Factors Associated With Adherence To Anti-Epileptic Drugs Among Children With Epilepsy At Tertiary Care Hospital: A Cross Sectional Study

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Abstract

Background: Childhood epilepsy causes a tremendous burden for the child, the family, society as well as the healthcare system. Adherence to antiepileptic drugs (AEDs) is key to treatment success, one of the main causes of unsuccessful treatment for epilepsy is poor adherence to medications. Non-adherence in children with epilepsy presents a potential ongoing challenge for achieving a key therapeutic goal of seizure control. In this study we will assess the level of adherence to AEDs in children and the factor associated with non-adherence.
Methodology: A cross-sectional prospective descriptive design study, conducted in NRIIMS medical College and hospital, Visakhapatnam, Andhra Pradesh from December 2021 to May 2022. 60 patients were included in this study who gave written consent and had been taking at least one AEDs for at least 6 months. Only those patients with normal neurological and cognitive development and no other severe comorbidities were included in this study. A structured questionnaire was used to collect relevant information on the adherence of study subjects to AEDs based on self/ caregive report. Part of the questionnaire was derived from Morisky Medication Adherence Scale (MMAS-8). Data were analysed by using a statistical package for social science software and $P<0.05$ was considered significant to see association between factors and non-adherence.
Results: The most common reason for non-compliance was the problem with remembering which was seen in 41.8% of the patients. 21.8% of the patients had problems sticking themselves and 18.6% had problems with buying the drugs.
Conclusions: Poor adherence was seen in 31.7%% of our study participants. In our study, patients did not stick to their therapy, buy the drugs or had the problem to remember to take their medication. More efforts are required to scale up the provision of client-centered service (provision of appropriate health care delivery, focus on quality of treatment and providing health education/counseling to improve caregivers' knowledge and attitude towards epilepsy) to improve children's adherence status to their medication(s) and seizure control status.

Keywords: Epilepsy, Children, AEDss, Non- adherence, Prevalence, Associated factors.

INTRODUCTION

Epilepsy is a chronic non-communicable disorder of the brain that affects about 10.5 million children worldwide, with 80% of these children living in developing countries.[1,2] The goal of treatment of epilepsy includes minimizing the risk of recurrent seizures and antiepileptic drug (AED) side effects, and maintaining normal psychosocial and educational/vocational adjustment.[3] The treatment goals in epilepsy include the achievement of good clinical control of seizures, prevention of relapse and drug resistant epilepsy; these require antiepileptic drug (AED) compliance and adherence.[4,5] Non-adherence in children with epilepsy presents a potential ongoing challenge for achieving a key therapeutic goal of seizure control.[6] Non-adherence to AEDs leads to inadequate treatment with subsequent uncontrolled seizures which leads to more emergency room visits, hospitalizations, poor quality of life, morbidity, and mortality.[7-12] This reduces the benefits that could be gained from the medication.

Adherence is defined as the level to which a patient's behaviour including how the medication he or she is taking corresponds with the agreed prescription from the health care provider.[13] As reported by the World Health Organization (WHO), less than 50% of patients with chronic medical conditions in developing countries adhere to prescribed medications and this may be lower in children who depend on adults for the provision of their essential needs.[13] Studies on AEDs adherence reported variable rates with ranges between 20-80%. These rates are however, much lower among children.[14] The differences in the adherence rate reported depends on the study population and the methods used. Due to high cost and unavailability of serum AEDs level estimation, self-report has been the main method of assessing adherence

in developing countries as it is affordable and adaptable to the populace, however, it has been reported to overestimate adherence.[14]

Factors that determine adherence to medications among children on treatment includes socioeconomic factors, age, sex, the availability of drugs, ignorance and the level of education of care givers.[15] Poor adherence to AEDs have been linked to suboptimal seizure control, frequent hospitalization, reduced quality of life of children living with epilepsy as well as avoidable negative psychosocial impact on the parents of affected children.[16,17] Out of pocket payment for health related conditions and negligible subscription to health insurance services as obtained in most developing countries contributes to poor health seeking behaviours and poor adherence to prescribed treatment.[17]

This study sought to assess the level of adherence and identify the factors associated with adherence to antiepileptic drugs among children with epilepsy attending the child clinic at the NRIIMS medical college and hospital.

METHODS

Study Site:

Study was conducted in NRIIMS medical college and hospital, Visakhapatnam, Andhra Pradesh, India from December 2021 to May 2022.

Study Design:

Cross-sectional Prospective Descriptive design study

Study Procedure/Sampling Method:

Children with a diagnosis of epilepsy who presented to the clinic within the period of study were enrolled for the study. The diagnosis of epilepsy was based on clinical history and examination finding. Electroencephalogram (EEG) was not mandatory but where available was used to support the diagnosis of epilepsy. Using a convenience sampling method, 60 children on AED who met the inclusion criteria were consecutively enrolled into the study who gave written consent and had been taking at least one AEDs for at least 6 months.

Inclusion criteria

Children between 6 month - < 18years of age having epilepsy visiting NRIIMS medical college and hospital, Visakhapatnam, Andhra Pradesh, India and those who fulflled the eligibility criteria were enrolled in this study. Patients diagnosed with epilepsy for at least 6 months, administered at least one AEDs, with normal neurological and cognitive development, without other severe co-morbidities and consented to participate in the current study were included in the study.

Exclusion criteria

Patients with ages <6 months and > 18 years, taking AEDs for treatment other than epilepsy were excluded from the study.

Data Collection:

We used structured researcher-administered questionnaire to collect information from the caregivers of the subjects. Some of the subjects who take medications by themselves also provided relevant information. The questionnaire consisted of three sections. Section 1 contained information onsocio-demographic data. Section 2 which was derived from Morisky Medication Adherence Scale (MMAS-8)[18] was used to assess adherence based on self/caregiver report. The scale is composed of 8 items. Items 1-7, except item 5, are yes/no questions, where no answers receive a score of 1 while yes answers receive a score of 0. For item 5, the score is reversed. Item 8 is measured based on 1-5 Likert scale. The total scores range between 0 and 8, where 8 is regarded as high adherence, 6-7 moderate adherence, and less than 6 low adherence.Based on the scale, patients who scored less than 6 were classified as non-adherent. The MMAS-8 has widespread acceptance in clinical settings and advantages of MMAS-8 include cost-effectiveness, ease of use and convenience. Disadvantages of the scale include recall bias and participants feeling pressured to give acceptable responses in an effort to elicit positive reaction from their healthcare provider. Section 3 contained information on reasons for non-adherence.

Ethical approval

Before the initiation of the study, ethical approval was taken from the ethics committee of NRIIMS medical College and hospital, Visakhapatnam, Andhra Pradesh.

Statistical analysis

Data obtained was analyzed with statistical package for social sciences (SPSS) software version 20. Results were presented in descriptive statistics using frequency tables. Chi-square test was used to determine significance of association between non - adherence and patients' characteristics. *P value < 0.05 was considered significant.

RESULTS

The study was conducted in a tertiary care hospital in NRIIMS medical college and hospital, Visakhapatnam, Andhra Pradesh, India. 60 pediatric patients were enrolled in this study. The baseline characteristics of the study population and their correlation with adherence were mentioned in Table 1 and Table 2. Low adherence were seen in 10 patients in the age group of 11 to 17 years with p = 0.20. High adherence was found in males (66.7% as compared to females (33.3%); however, the difference was not statistically significant (p=0.39). The non-adherence in the urban population (16.7%) was found to be lesser as compared to the rural population (46.7%) with p=0.01* which was statistically significant . 46.7% of the high adherence population belonged to the upper lower class as compared to the poor adherence population among which 57.8% belonged to the lower class (p=0.17). Those patients who were on multiple AEDs had poor compliance as compared to those on only one AEDs but not statistically significant (p=0.43). The most common reason for non-compliance (poor / low adherence) was a problem with remembering which was seen in 31.7% of the patients. 21.7% of the patients had problems sticking themselves and 13.3% had problems with buying the drugs Figure 1 and Table 3. 50% of the study population belongs to urban areas. 63.3% of the study population belongs to the lower and lower middle class .

Characteristics	High Adherence n(%)	Moderate Adherence n(%)	Low Adherence n(%)	Chi-Square test ($X^{2)}$	P-value
SEX					
Male	20 (66.7%)	05 (45.5%)	10 (52.6%)	1.86	0.39
Female	10 (33.3%)	06 (54.5%)	09 (47.4%)		
Age					
<1 year	02 (06.2%)	02 (22.2%)	01 (05.3%)		
1-5 years	11 (34.3%)	02 (22.2%)	04 (21.0%)	8.02	0.24
6-10 years	12 (37.5%)	02 (22.2%)	04 (21.0%)		
11-17 years	07 (21.2%)	03 (33.3%)	10 (52.7%)		
Region					
Rural	11 (36.7%)	05 (45.5%)	14 (73.7%)	6.49	0.04*
Urban	19 (63.3%)	06 (54.5%)	05 (26.3%)		
Socio-Economic Status					
Lower	06 (20.0%)	06 (54.5%)	11 (57.8%)		
Lower middle	09 (30.0%)	02 (09.1%)	04 (21.1%)	9.31	0.16
Upper lower	14 (46.7%)	03 (27.3%)	04 (21.1%)		
Upper middle	01 (03.3%)	00 (00.0%)	00 (00.0%)		
Type of Epilepsy					
Generalized	20 (66.7%)	06 (54.5%)	15 (78.9%)	1.00	0.61
Focal	10 (33.3%)	05 (45.5%)	04 (21.1%)		
Number of AEDs					
Monotherapy	22 (73.3%)	06 (45.5%)	11 (57.8%)	2.13	0.35
Polytherapy	08 (26.7%)	05 (54.5%)	08 (42.2%)		
Duration of AED therapy					
<6 months	02 (13.3%)	03 (11.5%)	01 (05.3%)		
6 - 12 months	04 (26.6%)	10 (38.5%)	03 (15.8%)	6.48	0.37
13 - 24 months	08 (53.3%)	11 (42.3%)	10 (52.6%)		
>24 months	01 (06.6%)	02 (07.7%)	05 (26.3%)		

TABLE:1 Correlation of different variables with adherence levels.

Among low adherence (non-adherence) patients,the commonest reason for non-adherence was geographical distribution (rural vs urban) followed by 100% low adherence patients had a problem remembering which was statically significant. 36.8% of low adherence patients had a problem with taking, 68.4% with sticking and 42.1% with buying which was statistically significant with p<0.001. Only 5.3% of low adherence patients had the reason for drug side effects which was statistically not significant with p=0.30 .

Characteristics	Adherence	Non-adherence	Total (n %)	Chi-Square test ($X^{2)}$	P-value
SEX					
Male	25	10	35 (58.3%)	0.37	0.54
Female	16	09	25 (41.7%)		
Age					
<1 year	04	01	05 (08.3%)		
1-5 years	13	04	17 (28.3%)	13.3	0.20
6-10 years	14	04	18 (30.0%)		
11-17 years	10	10	20 (33.3%)		
Region					
Rural	16	14	30 (50.0%)	6.24	0.01*
Urban	25	05	30 (50.0%)		
Socio-Economic Status					
Lower	12	11	23 (38.3%)		
Lower middle	11	04	15 (25.0%)	4.96	0.17
Upper lower	17	04	21 (35.0%)		
Upper middle	01	00	01 (01.6%)		
Type of Epilepsy					
Generalized	26	15	41 (68.3%)	1.45	0.23
Focal	15	04	19 (31.6%)		
Number of AEDs					
Monotherapy	28	11	39 (65.0%)	0.62	0.43
Polytherapy	13	08	21 (35.0%)		
Duration of AED therapy	05	01	06 (01.0%)		
<6 months	18	03	21 (35.0%)	4.98	0.17
6 - 12 months	12	10	22 (36.7%)		
13 - 24 months	06	05	11 (18.3%)		
>24 months					

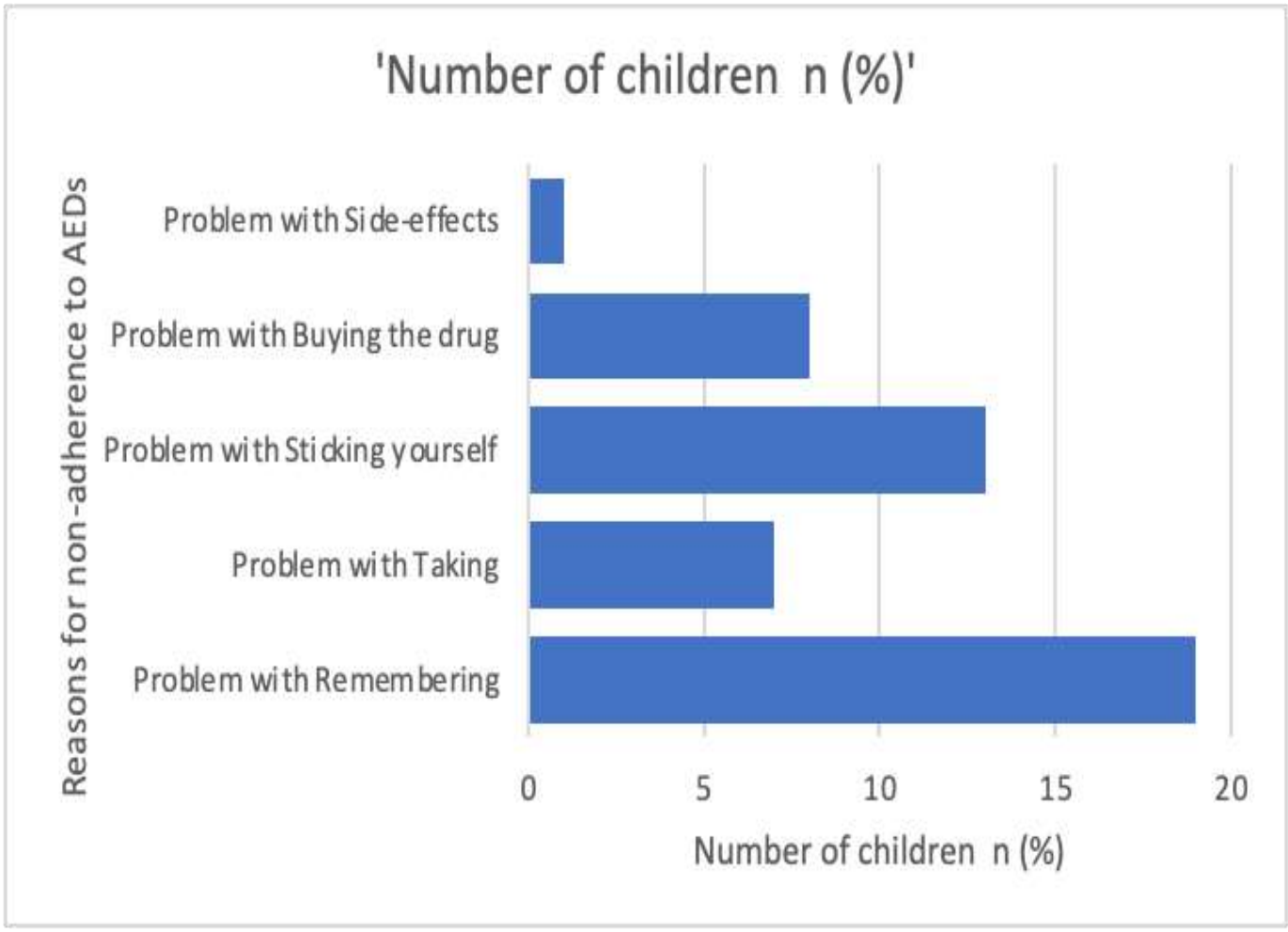
TABLE: 2 Factors associated with non-adherence to AED

Reason for Non-Compliance	High adherence n(%)	Moderate adherence n(%)	Low adherence n(%)	Chi-Square test ($X^{2)}$	P-value
Problem with Remembering					
YES	00 (0.0%)	03 (27.3%)	19 (100.0%)	50.6	<0.01*
NO	30 (100.0%)	08 (72.7%)	00 (0.0%)		
Problem with Taking					
YES	00 (0.0%)	01 (9.1%)	07 (36.8%)	13.9	<0.01*
NO	30 (100.0%)	10 (90.9%)	12 (63.2%)		
Problem with Sticking yourself					

YES **NO**	00 (0.0%) 30 (100.0%)	08 (72.7%) 03 (27.3%)	13 (68.4%) 06 (31.6%)	32.4	<0.01*
Problem with Buying the drug **YES** **NO**	00 (0.0%) 30 (100.0%)	02 (18.2%) 09 (91.8%)	08 (42.1%) 11 (57.9%)	14.87	<0.01*
Problem with Side-effects **YES** **NO**	00 (0.0%) 30 (100.0%)	01 (9.1%) 10 (90.9%	01 (5.3%) 18 (94.7%)	2.40	0.30

TABLE 3: Therapy related factors effect on adherence.

FIGURE1 : Reasons for non-adherence to AEDs



DISCUSSION

AED adherence is often a factor that affects the management of childhood epilepsy. Poor adherence levels to AEDs have been reported with non-adherent patients prone to poorly controlled seizures with frequent hospital admissions. Assessing blood level of AEDs is expensive and not readily available in our setting hence, self - reporting can be used. 60 patients were enrolled in this cross-sectional study. In our study, 50%, 18.3% and 31.7% had high adherence, moderate adherence and low adherence respectively. Similar studies were conducted by Fadare et al, Pattoo et al and Yang et al the proportion of patients having high, moderate and low adherence were 17.2%, 38.3%, and 44.5%, 48%, 34%, and 19%, 21.3%, 51.4%, and 27.3%, respectively.[19-21]

In other studies that were conducted in Nigeria and Uganda, the prevalence of non-adherence was 21% and 46%.[22,23] Multiple factors are associated with non-adherence to the AEDs among epilepsy patients like low socio-

economic status, type of seizures, number of AEDs, duration of therapy, and cost of therapy.[24] 57.8% of the patients in the poor adherence group in the study belonged to lower class socioeconomic status. The non-adherence in the urban population (16.7%) was found to be lesser as compared to the rural population (46.7%). It might be because of low education status to release the importance of AEDs and their adherence, low-income source to afford AEDs.

Mbuba et al in did the study and revealed factors associated with non-adherence and association of low socioeconomic among poor adherence patients.[25] Males (66.7%) were found to have high adherence as compared to female patients (33.3%). Liu J et al in 2013 also observed adherence to AEDs among males was more as compared to females.[26] Women were found often more negative than men about the use of drugs in the study conducted by Jung et al. It might be because women are more sensitive to adverse drug reactions due to these drugs.[27]

Furthermore, the discontinuation ratio was Generalised tonic clonic seizures were more common as compared to focal seizures in our study. Patients on monotherapy were more adherent as compared to multiple AED therapy but this correlation was statistically not significant. It might be because monotherapy improves adherence by offering better tolerability and avoidance of drug interaction. Chauhan et al from India, Hovinga et al from the United States in 2008 and Tan et al from Malaysia revealed in their studies that monotherapy improved adherence by providing better tolerability and decreasing drug interactions [28-30]

In our study, the most common reason for poor adherence was the problem remembering (100%)of to take drugs with $p<0.001$ which was statistically significant. 68.3% and 36.8% had a problem with sticking and taking the drugs respectively with $p<0.001$, which was statistically significant. 42.1% of patients were not able to buy drugs which were statistically significant ($p<0.001$). Mbuba et al conducted a similar study in Kenya and revealed similar results.[25] A similar study was conducted by Gurumurthy et al in which 94.6% of poor adherence patients had a problem remembering drug intake as seen in our study.[31] This is supported by many researchers such as Hasiso and Desse (75.4%), Liu et al (69.6%), Kassahun et al (53.5%), Al-Ramahi argued that forgetfulness is a significant factor affecting the adherence of patients toward their medications, which emphasizes our finding.[32-35]

Limitation

This study is limited by the use of questionnaires since it is prone to recall bias, especially where caregivers or patient report on adherence and are likely to overestimate it. The research was done in single institution which may not help to generalize the findings of this study for regional or country level and samples were taken from hospital which might not be representative as many patients may not come to hospital despite their illness for diferent reasons. Further, many patients were not had EEG for the diagnosis of epilepsy; thus diagnosis of epilepsy and initiation of AEDs was based on clinical evidences.

CONCLUSION

Low / Poor adherence was seen in 31.7% of our study participants. Illiteracy, low socio-economic status, gender, multiple AEDs, and adverse effects are the important parameters of poor adherence to the medication. In our study, patients are not sticking to their therapy, buying the drugs or having the problem to remember to take their medication are the main reasons for poor adherence to AEDs. Free supply of AEDs, and provision of regular information about the significance of treatment may help improve adherence. By improving adherence to AEDs, we can decrease the morbidities and mortality associated with non-adherence.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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