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Factors Associated with Poor Compliance of Antiepileptic Drugs in Children with Epilepsy

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ABSTRACT

Epilepsy is a chronic neurological disorder characterized by recurrent seizures resulting from abnormal electrical discharges in the brain. **Objectives:** To determine the factors associated with poor compliance with antiepileptic drugs in children with epilepsy. **Methods:** This cross-sectional study was conducted at the Outpatient Department of Neurology of the National Institute of Child Health, Karachi, Pakistan, from January 2025 to June 2025. A total of 185 children aged 1–12 years with epilepsy, diagnosed ≥6 months earlier, were recruited by non-probability consecutive sampling. Compliance with antiepileptic drugs was assessed using the Morisky Medication Adherence Scale (MMAS-8), classifying scores ≥6 as compliant. Factors behind non-compliance were noted. Data were analyzed using SPSS v26 with chi-square and binary logistic regression applied, taking $p<0.05$ as significant. **Results:** In a total of 185 children, the mean age was 7.4 ± 3.1 years, and 104 (56.2%) were males. Respondents were 117 (63.2%) mothers and 68 (36.8%) fathers, with a mean parental age of 34.8 ± 6.7 years. Residence was urban in 118 (63.8%), and rural in 67 (36.2%). Low socioeconomic status was noted in 92 (49.7%), and 47 (25.4%) parents were illiterate. Overall, 119 (64.3%) children were compliant and 66 (35.7%) non-compliant. Non-compliance was significantly associated with rural residence (AOR 1.9, 95% CI 1.0–3.6), low socioeconomic status (AOR 2.5, 95% CI 1.1–5.7), and illiteracy (AOR 6.9, 95% CI 2.4–20.5). **Conclusions:** Non-compliance with AEDs in children with epilepsy in Karachi was strongly influenced by rural residence, low socioeconomic status, and low parental education.

INTRODUCTION

Epilepsy is a chronic neurological disorder characterized by recurrent seizures resulting from abnormal electrical discharges in the brain [1]. Approximately 7.6 per 1000 individuals are affected by epilepsy globally, accounting for nearly 70 million people across all age groups [2]. The highest incidence is reported during infancy, with 102 new cases per 100,000 annually, particularly within the 1–12 years age range [3]. In contrast, children aged 11–17 years demonstrate a lower incidence, ranging between 21 and 24 per 100,000 annually [4]. In the context of epilepsy, compliance refers to the degree to which patients follow prescribed antiepileptic drug (AED) regimens in terms of both dosage and timing. Medication adherence is fundamental for seizure prevention and reduction, with significant implications for overall quality of life [5]. Poor adherence represents one of the most critical challenges in epilepsy management, as it compromises seizure control and undermines therapeutic outcomes. Evidence suggests that with appropriate and consistent use of AEDs, seizure freedom can be achieved in nearly 70% of individuals; non-adherence therefore constitutes a major barrier to attaining this goal [6]. Rates of adherence to AEDs are variable in different studies, ranging between 20 and 80%. In children, however, these rates are even lower, estimated between 25 and 75% [7]. A study by Dima and Shibeshi on adherence of AEDs in children reports 65.0% adherence and 35.0% non-adherence. Commonly reported factors of non-adherence were family size (>5), 59.7%, low

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monthly income, 31.3%, financial problems, 59.7%, duration of illness (≥3 years), 43.3%, seizure attacks in the last three months, 77.6%, and duration of treatment (≤2 years), 56.7% [8]. Another study by Ejeliogu *et al.* reported 44.8% non-adherence in children [9]. A Pakistani study by Malik *et al.* on factors influencing medication adherence in children with epilepsy reported 58.0% non-adherence in children. Factors significantly associated with non-adherence were polypharmacy (79.0%), uncontrolled seizure (57.0%), unaffordability (71.0%), poor counseling (86.0%), unavailability of AEDs (29.0%), and no parental/caretaker education (43.0%) [10]. Continuous efforts are being advocated to raise awareness of epilepsy related disorders, strengthen health system responses, and reduce its global burden [11].

Despite these efforts, research addressing medication adherence in children with epilepsy remains limited, and the factors influencing adherence are not fully understood. In Pakistan, data on pediatric adherence to AEDs are particularly scarce. This study was planned with a research question: What are the factors behind non-compliance to AEDs among children with epilepsy attending a tertiary care hospital in Karachi, Pakistan? There is a pressing need to characterize adherence patterns in this population, identify determinants of non-adherence, and develop evidence-based strategies to improve compliance. This study aimed to determine factors associated with poor compliance with antiepileptic drugs in children with epilepsy among the local population of Karachi, Pakistan.

METHODS

This cross-sectional study was commenced at the Outpatient Department of the Neurology, National Institute of Child Health, Karachi, Pakistan, from January 2025 to June 2025, after obtaining prior approval from the ethical review committee of the institution (IERB-41/2024). A sample size of 185 was calculated using the "Online Open Epi Sample Size Software", considering the poor counseling by physicians as the most common factor of non-adherence occurring in 86.0% of the children with epilepsy, taking the confidence level at 95%, and the margin of error at 5% [10]. All enrolled children were evaluated and diagnosed by consultant pediatric neurologists at the Department of Neurology, NICH, Karachi, Pakistan. Inclusion criteria comprised children aged 1–12 years of either gender with a confirmed diagnosis of epilepsy. Diagnosis of epilepsy was made in accordance with the International League Against Epilepsy (ILAE) criteria, based on clinical history, neurological examination, and supporting investigations such as electroencephalography (EEG) and neuroimaging (CT or MRI) when indicated. Only those children with a confirmed diagnosis of epilepsy for at least six months and who were currently receiving antiepileptic therapy were included. Children with acute symptomatic seizures due to infection, trauma, metabolic abnormalities, or other transient causes were excluded. Each child had a documented neurological evaluation in their hospital record at diagnosis, and the appropriateness of the prescribed treatment plan was verified by the attending neurologist. The sample selection was carried out using the non-probability consecutive sampling technique. Informed and written consent was obtained from all parents once they were informed of the objective of the study. They were also assured about the secrecy of their provided information. Demographics of the eligible subjects, which included gender (male/female), age, age group, residential status (rural/urban), monthly income (PKR), and level of education (illiterate/primary/matric/intermediate/graduation/post-graduation), along with socioeconomic status (low/middle/high), were documented. Parents were interviewed using the Morisky Medication Adherence Scale (MMAS-8) to assess the compliance of children towards AEDs. MMAS contained 8 questions, having a response choice of yes or no for questions 1-7 [12]. Each question (1-7) was given a score of 1 for 'no' and 0 for 'yes', except question 5, where a score of 1 was given for 'Yes' and 0 for 'No'. Question 8 had a five-point Likert response scale and was measured based on 0-4 scores standardized by dividing the result by 4 to calculate a summated score. Total scores on the MMAS-8 ranged from 0 to 8 and were classified as compliance (scores 6-8) and non-compliance (scores <6) [12]. The eight-item MMAS-8 was used under fair academic use for non-commercial, hospital-based research. All rights to the scale remain with the original developer [12]. Each parent was investigated about different factors of non-compliance, which comprised polypharmacy (children on treatment of more than one AED), uncontrolled seizures (children having seizure attacks in the last three months), financial problems (parents either unable or having difficulty affording medications), availability of prescribed AEDs (prescribed AEDs either easily available or not available), physician counseling (parents either properly counseled or poorly counseled or not counseled about appropriate use of AEDs), parental education (parents either illiterate or having some level of education), and adverse effects (children suffer either from minor or significant adverse effects). The data were recorded on a specifically predesigned proforma by the researchers themselves. The statistical analysis was performed using "IBM-SPSS Statistics" version 26.0. The qualitative variables were shown as frequency and percentage. The normality of the quantitative data was checked using the Shapiro-Wilk test. For the numeric variables, means and standard deviations (SD) or medians and interquartile

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ranges (IQR) were computed. The effect modifiers were controlled through stratification, and a post-stratification chi-square test was applied to see the effect of effect modifiers on the outcome (non-compliance), taking a p-value <0.05 as significant. To identify independent predictors of non-compliance with AEDs, binary logistic regression analysis was performed. Variables with a p-value <0.10 in univariate analysis were subsequently entered into a multivariate binary logistic regression model using the enter method. The results were expressed as adjusted odds ratios (AOR) with 95% CI, and a p-value <0.05 was considered statistically significant.

RESULTS

In a total of 185 children, the mean age was 7.4 ± 3.1 years, and 104 (56.2%) were male. The respondents were 117 (63.2%) mothers, 68 (36.8%) fathers, and the mean age of parents was 34.8 ± 6.7 years. In terms of residence, 118 (63.8%) belonged to urban areas, while 67 (36.2%) lived in rural areas. Based on socioeconomic status, 92 (49.7%) families were classified as low income, 63 (34.1%) as middle income, and 30 (16.2%) as high income. Regarding parental education, 47 (25.4%) were illiterate, 39 (21.1%) had primary to secondary education, 58 (31.4%) had matriculation to intermediate education, and 41 (22.1%) were graduates or above (Table 1).

Table 1: Characteristics of Children (n=185)

Characteristics		Frequency (%)
Gender (Child)	Male	104 (56.2%)
	Female	81 (43.8%)
Parents	Mother	117 (63.2%)
	Father	68 (36.8%)
Age in Years (Child)	1-5	63 (34.1%)
	>5 to 12	122 (65.9%)
Age in Years (Parents)	20-29	42 (22.7%)
	30-40	108 (58.4%)
	>40	35 (18.9%)
Residence	Urban	118 (63.8%)
	Rural	67 (36.2%)
Socio-Economic Status	Low	92 (49.7%)
	Middle	63 (34.1%)
	High	30 (16.2%)
Parental Education	Illiterate	47 (25.4%)
	Primary to Secondary	39 (21.1%)
	Matriculation to Intermediate	58 (31.4%)
	Graduate or above	41 (22.1%)

On assessment with the MMAS-8 tool, 119 (64.3%) children were compliant, and 66 (35.7%) were non-compliant with AEDs. The reported factors of non-compliance are shown in figure 1, where poor physician counselling was documented in 57 (30.8%) cases, financial difficulties in 51 (27.6%), and unavailability of prescribed AEDs in 38 (20.5%) (Figure 1).

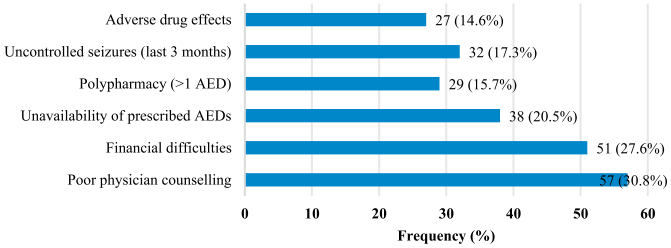

Figure 1: Factors Behind Non-Compliance with Antiepileptic Drugs

Non-compliance was observed in 35 (33.7%) males, and 31 (38.3%) females (p=0.515). Among parents, 44 (37.6%) of 117 mothers, and 22 (32.4%) of 68 fathers had non-compliant children (p=0.472). Non-compliance was reported in 19 (30.2%) children aged 1–5 years and 47 (38.5%) of 122 children aged >5–12 years (p=0.260). Among parents aged 20–29, 16 (38.1%) were associated with non-compliance, compared with 37 (34.3%) aged 30–40 years, and 13 (37.1%) aged >40 years (p=0.747). Non-compliance was significantly higher in children from rural areas, reported in 31 (46.3%), compared with 35 (29.7%) from urban areas (p=0.023). With respect to socioeconomic status, non-compliance was identified in 43 (46.7%) families with low income, 16 (25.4%) with middle income, and 7 (23.3%) with high income (p=0.007). For parental education, non-compliance was found in 29 (61.7%) children of illiterate parents, 17 (43.6%) with primary to secondary education, 14 (24.1%) with matriculation to intermediate education, and 6 (14.6%) of graduate or above parents (p<0.001) (Table 2).

Table 2: Association of Children and Parental Characteristics with Respect to Compliance Status of Antiepileptic Drugs (n=185)

Characteristics		Compliant (n=119)	Non-Compliant (n-66)	p-value
Gender (Child)	Male	69 (57.9%)	35 (53.0%)	0.515
	Female	50 (42.1%)	31 (47.0%)	
Parents	Mother	73 (61.3%)	44 (66.7%)	0.472
	Father	46 (38.7%)	22 (33.3%)	
Age in Years (Child)	1-5	44 (37.0%)	19 (28.8%)	0.260
	>5 to 12	75 (63.0%)	47 (71.2%)	
Age in Years (Parents)	20-29	26 (21.8%)	16 (24.2%)	0.747
	30-40	71 (59.7%)	37 (56.1%)	
	>40	22 (18.5%)	13 (19.7%)	
Residence	Urban	83 (69.7%)	35 (53.0%)	0.023
	Rural	36 (30.3%)	31 (47.0%)	
Socio-Economic Status	Low	49 (41.2%)	43 (65.2%)	0.007
	Middle	47 (39.5%)	16 (24.2%)	
	High	23 (19.3%)	7 (10.6%)	
Parental Education	Illiterate	18 (15.1%)	29 (43.9%)	<0.001
	Primary to Secondary	22 (18.5%)	17 (25.8%)	
	Matriculation to Intermediate	44 (37.0%)	14 (21.2%)	
	Graduate or above	35 (29.4%)	6 (9.1%)	

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Children residing in rural areas had 1.9-fold higher odds of non-compliance (95% CI 1.0–3.6, p=0.041) compared with urban residents. Low socioeconomic status was significantly associated with non-compliance (AOR 2.5, 95% CI 1.1–5.7, p=0.034), while middle socioeconomic status showed no significant effect (AOR 1.1, 95% CI 0.4–2.8, p=0.923) compared with high socioeconomic status. Parental education was a strong predictor of non-compliance as children of illiterate parents had 6.9 times higher odds of non-compliance (95% CI 2.4–20.5, p<0.001), and those with parents educated up to primary to secondary level had 3.3 times higher odds (95% CI 1.1–10.2, p=0.041) compared with those of graduate or above parents. Matriculation to intermediate education did not show a statistically significant association (AOR 1.4, 95% CI 0.5–4.3, p=0.537)(Table 3).

Table 3: Multivariate Binary Logistic Regression Analysis for Predictors of Non-Compliance of Antiepileptic Drugs

Variables		95% Confidence Interval	P-value
Residence	Rural	1.9 (1.0-3.6)	0.041
	Urban	Reference	
Socio-Economic Status	Low	2.5 (1.1-5.7)	0.034
	Middle	1.1 (0.4-2.8)	0.923
	High	Reference	
Parental Education	Illiterate	6.9 (2.4-20.5)	<0.001
	Primary to Secondary	3.3 (1.1-10.2)	0.041
	Matriculation to Intermediate	1.4 (0.5-4.3)	0.537
	Graduate or above	Reference	

DISCUSSION

The current study identified non-compliance with AEDs in 35.7 with epilepsy. Wang *et al.* reported a 37.2% rate of poor compliance in China [13], while a study from Ethiopia identified non-adherence in 35% of children with epilepsy [8]. In India, Singh *et al.* pooled nine studies with 1772 participants and found that almost half were non-adherent to AEDs, with a prevalence of 50.1% [14]. In Uganda, Nazziwa et al. reported markedly higher adherence by self-report at nearly 80%, though serum drug levels showed only 22.1% had therapeutic concentrations [7]. Variations across studies can be partly explained by differences in measurement tools, population characteristics, and healthcare delivery systems. The factors of non-compliance identified in this study included poor physician counselling (30.8%), financial difficulties (27.6%), and non-availability of prescribed drugs (20.5%). Clinical contributors were polypharmacy in 15.7%, uncontrolled seizures within three months in 17.3%, and adverse effects in 14.6%. Rana *et al.* in a local study from Lahore, observed that high cost and forgetfulness were the most frequent factors of non-compliance to AEDs, with financial barriers reported by 57.5% of patients [15]. Shahbaz *et al.* in another study from Karachi, demonstrated high cost as the leading factor in 62.1%, and drug non-availability in 5.9% [16]. Bekele in Ethiopia confirmed that side effects and polypharmacy were independent predictors of poor adherence [17]. The alignment between the present study and others across Asia and Africa highlights that adherence is influenced by a combination of financial constraints, medication complexity, inadequate counselling, and drug side effects. Clinically, these findings support the need for improved drug availability in public hospitals, simplification of regimens where feasible, and consistent reinforcement of counselling at each clinic visit. The association of residence with adherence status was evident in this study, where 46.3% children from rural areas were non-compliant, compared with 29.7% children living in urban areas, whereas logistic regression confirmed rural residence as an independent predictor with nearly two-fold higher odds of non-compliance. Data from western China demonstrated that place of residence was significantly associated with treatment adherence [18]. The barriers described in that population included difficulty in scheduling appointments and receiving timely feedback from the care team. In the present context, rural settings may limit access to specialist centers, continuity of drug supply, and counselling opportunities. The linkage of rural living with poor adherence has clinical implications for Pakistan, where pediatric neurology services are concentrated in a few tertiary centers [19]. Expanding outreach clinics and ensuring community-level counselling may reduce the rural–urban disparity. Socioeconomic status was also a major determinant of non-compliance to AEDs in this study, as low socioeconomic status independently predicted non-compliance (AOR 2.5, 95% CI 1.1–5.7). Wang *et al.* from China where a monthly household income of less than 5000 RMB was associated with nearly 3-fold increased odds of poor compliance [13]. Rana *et al.* also identified high medication cost as the leading factor for non-compliance in adults with epilepsy in Lahore, where 57.5% cited financial burden as the main barrier [15]. Shahbaz *et al.* from Karachi reported that 62.1% of patients attributed poor adherence to high drug cost [16]. The repeated observation of financial constraint across settings highlights its clinical significance. The results suggest that provision of subsidized or free antiepileptic drugs in public sector facilities could markedly improve adherence in lower-income families [20, 21]. Parental education was the most powerful predictor of non-compliance, as 61.7% of these parents were illiterate, and 43.6% had an education to primary or secondary level, compared with 14.6% graduated or above. These findings mirror those of Zhang *et al.* who reported parental educational level as a key determinant with an odds ratio of

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2.8 [22]. Wang *et al.* also found that lower parental education strongly correlated with poor adherence [13]. The consistency of these results across diverse contexts underscores the central role of caregiver understanding. Lack of comprehension of disease chronicity, drug dosing schedules, and side effects may increase the likelihood of missed doses and premature discontinuation [23]. Education-based interventions for parents are therefore a cornerstone for improving adherence in pediatric epilepsy [24, 25].

There are few limitations to the present study. The potential for social desirability bias in self-reported adherence is present. The single-center design, which may limit generalizability to the whole of Pakistan. The lack of objective adherence measures (e.g., pill counts, serum levels) was also another limitation. Prospective cohort designs with follow-up over time would better clarify temporal associations. Compliance was measured using the MMAS-8 scale, which though validated, relies on self-report and may be influenced by recall or social desirability bias.

CONCLUSIONS

Non-compliance with AEDs in children with epilepsy in Karachi was strongly influenced by rural residence, low socioeconomic status, and low parental education. These findings highlight that social and educational determinants are as important as clinical ones in shaping adherence. Addressing these factors through system-level interventions, including subsidized drug provision, decentralized epilepsy services, and structured caregiver education, may improve compliance, enhance seizure control, and reduce the long-term burden of pediatric epilepsy.

Authors' Contribution

Conceptualization: SK
Methodology: LK, SK, WH
Formal analysis: LK
Writing and Drafting: LK, WH
Review and Editing: LK, SK,WH

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

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