the description of the clinical features. SCID I has been widely used and its utility, validity and reliability has been well established with it being translated into more than 10 languages.<sup>16</sup>

##### Rating of Depression

The Hamilton Depression Rating Scale (HDRS) was used to assess the severity of the co-morbid depression. It is a twenty one item likert scale used to measure depressive symptoms on various parameters including mood, sleep, suicidal ideation, diurnal variation of mood, somatic symptoms, appetite, depersonalization, obsessions and paranoid symptoms. The total score was obtained by summation of the scores. It has a reliability coefficient above 0.92 and validity with good sensitivity (0.95) and specificity (0.94).<sup>17</sup>

##### Rating of Anxiety

Hamilton Anxiety Rating Scale (HARS) a fourteen-item likert questionnaire was used to measure various factors including autonomic symptoms, psychic symptoms, and somatic anxiety symptoms and gives the degree of anxiety and pathological condition. The total score was obtained by summation of the scores. HARS has good validity and reliability with Cronbach alpha of 0.75.<sup>18</sup>

All patients were explained about the nature of the study and its applications and informed consent was obtained from the patients or the guardian in case of minor subjects. A proforma was designed in the form of a semi-structured interview to obtain information on the socio demographic profile, investigations and questions pertaining to the aims of the study. All the patients having NEAD were then divided into two groups depending upon the presence or absence of existing co-morbid psychopathology. Thus the resultant groups were:

*Group A:* Patients of NEAD with co-morbid psychopathology.

*Group B:* Patients of NEAD without co-morbid psychopathology

All the enrolled patients having anxiety, depression, panic disorder as psychiatric morbidity (Group A) were then started on medications available from the hospital pharmacy viz. Tab escitalopram doses ranging from 5 to 20 mg per day and /or Tab imipramine in doses ranging from 25 to 75 mg per day. Patients of schizophrenia were started on Tab risperidone in doses ranging from 2 to 6mg per day. Oral benzodiazepines, lorazepam (max upto 4 mg) and clonazepam (max upto 1mg) were used when required for anxiety or panic attacks.

All patients were asked for a regular biweekly follow up for the initial 3 months and then once a month follow ups over the next 3 months (total 10 consultations). Group A patients' medication doses were titrated accordingly as per improvement or side effects. Both group patients were also taken up for 30 minutes of individual supportive psychotherapy sessions by either of the investigators, where there was a therapeutic alliance formed and either of the investigators addressed the problems and conflicts that the patient was aware of and used the techniques of praise, encouragement, reassurance, normalizing, reframing and advice to help achieve symptom improvement during each follow up session.

The HDRS and HARS was applied to patients of both groups at baseline and then at 3 and 6 months respectively to Group A patients. 12 patients dropped out of the study in Group A during the 3 month follow-up and so there were 38 patients for the HDRS and HARS analysis at the end of 3 months. The next assessment at 6 months revealed a further drop out with only 27 patients of Group A completing the study.

Among the Group B patients the outcome assessment at the end of 6 months had only nine patients completing the 6 month follow up with three patients dropping out after 3 weeks, three patients after 12 weeks, two after 13 weeks and four patients after 16 weeks.

### Statistical analysis

The group differences were analyzed using parametric tests like paired t test with correction, student t test, and frequency distribution wherever applicable. Two tailed 'p' values were obtained for all statistical analysis. The changes in psychopathology and NEAD after treatment were studied by paired t-test in the patient group as per protocol analysis.

## Results

### Demographic variables

Majority of the sample of both groups A & B were less than 35 years of age [88% (n=44), 100% (n=21)], females outnumbered males at 88%(n=44) & 52%( n=11) in Groups A& B respectively. 27(54%) patients of Group A and 8 (38%) patients of Group B were married. Higher secondary and above education was achieved by nearly 70 % (n=47) patients of both the groups, 80% (n=55) of patients in both groups were unemployed and nearly 60 % (n=46) patients of both groups belonged to upper lower class.

### Presence and Type of Psychopathology

When all the patients with NEAD (n=71), were assessed for associated psychiatric co morbidity, then 70.42% (n=50) of the patients were seen to be having co

morbid psychopathology as compared to 29.6% (n=21) who did not have any psychiatric co morbidity. The sample of the two study groups was:

Group A = NEAD with psychiatric co morbidity (n=50)

Group B = NEAD without psychiatric co morbidity (n=21).

Nearly 46 patients in our sample had predominant neurotic disorders as compared to psychotic or substance use disorders when assessed for associated psychiatric co morbidity. The type of psychiatric morbidity as per SCID revealed anxiety disorders NOS in 26%, minor depression in 24%, dysthymia in 6%, schizophrenia 4%, substance abuse disorders in 4% and phobia and panic disorder each in 2% of the patients ( Table1). Thus psychiatric co morbidity was quite prevalent among the NEAD patients which may often go undetected.

### Outcome of anxiety and depression from baseline, 3 months and 6 months follow up

As most of the patients had predominant depressive and anxiety symptoms clinically at baseline, the HDRS and HARS were administered to objectively rate the severity of these symptoms. On comparing both the groups for difference in severity of the symptoms, those patients who had clinical manifestations scored significantly higher on both the scales and an extremely significant difference was seen. (HDRS:  $t = 8.91$ ,  $p < 0.01^*$ ), (HARS:  $t = 6.19$ ,  $p < 0.01^*$ ). Thus this data confirms the clinical diagnosis in these patients of NEAD with associated psychiatric co morbidity (see Table 2a).

Patients who were initially diagnosed as having psychiatric co morbidity at baseline were started on a combination of pharmacotherapy and supportive psychotherapy and were assessed at 3 and 6 months for the outcome of depressive and anxiety disorders.

An analysis of the data of thirty eight patients of Group A who followed up after three months, revealed a reduction in the total mean scores of both HDRS and HARS and a further slight reduction at the end of 6 months. However there was a significant rate of drop out with only 27 patients following up at the end of 6 months (See Table 2b)

### Outcome of NEAD at end of six months in both Groups

Along with the psychiatric co morbidity, patients of both the groups were also assessed for the outcome of NEAD at the end of six months. Group A patients were treated with pharmacotherapy and supportive psychotherapy whereas Group B patients received only supportive psychotherapy. The analysis revealed a 100% reduction in the non-epileptiform attacks in 28% (n=14) of the patients, followed by a 50% reduction in

approximately 15 – 16% (n=8 &3) of both group patients respectively. 10% (n=5) of Group A patients claimed no improvement at all in the non-epileptiform attacks since the time of enrollment in the study. It was also seen that approximately 50% (n=23 & 12) of patients were lost to follow up in both the groups respectively which makes it difficult to comment on the outcome. Both groups however seemed to have a similar outcome at the end of 6 months in terms of reduction of NEAD. (See Table 3)

## Discussion

### Psychiatric comorbidity in NEAD

In our study nearly 46 patients (92%) had neurotic disorders like major/minor depression, anxiety, panic disorder etc as compared to psychosis or substance use disorders. Several studies have reported the presence of co morbid psychopathology in patients of pseudo seizures to be around 50 – 96% which is in keeping with our study.<sup>2-7</sup>

Most of the studies have documented depression in the range of 25-45% of the NEAD patients and dysthymia ranging from 7 – 13%.<sup>2-7</sup> Kanner et al reported adjustment disorders in 13% of his NEAD patients which is more or less in keeping with the findings of our study.<sup>2</sup> One of the reasons for having more depressive disorders could be due to the female preponderance which was seen in our sample where 44 patients of Group A were females and depression is known to occur more in females.<sup>1</sup>

An Indian study by Patidar et al<sup>19</sup> also found a high incidence of depressive (90.16%) and anxiety disorders (62.3%) in their NEAD patients where most patients had moderate to severe depression and mild to moderate anxiety scores respectively. However our findings of anxiety disorders were not as high as those of Patidar et al<sup>19</sup> and other researchers where the prevalence for anxiety disorders ranged from 9 – 71%.<sup>14</sup> We did find anxiety

Type of psychiatric morbidity (SCID-1 Diagnosis)	Group A (n=50)
Anxiety disorders NOS	13 ( 26% )
Minor depression	12 (24% )
Major depressive disorder	11 (22% )
Adjustment disorder	5 (10% )
Dysthymia	3 ( 6% )
Schizophrenia	2 ( 4% )
Social phobia with panic attacks	1 (2% )
Panic disorder	1 (2% )
Alcohol dependence with adjustment disorder	1 (2% )
Alcohol and cannabis abuse	1 (2% )
<b>Total</b>	<b>50 ( 100% )</b>

Table 1: Type of Psychiatric Co morbidity in Group A Patients

Scores	Group A (n=50)		Group B (n=21)		Student 't' test	p value
	Mean	SD	Mean	SD		
HDRS	16.31	5.67	6.85	2.37	8.91	<0.01*
HARS	14.5	5.24	8.19	2.69	6.19	<0.01*

Table 2a : HDRS And HARS At Baseline Visit. \* significant

Scores	0 months Baseline visit (n= 50)		3 months Follow up (n= 38)		6 months Follow up (n= 27)	
	Mean	SD	Mean	SD	Mean	SD
HDRS	16.31	5.67	14.76	4.91	11.64	4.78
HARS	14.5	5.24	11.28	4.32	10.75	4.94

Table 2b: Improvement in HDRS and HARS in Patients of Group A on Follow Up

Reduction in symptoms of NEAD at 6 months	Group A (n=27)	Group B (n=9)
100 % ( Complete reduction )	14 (28%)	6 (28.57%)
50% (Partial reduction with decreased frequency)	8 (16%)	3 (14.28%)
0% (No reduction at all)	5 (10%)	0(0%)
Lost to Follow up	23 (46%)	12 (57.14%)
<b>Total</b>	<b>50</b>	<b>21</b>

Table 3: Outcome of NEAD in both groups at end of 6 months

disorders NOS to be prevalent in about 26% of the cases which is in keeping with those who have documented panic disorder, phobia and generalized anxiety disorder in about 10-30% of the cases.<sup>2,3</sup> The reason for lowered anxiety rates in our study could be due to higher levels of major and minor depression as we had used diagnostic criteria as compared to previous researchers who only diagnosed anxiety with the help of rating scales.

Substance use disorders in NEAD accounted for 4-11% of the patients as per a study by Kanner et al<sup>2</sup> which is at a higher frequency than our study sample. This could be due to the fact that in our study females outnumbered in both groups and substance disorder was seen in 2 male patients. Sociocultural and religious factors could also be responsible for differences seen across various studies. Several researchers have also found associated personality disorders in 16-46% of patients with NEAD,<sup>3</sup> post traumatic stress disorder (PTSD) (35– 49%),<sup>20</sup> dissociative disorders (22–91%),<sup>21</sup> and personality disorders (10–86%),<sup>6,7</sup> though we did not find the same in our sample of patients.

The presence of psychiatric co morbidities has been correlated with more severe dysfunction and impaired quality of life in this population having NEAD.<sup>1</sup> Also NEAD usually present with another co morbid psychopathology which has now become very evident in the various studies.<sup>3-6,8</sup>

Most of these disorders may have a multi-factorial etiology where factors such as stressful life events, history of trauma or sexual abuse, faulty coping, environmental factors like relationship problems & financial burden etc all may cause both NEAD as well as other psychopathologies.<sup>1-22</sup> Freud had proposed a psychodynamic explanation for the development of conversion symptoms where the unconscious intra psychic conflict between instinctual impulses and the prohibition against its expression results in anxiety which gets converted into a physical symptom.<sup>1</sup>

### **Outcome of anxiety and depression at baseline, 3 months and 6 months follow up**

Previous studies have focused more on the outcome of NEAD in the follow up phase and have documented a poorer outcome in patients with associated psychiatric co morbidity.<sup>23</sup> An improvement in the underlying psychiatric morbidity would also influence the outcome of NEAD as patient's coping and frustration tolerance would improve with an overall effect seen in various spheres of functioning viz. emotional, social and occupational.

In our study it was seen that there was a 24% dropout at the end of three months which became approximately 50% by the end of six months. An improvement in the associated psychiatric co morbidity probably accounted for the dropout in the follow up of the patients over the next three months. There are very few studies available

documenting the outcome of NEAD and associated psychiatric co morbidity. Several other researchers have found a poorer outcome in patients having NEAD with psychiatric co-morbidity and personality disorder.<sup>2,23</sup>

### **Outcome of NEAD at end of six months**

All our patients were referred by the neurologist to the psychiatry department. Hence the stigma of having psychiatric disorder overrode their need of treatment. This is very much in keeping with the cultural attitudes in the Indian society. Also each follow up session included time spent with the patient addressing their stressors and probably also some of their conflicts though the sessions were not planned for conflict resolution but to help improve both their depressive anxiety states and NEAD. Patidar et al also felt that the most important prognostic factor in their sample was probably the acceptance of the diagnosis of psychogenic non-epileptiform seizures (PNES) by patients and their family members.<sup>19</sup>

Most of the studies have assessed the outcome of pseudo seizures after 1 year and above. A wide range of cessation of non epileptic attacks was seen by several researchers over varying periods of time ranging from 29 to 58%.<sup>2,3,23</sup> This is more or less in keeping with our findings where 28% of the patients gave a complete reduction of NEAD symptoms within six months on enrollment in the study. Though only Group A patients were on medication for their co morbidity, patients from both the groups were on supportive psychotherapy; which probably helped in reduction of NEAD as both the groups had similar outcomes at end of 6 months. Medication therefore helped in resolving the depressive anxiety states of Group A patients and also helped the NEAD symptoms in those who followed up. Researchers have noted that psychotherapy in NEAD like CBT was not always beneficial in reduction of NEAD symptoms.<sup>14,15</sup> Patidar et al reported cessation of seizures in 46.66% and less than 50% reduction in seizure frequency in 24.44% patients in a 6- 12 month follow up which was higher than our findings.<sup>19</sup> McKenzie in their follow up of 260 patients over 6-12 months found that 38% of patients had been free of spells and 23% patients had at least 50% reduction in spell frequency.<sup>24</sup>

Kanner et al on their six month follow up of patients with NEAD found 29% to be having complete cessation of symptoms, 27% having occasional attacks and 44% having persistent attacks.<sup>2</sup> Though a similar finding was seen in our group for complete cessation, the findings did not corroborate for partial and no reduction in symptoms. The 44% in the above study who did not show improvement had a high frequency of major depression, dissociative disorders, personality disorders and abuse. All the patients in Kanner's study<sup>2</sup> followed up over six months which is not in keeping with our study where a

high 6 month dropout rate of 50% was seen. The reasons for dropout in our study could be that some of the patients were from outstation and had sought a referral to this tertiary centre for only diagnosis; many did not have relatives staying in the city; some did not believe in the psychopathology when they were explained and educated regarding the nature of their condition or some who had partial improvement in their underlying psychopathology, then had a decreased need to see the doctor.

Riaz et al had looked at the outcome of NEAD and patient satisfaction with majority of the sample reporting reduction in seizures and improved quality of life in a follow up period of 8-21 months, with 20% patients following up with a psychiatrist, 40% in epilepsy clinics and 40% having no follow up.<sup>25</sup> Studies by researchers with a long term (1-14 years) follow-up have reported seizure freedom rates from 16- 40%.<sup>26,27</sup>

Despite the fact that this study was done nearly 15 years ago, it still holds clinical relevance today, as there is a paucity of Indian data on the short or long outcomes of NEAD and psychiatric comorbidities. Liaison with the neurologist, early referral and treatment of NEAD and its comorbidities definitely affects the outcome and quality of life of these patients.

### Conclusions

This was the first prospective study of its kind in India to study the psychiatric co-morbidities associated with NEAD and their outcomes at the end of 6 months but it had certain limitations, as the sample was from a tertiary centre and hence not reflective of the general population. We included patients with or without true seizures which could be a confounding factor. We did not assess the personality profile of our patients and had a high dropout rate. Future long term prospective studies looking at the various risk factors, other therapies for NEAD and associated psychiatric co-morbidities would definitely help in the understanding of these patients.

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