

Anti-seizure Medication Adherence among Adolescents with Epilepsy in a Tertiary Hospital in the Philippines

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ABSTRACT

Background and Objectives. Epilepsy is a very common pediatric neurologic disorder, and the mainstay of treatment is the use of anti-seizure medication. Several factors may cause inadequate adherence leading to uncontrolled seizures, lower quality of life, and neurodevelopmental consequences. This study aimed to determine medication adherence of adolescents with epilepsy and identify factors that may be associated in medication adherence.

Methods. This is a prospective cross-sectional study involving adolescents with epilepsy. A self-reported survey was used to measure adherence. Data on demographics and epilepsy were then assessed for presence of association with adherence.

Results. Fifty-one participants were included. Of these, 19.6% were non-adherent, 35.3% had medium adherence, and 45.1% had high adherence. Simple logistic regression analysis showed that unemployed primary caregiver is associated with 7.0 times higher odds of having moderate-high adherence and consuming at least three drugs is associated with 0.3 lower odds of having moderate-high adherence.

Conclusion. As high as 80.4% of adolescents were adherent to their medications. The presence of a caregiver who can closely monitor the patient is associated with adherence while intake of several drugs is associated with non-adherence. Future studies may need larger sample size and explore knowledge, attitude, and other social factors that may influence medication adherence.

Keywords: anti-seizure medication, adherence, adolescents, epilepsy

INTRODUCTION

Epilepsy is one of the most common neurologic disorders affecting the pediatric population. It is a disease characterized by its chronicity, enduring predisposition, neurobiological, cognitive, psychological, and social consequences.¹ One of the mainstays of treatment is the use of anti-seizure medication/s (ASM) to attain seizure freedom and a good quality of life, while minimizing drug side effects.²

Medication adherence, or compliance, according to Cramer³ is “the extent to which a patient acts in accordance with the prescribed interval and dose of a dosing regimen”. There are five factors that interact and come into play in determining adherence to medications⁴: (1) social and economic, (2) health care team and system-related, (3) condition-related, (4) therapy-related, and (5) patient-related factors. Social and economic factors include age, race, socio-economic status, logistics in getting and sustaining medication, cultural beliefs about an illness, and family dynamics. Health care team and system-related factors are those pertaining to the dynamics

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of how the patient is in relation to the medical care providers and medical institution. Condition-related factors tackle on the patient's symptomatology, disease severity, comorbidities, and treatment availability. Therapy-related factors include complexity, duration, side-effects, and failures of treatment. Patient-related factors pertain to the knowledge, attitude, motivation, and expectations of the patient.⁴

The World Health Organization (WHO) states that there is a 50% compliance rate to chronic medication in developed countries, and a lower rate in their developing country counterparts.⁴ Medication adherence can be measured subjectively or objectively. Subjective measures include patient self-report or clinician assessment. These methods are practical, flexible, and low-cost but may not be reliable due to underreporting. Direct measures include drug levels in body fluids, evaluation of a biological marker, or observation of drug intake. Although reliable, they are expensive and may not reveal the underlying causes and patterns of non-adherence.⁵

In epilepsy, non-adherence may mean uncontrolled seizures, status epilepticus, increased risk for sudden unexplained death in epilepsy (SUDEP), lowered quality of life, decreased job-related productivity in adults, and developmental sequelae in children.⁶⁻⁹ Non-adherence to ASMs has also been associated with increased financial costs due to increased utilization of inpatient and emergency department services.¹⁰ Meanwhile, good ASM adherence is associated with better seizure control and higher chances of long-term seizure freedom.^{11,12}

One of the validated self-reported tools on medication adherence is the Morisky, Green, and Levine Scale. Published in 1986, it sits on the premise that omission of drugs happens due to one of the following items: forgetting, carelessness, stopping the drug when feeling better, or stopping the drug when feeling worse.¹³ The scale is a valid and reliable measure, and can be used as an initial diagnostic tool in which a patient's adherence can be assessed.¹³ It groups patients into three categories: high, medium, and low adherence. It has a sensitivity of 81%, specificity of 44%, a positive predictive value of 75%, and a negative predictive value of 47%.¹³

Prevalence of ASM adherence in children with epilepsy varies worldwide. A meta-analysis done by Yang¹⁴ investigated the different studies done from 1990 to 2016 to determine pooled adherence rates of children to their medication. Adherence rates reported were from 22.1 to 96.5%.

Numerous factors can affect adherence to ASM in the pediatric population. Aside from the non-modifiable factors (epilepsy type, age of onset, duration of disease), the following can affect adherence: parent's knowledge about epilepsy¹⁵, availability of emotional support¹⁶, stigma of the disease, good doctor-patient relationship¹⁵⁻¹⁸, number of medication and complexity^{17,18}, sense of normality^{15,18}, and motivation^{15,18}.

A study done by de Roxas and colleagues¹⁹ in 2017 investigated factors and issues affecting treatment adherence of adult Filipino patients with epilepsy and their caregivers. Via Focus Group Discussions, the following factors were identified: good patient-doctor relationship, treatment side-

effect/s, financial resources and government support, and religious beliefs.

As of writing, there are limited studies regarding ASM adherence in Filipino children diagnosed with epilepsy. Therefore, there is a need to determine the adherence of pediatric patients with epilepsy to their ASM to establish the burden of this situation in a resource-limited country like the Philippines. Moreover, adapting a validated tool on self-reported measure of adherence would help clinicians determine adherence and/or non-adherence quickly and effectively. To our knowledge, this is the first local study on this topic. We aimed to translate and validate a Filipino version of the Morisky, Green, and Levine (MGL) Adherence Scale for epilepsy, categorize the degree of adherence of adolescents taking ASMs, and identify possible factors that could be associated with medication adherence.

METHODS

Study Design and Participants

A prospective cross-sectional study involving adolescents diagnosed with epilepsy was employed. Adolescents aged 10-19 years old, as defined by the WHO, diagnosed with epilepsy at the Philippine General Hospital (PGH), Division of Pediatric Neurology from 2015 to 2023 were included in the study from February 2023 to July 2023 via convenience sampling. PGH is the largest tertiary referral center and one of the three institutions with a training program for Child Neurology in the country. Participants included were diagnosed with epilepsy based on these definitions by the International League Against Epilepsy⁴:

1. At least 2 unprovoked (or reflex) seizures occurring more than 24 hours apart
2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after 2 unprovoked seizures, occurring over the next 10 years
3. Diagnosis of an epilepsy syndrome

Moreover, patients who were taking their anti-seizure medication/s for a minimum duration of one month^{20,21} and able to answer the questions independently were also included. Patients with cognitive or communication impairment which can affect their ability to answer the self-administered tool were excluded. Likewise, patients and/or parents who did not assent/consent in answering the questionnaire during clinic visit were excluded (Figure 1). The study had 2 phases: 1) tool translation and validation (Phase 1) and 2) survey proper (Phase 2).

Data Collection

Phase 1. Translation and Validation of Scale

Phase 1 consisted of translation and validation of the Morisky, Green, and Levine (MGL) Adherence Scale

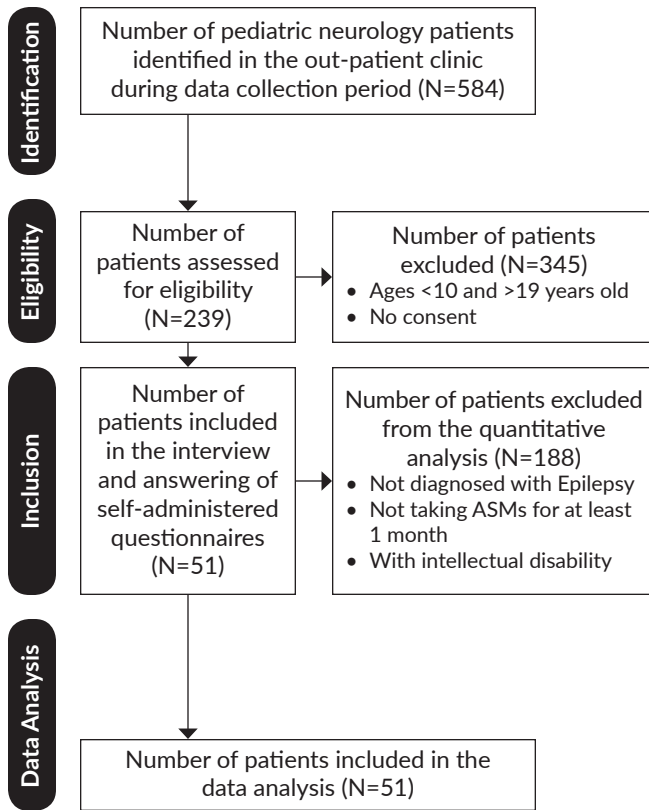


Figure 1. Flow diagram of patient inclusion in the study.

(Appendix A) which was patterned after published guidelines and principles of good practice.^{17,22} Forward translation of the English version of the Morisky, Green, and Levine Self-reported Medication-taking Scale to Filipino by a certified language professor/linguist was made. After translation, evaluation by an expert in the field (pediatrician) was performed by reviewing and checking the Filipino translation. This was done to see if the translation was able to correctly capture what was meant to be translated and corrections were incorporated in the questionnaire. A backward translation of the Filipino version of the questionnaire to English was done by another independent language professor/linguist. Similar to the previous process, the back-translated questionnaire was compared to the original version of the scale. This was done by independent expert in the field (pediatrician) to check if the translation correctly captured what was meant to be translated. Any changes were incorporated in the questionnaire to finalize the Filipino-translated adherence scale.

Content validity of the translated tool was performed by evaluation of experts and target population. Eight experts (pediatricians and pediatric neurologists) were asked to review the items on the translated scale. Each item was rated as follows: 1 – not relevant, 2 – somewhat relevant, 3 – quite relevant, 4 – highly relevant. Evaluation was done using the Content Validity Index (CVI) and each item should have a

CVI score of 0.80 for the item to be accepted as valid. Ten adolescents²³ from the intended population will answer and review the translated questionnaire. They were asked to answer the following questions: 1) Did you have any difficulty understanding this question?, 2) What does this question mean to you?, 3) Is the question relevant to you?. To determine the test-retest reliability, the questionnaire was re-administered after a week of the interview to the participants and answers should not have changed over the said period.

Phase 2. Survey Proper

The survey proper utilized two forms, the Filipino-translated Morisky, Green, and Levine (MGL) Adherence Scale (Appendix B) and a questionnaire regarding factors that might affect adherence (Appendix C). Sample size computation showed a minimum of 50 patients required for this study based on 125 out of 451 (27.72%) non-adherent epilepsy patients to their medication²⁴, 5% level of significance and 12.5% desired half-width of the confidence interval.

The questionnaires were administered during face-to-face consult at the Pediatric Neurology clinic visit from February to July 2023 and was performed by the principal investigator. Observation of proper health protocols was strictly enforced following the guidelines set by the institution to ensure safety of all participants. Patients who fulfilled the inclusion criteria and seen during clinic consult were involved in the recruitment process. The study was thoroughly discussed with the parent or primary caregiver and the patient. Afterwards, informed consent and assent were obtained while explaining the purpose of the study, risks and benefits, and confidentiality for which full understanding was ensured. Those who gave their voluntary consent and assent were ultimately included in the study while those without consent were excluded. Prior to answering the questionnaire, the parent or caregiver was instructed to go outside the clinic and wait until the subject finishes answering the self-administered questionnaires. Likewise, the primary investigator allowed the subject to answer independently and the whole process lasted approximately 20 to 30 minutes. Should there be any questions or clarifications, the attention of the primary investigator was called to answer the subject.

The Filipino-translated Morisky, Green, and Levine Adherence Scale¹³ (Appendix B) has items that were answerable by yes/"oo" (0) or no/"hindi" (1). Every "no/hindi" answer garnered 1 point. The score of each item was summed to give a range of 0-4. Based on their answers, the respondent was categorized according to the level of adherence:

1. Adherent: score of 3-4²⁴
 - a. High adherence: score of 4
 - b. Medium adherence: score of 3
2. Non-adherent: score of 0-2²⁴

This form on possible factors affecting adherence included questions regarding demographic data, features associated with epilepsy including type, duration, seizure

frequency, and number of medications in the regimen, and adverse events. Likewise, limitations in performing usual activities due to epilepsy and medication side effect were asked. Perceived support from the healthcare team, family members, and friends were also included in the questionnaire. Lastly, changes brought about by the COVID-19 pandemic on adolescents with epilepsy was explored which could possibly affect adherence because of lack of follow-up and difficulties procuring ASM.

Statistical Analysis

For Phase 1, face validation was analyzed qualitatively. For validation, content validity index (CVI) was used. A CVI score of 0.80 was accepted as valid. For test-retest reliability, the intraclass correlation coefficient (ICC) was determined. ICC interpretation of reliability according to Fleiss²⁵ is as follows: 0.40 is poor, 0.40 to 0.75 is fair to good, and 0.75 is excellent.

For Phase 2, descriptive statistics was used for the general data of the participants. Frequency and proportion were used for nominal variables. Odds ratio and corresponding 95% confidence intervals from simple logistic regression was computed to determine significant factors of ASM adherence. Missing variables were neither replaced nor estimated. STATA 13.1 was used for data analysis.

Ethical Considerations

This study was carried out in accordance with the recommendations of the University of the Philippines – Manila Research Ethics Board (UPMREB). All participants gave written assent and/or informed consent.

RESULTS

Eight experts in the field composed of five pediatricians and three pediatric neurologists rated the content of each item of the scale based on its relevance. The Filipino-translated Morisky, Green, and Levine Self-reported Medication-taking Scale showed an overall CVI of 0.969 which supports the content validity of the questionnaire (Table 1). All items in the scale have 100% rating in terms of clarity and simplicity which supports the face validity of the tool. Lastly, the computed ICC for its test reliability was 0.92 which was excellent.

A total of 51 participants were included in the study. Table 2 shows the summary of patient demographics and characteristics. Majority of the participants were males

(60.8%). In terms of age, 35.3% were early adolescents (10-12 years old), 37.2% were middle adolescents (13-16 years old), and 27.5% were late adolescents (17-19 years old). Most of the subjects are enrolled in high school (60.8%). Of these, 19.6% were non-adherent, 35.3% had medium adherence, and 45.1% had high adherence as seen in Table 3.

Most of the participants had their mother as primary caregiver (76.5%). About half of their caregivers were employed (51.0%). The most common type of seizure was focal type (82.4%). Most of the participants had epilepsy for more than 6 years already (43.1%) and frequency of seizure was mostly >4 times per month (35.3%). In terms of ASM regimen, most only had 1 (72.5%) while majority did not experience side effects (86.3%). Only 7.8% experience limitation of activity due to ASM side effect while 70.6% experience limitation of activity due to epilepsy. All of the participants perceived good support from health care provider and family members while 90.2% perceived good support from friends. About one-fourth (25.5%) mentioned that changes in treatment were experienced because of COVID-19. As seen in Table 2, none of the demographic and clinical characteristics differed significantly across levels of adherence among adolescents with epilepsy (p-values>0.05).

Simple logistic regression analysis showed that having an unemployed primary caregiver is associated with 7.0 times higher odds (95%CI=1.1-43.5, p-value=0.035) of having moderate to high adherence. Moreover, having at least three anti-seizure medication in the treatment regimen is associated with 0.3 lower odds (95%CI=0.09-0.8, p-value=0.045) of having moderate to high adherence (Table 4). The other demographic and clinical characteristics were not significant factors associated with adherence (p-values>0.05).

DISCUSSION

Adherence to anti-seizure medications is essential for successful treatment, and poor adherence to prescribed drugs is one of the main reasons pharmacological treatments fail.^{26,27} Medication adherence reduces relapses and seizure frequency, lowers healthcare costs, increases therapeutic benefits, and improves patient outcomes.²¹ The current study shows that 45.1% of adolescents had high adherence, 35.3% had medium adherence, while 19.6% had low adherence. Overall, the adherence rate found in this study is way higher from the results seen in studies conducted in China, India, Malaysia, Nigeria, Saudi Arabia, South Africa, and Turkey, ranging from 47% to 61.7%.^{18,28-33} The variations of results among

Table 1. Content Validity Indices for the Items in the Filipino-translated MGL Adherence Scale

Item #	Rater 1	Rater 2	Rater 3	Rater 4	Rater 5	Rater 6	Rater 7	Rater 8	I-CVI	Decision
1	4	4	4	4	4	4	4	4	100%	Retain
2	3	3	4	3	2	4	4	4	87.5%	Retain
3	3	4	4	4	4	4	4	4	100%	Retain
4	4	4	4	4	4	4	4	4	100%	Retain

Table 2. Characteristics of Filipino Adolescents with Epilepsy

	Total	Low Adherence	Medium Adherence	High Adherence	P-value
	Frequency (%)				
Age					
Early	18 (35.3)	2 (20.0)	6 (33.3)	10 (43.5)	0.129
Middle	19 (37.2)	2 (20.0)	7 (38.9)	10 (43.5)	
Late	14 (27.5)	6 (60.0)	5 (27.8)	3 (13.00)	
Sex					
Female	20 (39.2)	3 (30.0)	7 (38.9)	10 (43.5)	0.814
Male	31 (60.8)	7 (70.0)	11 (61.1)	13 (56.5)	
Educational Attainment					
Out of school	4 (7.8)	0 (0.0)	1 (5.6)	3 (13.0)	0.410
Grade school	16 (13.4)	2 (20.0)	5 (27.8)	9 (39.1)	
High School	31 (60.8)	8 (80.0)	12 (66.7)	11 (47.8)	
Primary caregiver					
Mother	39 (76.5)	7 (70.0)	13 (72.2)	19 (82.6)	0.695
Father	7 (13.7)	1 (10.0)	3 (16.7)	3 (13.0)	
Others	5 (9.8)	2 (20.0)	2 (11.1)	1 (4.4)	
Occupation of primary caregiver					
Unemployed	25 (49.0)	2 (20.0)	11 (61.1)	12 (52.2)	0.105
Employed	26 (51.0)	8 (80.0)	7 (38.9)	11 (47.8)	
Epilepsy Type					
Generalized	9 (17.6)	1 (10.0)	6 (33.3)	2 (8.7)	0.095
Focal	42 (82.4)	9 (90.0)	12 (66.7)	21 (91.3)	
Duration of epilepsy					
2-6 months	2 (3.9)	0 (0.0)	1 (5.6)	1 (4.4)	0.448
>6 months-1 year	2 (3.9)	0 (0.0)	2 (11.1)	0 (0.0)	
2-3 years	9 (17.6)	2 (20.0)	4 (22.2)	3 (13.0)	
3-6 years	16 (13.4)	5 (50.0)	5 (27.8)	6 (26.1)	
>6 years	22 (43.1)	3 (30.0)	6 (33.3)	13 (56.5)	
>6 years	22 (43.1)	3 (30.0)	6 (33.3)	13 (56.5)	
Frequency of seizures					
0	17 (33.3)	3 (30.0)	5 (27.8)	9 (39.1)	0.437
<10/year	13 (25.5)	1 (10.0)	6 (33.3)	6 (26.1)	
1-2/month	2 (3.9)	1 (10.0)	1 (5.6)	0 (0.0)	
3-4/month	1 (2.0)	1 (10.0)	0 (0.0)	0 (0.0)	
>4/month	18 (35.3)	4 (40.0)	6 (33.3)	8 (34.8)	
>4/month	18 (35.3)	4 (40.0)	6 (33.3)	8 (34.8)	
ASM Regimen					
1	37 (72.5)	6 (60.0)	12 (66.7)	19 (82.6)	0.293
2	12 (23.5)	3 (30.0)	6 (33.3)	3 (13.0)	
≥3	2 (3.9)	1 (10.0)	0 (0.0)	1 (4.4)	
Side effects of ASM					
Present	7 (13.7)	3 (30.0)	2 (11.1)	2 (8.7)	0.243
None	44 (86.3)	7 (70.0)	16 (88.9)	21 (91.3)	
Limitation of activity due to ASM side effect					
Yes	4 (7.8)	2 (20.0)	1 (5.6)	1 (4.3)	0.278
No	47 (92.2)	8 (80.0)	17 (94.4)	22 (95.6)	
Limitation of activity due to epilepsy					
Yes	36 (70.6)	8 (80.0)	12 (66.7)	16 (69.6)	0.751
No	15 (29.4)	2 (20.0)	6 (33.3)	7 (30.4)	
Perceived support from health care provider					
Yes	51 (100.0)	10 (100.0)	18 (100.0)	23 (100.0)	n/a
No	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Perceived support from family					
Yes	51 (100.0)	10 (100.0)	18 (100.0)	23 (100.0)	n/a
No	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Perceived support from friends					
Yes	46 (90.2)	9 (90.0)	17 (94.4)	20 (87.0)	0.726
No	5 (9.8)	1 (10.0)	1 (5.6)	3 (13.0)	
COVID changes					
Yes	13 (25.5)	2 (20.0)	6 (33.3)	5 (21.7)	0.634
No	38 (74.5)	8 (80.0)	12 (66.7)	18 (78.3)	

Table 3. Prevalence of Adherence to Anti-seizure Medications (n=51)

	Prevalence	Frequency
Adherent	High adherence	23 (45.1)
	Medium adherence	18 (35.3)
Non-adherent		10 (19.6)

studies may be explained by differences in demographic characteristics, study population and sample size used, and the use of different scales to measure adherence in their respective studies³⁴, along with variations in cultures, beliefs, educational systems, approaches of clinicians to patients with epilepsy, or levels of parental and medical support. Other studies also suggest that difference in results may also be associated with variations in the frequency and side effects of the medications, severity of the disease, accessibility to medical treatment, and availability of medications.³⁵

The factors found to be significantly associated with higher adherence level were employment status of the parents and intake of three or more anti-seizure medication. Adolescents with unemployed primary caregiver had significantly higher adherence (OR=7.0, p-value=0.035) to their medications. This may possibly be attributed to primary caregivers having more time and attention to focus on caring for their children and do close monitoring in terms of following instructions

on intake of medications. This situation may then lead to improved adherence among adolescents with epilepsy.

As mentioned, it was likewise found out that patients who had three or more medications have lower adherence (OR=0.3, p-value=0.045) as compared to those who have fewer drugs in their regimen. This may be attributed to various factors such as higher cost of maintenance medication and complexity of medication regimen in terms of frequency as well as timing. This result was consistent to previous studies showing that those receiving monotherapy exhibit much higher adherence compared to patients prescribed with polypharmacy.¹⁸ The complex nature of the treatment, where taking numerous medications at various times can cause patients to skip doses have an impact on drug adherence.³⁶ Contradictory to the current study, it was seen in the study of Carbone et al.¹⁷ that improved adherence was associated with more anticonvulsant prescriptions. However, analyzing the previous study more closely, it was explained that increased number of medications prescribed is a marker of more difficult to control or complex epilepsy which led to greater parental vigilance regarding administration of drugs but the self-reported adherence by the adolescents with epilepsy was not predicted by the number of medications prescribed. Sweileh et al.³⁷, on the other hand, claimed that there was significant difference in the rate of adherence between patients receiving monotherapy and those receiving polypharmacy.

Table 4. Factors Associated with Moderate to High Adherence

	Odds Ratio	95% CI	P-value
Age	0.3	0.06-1.5	0.143
Sex			
Female	0.9	0.1-8.3	0.967
Higher educational attainment	2.4	0.4-13.1	0.301
Primary caregiver			
Mother	Comparator	N/A	N/A
Father	1.3	0.1-12.7	0.814
Others	0.3	0.05-2.3	0.267
Unemployed primary caregiver	7.0	1.1-43.5	0.035
Epilepsy Type			
Generalized	Comparator	N/A	N/A
Focal	1.6	0.09-27.9	0.757
Duration of epilepsy	0.7	0.2-2.1	0.476
Frequency of seizures	0.9	0.4-1.7	0.688
ASM regimen			
≥3	0.3	0.09-0.8	0.045
Side effects of ASM are present	0.7	0.03-18.4	0.243
Limitation of activity due to ASM side effect	0.2	0.01-16.1	0.504
Limitation of activity due to epilepsy	0.2	0.01-3.2	0.271
Perceived support from health care provider	N/A*	N/A	N/A
Perceived support from family	N/A*	N/A	N/A
Perceived support from friends	2.2	0.1-43.6	0.618
COVID changes	2.8	0.2-41.7	0.454

N/A - not applicable

*Odds Ratio cannot be computed since all reported yes.

However, the latter study included participants of all ages and not only adolescents which may partially contribute to the difference in results.³⁷

Age (OR=0.143, p-value=0.143) and gender (OR=0.967, p-value=0.967) were not seen as significant factors in medication adherence of adolescents with epilepsy. These findings concur with those of Johnbull et al.³⁶, Liu et al.³³, and Gabr et al.¹⁸ who found that age has no bearing on adherence rate and no gender-based demographic differences between adherent and non-adherent patients. In other studies, results showed that adolescents who understood more about epilepsy and its treatment had higher self-reported adherence rates. Although higher educational attainment showed no significant association with adherence (OR=2.4, p-value=0.301), the criteria of knowledge on epilepsy and/or its treatment cannot be directly measured in the current study.

Furthermore, in the current study, 100% of the participants answered having perceived support from family, friends, and health care provider. Support from parents, other family members, and friends is regarded as the cornerstone of medication compliance for adolescents with epilepsy.³⁸ Parents and/or caregivers who provide self-care planning with adolescents, consistent positive reinforcement, and offering other incentives to encourage medication adherence were seen to work well to promote adherence. With the developmental stage that the adolescents are in, desire to talk to significant persons like their family members and friends may help in ensuring adherence to anti-seizure medications.¹⁸ Furthermore, a good relationship with the patient and the healthcare team provides better adherence to medication and treatment regimen in general. Gabr and colleagues¹⁸ emphasized that patients who felt that their regular medical relationships, monitoring, and support were good were significantly more likely to take their medication as prescribed than patients who felt that there was not enough of it, while Liu et al.³³ found that a poor patient-prescriber interaction was the root of non-adherence in 9.5% of his study's patient group.

In general, stronger adherence was associated with having fewer adherence barriers over time. Earlier studies^{18,39,40} showed that barriers provide an excellent target for enhancing adherence. According to a recent study⁴¹, barriers to adherence remain steady over a period of two years with difficulties swallowing medications, forgetting about them, and refusing to take them being associated to adherence over time. Individual-specific barriers can be addressed and handled in the clinical setting by frontline healthcare professionals to increase adherence.^{42,43} It is then the duty of physicians to identify, address, and discuss these factors with the adolescents to be able to arrive at a common goal of enhancing medication adherence and ultimately leading to good control of seizures and better quality of life.

Limitations also exist in the study. The smaller sample size, as well as data being collected from a single center, might not generally reflect all adolescents with epilepsy in

the country. It is suggested that additional research with more participants involving multi-center studies could be done in the future. On the other hand, since the measures relied on self-reporting, the level of adherence may have been overestimated or underestimated; while the study's cross-sectional design makes it impossible to evaluate patients' changing adherence behaviors. It is also recommended to conduct future studies that may include wider social factors including family's influence in predicting adherence among adolescents. Understanding how adolescents adhere to their epilepsy medication may also depend on their family context.¹⁷ Additionally, understanding the knowledge, perception, and attitude of the patients, as well as their parents or primary caregivers, may give a more meaningful evaluation of the current adherence of adolescents in medication adherence.

CONCLUSION

Among adolescents with epilepsy, 80.4% were adherent to their anti-seizure medications. The presence of caregivers who can closely supervise is associated with adherence while having to take many drugs as part of their regimen is associated with non-adherence. The Filipino-translated self-reported adherence scale may be utilized due to its high CVI and 100% face validity. Future studies may need to have larger sample size and correlate medication adherence by exploring the patients' knowledge, attitude, perception, and other social factors.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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REFERENCES

1. Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross J, Elger C, et al. ILAE official report: a practical clinical definition of epilepsy. *Epilepsia*. 2014 Apr;55(4):475-82. doi: 10.1111/epi.12550. PMID: 24730690.
2. Saad K. Childhood epilepsy: an update on diagnosis and management. *American Journal of Neuroscience*. 2014;5(2):36-51. doi: 10.3844/amjnsp.2014.36.51.
3. Cramer JA, Roy A, Burrell A, Fairchild CJ, Fuldeore MJ, Ollendorff DA, et al. Medication compliance and persistence: terminology and definitions. *Value Health*. 2008 Jan-Feb;11(1):44-7. doi: 10.1111/j.1524-4733.2007.00213.x. PMID: 18237359.
4. World Health Organization, Adherence to Long-Term Therapies: evidence for action [Internet]. 2003 [cited 2023 Sep]. Available from: <https://apps.who.int/iris/handle/10665/42682>.
5. Lam WY, Fresco P. Medication adherence measures: an overview. *BioMed Res Int*. 2015 Oct;1-12. doi: 10.1155/2015/217047. PMID: 26539470; PMCID: PMC4619779.

6. Hovinga CA, Asato MR, Manjunath R, Wheless JW, Phelps SJ, Sheth RD, et al. Association of non-adherence to antiepileptic drugs and seizures, quality of life, and productivity: Survey of patients with epilepsy and physicians. *Epilepsy Behav.* 2008 Aug; 12(2):316-22. doi: 10.1016/j.yebeh.2008.03.009. PMID: 18472303.
7. Duggan M. Epilepsy and its effects on children and families in rural Uganda. *Afr Health Sci.* 2013 Sep;13(3):613-23. doi: 10.4314/ahs.v13i3.14. PMID: 24250298; PMCID: PMC3824457.
8. Ferrari CMM, de Sousa RMC, Castro LHM. Factors associated with treatment non-adherence in patients with epilepsy in Brazil. *Seizure.* 2013 Jun;22(5):384-9. doi: 10.1016/j.seizure.2013.02.006. PMID: 23478508.
9. Nei M Hays R. Sudden unexpected death in epilepsy. *Curr Neurol Neurosci Rep.* 2010 Jul;10(4):319-26. doi: 10.1007/s11910-010-0116-4. PMID: 20446062.
10. Faught RE, Weiner JR, Guerin A, Cunnington MC, Duh MS. Impact of non-adherence to antiepileptic drugs on health care utilization and costs: findings from the RANSOM study. *Epilepsia.* 2009 Mar;50(3):501-9. doi: 10.1111/j.1528-1167.2008.01794.x. PMID: 19183224.
11. Hill AC, Thomson KE, Newell TG, White HS. Correction of medication non-adherence results in better seizure outcomes than dose escalation in a novel preclinical epilepsy model of adherence. *Epilepsia.* 2019 Mar;60(3):475-84. doi: 10.1111/epi.14655. PMID: 30669183.
12. Modi AC, Wu YP, Rausch JR, Peugh JL, Glauser TA. Antiepileptic drug non-adherence predicts pediatric epilepsy seizure outcomes. *Neurology.* 2014 Nov; 83(22):2085-90. doi: 10.1212/WNL.0000000000001023. PMID: 25355825; PMCID: PMC4248449.
13. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care.* 1986 Jan;24(1):67-74. doi: 10.1097/00005650-198601000-00007. PMID: 3945130.
14. Yang C, Hao Z, Yu D, Xu Q, Zhang L. The prevalence rates of medication adherence and factors influencing adherence to antiepileptic drugs in children with epilepsy: A systematic review and meta analysis. *Epilepsy Res.* 2018 May;142:88-99. doi: 10.1016/j.eplepsyres.2018.03.018. PMID: 29609075.
15. Kyngas H. Compliance with health regimens of adolescents with epilepsy. *Seizure.* 2000 Dec;9(8):598-604. doi: 10.1053/seiz.2000.0470. PMID: 11162760.
16. Kyngas H. Predictors of good compliance in adolescents with epilepsy. *Seizure.* 2001 Dec; 10(8): 549-553. DOI: 10.1053/seiz.2001.0557. PMID: 11792154.
17. Carbone L, Zebrack B, Plegue M, Joshi S, Shellhaas R. Treatment adherence among adolescents with epilepsy: what really matters? *Epilepsy Behav.* 2013 Apr; 27(1):59-63. doi: 10.1016/j.yebeh.2012.11.047. PMID: 23376337; PMCID: PMC3615641.
18. Gabr WM, Shams MEE. Adherence to medication among outpatient adolescents with epilepsy. *Saudi Pharm J.* 2015 Jan;23(1):33-40. doi: 10.1016/j.jsps.2014.05.003. PMID: 25685041; PMCID: PMC4311017.
19. De Roxas RC, Abejero JEE, Cabral-Lim LI. Factors and issues on treatment adherence among Filipino patients with epilepsy and their caregivers. *Acta Med Philipp.* 2017;51(4):310-8. doi:10.47895/amp.v51i4.499.
20. Alsous M, Hamdan I, Saleh M, McElnay J, Horne R, Masri, A. Predictors of non-adherence in children and adolescents with epilepsy: A multimethod assessment approach. *Epilepsy Behav.* 2018 Aug;85:205-11. doi: 10.1016/j.yebeh.2018.06.022. PMID: 30032809.
21. Aylward BS, Rausch JR, Modi AC. An examination of 1-year adherence and persistence rates to antiepileptic medication in children with newly diagnosed epilepsy. *J Pediatr Psychol.* 2015 Jan;40(1):66-74. doi: 10.1093/jpepsy/jsu010. PMID: 24648257; PMCID: PMC4288300.
22. Sousa VD, Rojjanasrirat W. Translation, adaptation and validation of instruments or scales for use in cross-cultural health care research: a clear and user-friendly guideline. *J Eval Clin Pract.* 2011 Apr; 17(2):268-74. doi: 10.1111/j.1365-2753.2010.01434.x. PMID: 20874835.
23. Peacock JL, Peacock PJ. Research design. In: Peacock JL, Peacock PJ. *Oxford Handbook of Medical Statistics*, 2nd ed. Oxford University Press; 2011. pp. 60-61.
24. Gurumurthy R, Chanda K, Sarma GRK. An evaluation of factors affecting adherence to antiepileptic drugs in patients with epilepsy: a cross-sectional study. *Singapore Med J.* 2017 Feb;58(2):98-102. doi: 10.11622/smedj.2016022. PMID: 26805666; PMCID: PMC5311891.
25. Matheson GJ. We need to talk about reliability: making better use of test-retest studies for study design and interpretation. *Peer J.* 2019 May;7:e6918. doi: 10.7717/peerj.6918. PMID: 31179173; PMCID: PMC6536112.
26. Mitchell WG, Scheier LM, Baker SA. Adherence to treatment in children with epilepsy: who follows "doctor's orders"? *Epilepsia.* 2000 Dec;41(12):1616-25. doi: 10.1111/j.1499-1654.2000.001616.x. PMID: 11114221.
27. Snodgrass SR, Parks BR. Anticonvulsant blood levels: historical review with a pediatric focus. *J Child Neurol.* 2000 Nov;15(11):734-46. doi: 10.1177/088307380001501105. PMID: 11108507.
28. Burger JR, Jacobs K, Julyan M, Lubbe MS, Cockeran M. Medicine possession ratio as proxy for adherence to antiepileptic drugs: prevalence, associations, and cost implications. *Patient Prefer Adherence.* 2016 Apr; 10:539-47. doi: 10.2147/PPA.S98940. PMID: 27110104; PMCID: PMC4835143.
29. Ejelolu EU, Courage A. Prevalence and factors associated with non-adherence to antiepileptic drugs among children with epilepsy in Jos, Nigeria. *Niger J Paediatr.* 2020 Aug; 47(3):240-45. doi: 10.4314/njp.v47i3.8
30. Korkmaz MF, Erdem-Uzun M, Korkmaz M, Ekici A. Adherence to antiepileptic drugs and the health literacy of caregivers in childhood epilepsy. *P R Health Sci J.* 2020 Mar;39(1):45-50. PMID: 32383567.
31. Molugulu N, Gubbiyappa KS, Vasudeva Murthy CR, Lumae L, Mruthyunjaya AT. Evaluation of self-reported medication adherence and its associated factors among epilepsy patients in Hospital Kuala Lumpur. *J Basic Clin Pharm.* 2016 Sept-Nov;7(4):105-9. doi: 10.4103/0976-0105.189430. PMID: 27999469; PMCID: PMC5153886.
32. Wang S, Chen C, Jin B, Yang L, Ding Y, Guo Y, et al. The association of psychosocial variables with adherence to antiepileptic drugs in patients with temporal lobe epilepsy. *Epilepsy Behav.* 2017 Dec;77:39-43. doi: 10.1016/j.yebeh.2017.09.024. PMID: 29107200
33. Liu J, Liu Z, Ding H, Yang X. Adherence to treatment and influencing factors in a sample of Chinese epilepsy patients. *Epileptic Disord.* 2013 Sept;15(3):289-94. doi: 10.1684/epd.2013.0588. PMID: 23906632.
34. Mohammed H, Lemnuro K, Mekonnen T, Melaku T. Adherence to anti-seizure medications and associated factors among children with epilepsy at tertiary Hospital in Southwest Ethiopia: a cross-sectional study. *BMC Neurol.* 2022 Aug 22(1):310. doi: 10.1186/s12883-022-02842-8. PMID: 35999500; PMCID: PMC9395824.
35. Tesema AA, Ahmed I, Demeke T. Medication adherence and associated factors among patients with epilepsy at follow up clinics of Jimma town public hospitals, Jimma, South West, Ethiopia. *J Pharmacol Clin Res.* 2020 Jan;8(1):34-44. doi: 10.19080/JPCR.2019.08.555735.
36. Johnbull OS, Farouni B, Adeye AO, Ogunrin O, Uche AP. Evaluation of factors influencing medication adherence in patients with epilepsy in rural communities of Kaduna State, Nigeria. *Neuroscience and Medicine.* 2011 Dec;2(4):299-305. doi: 10.4236/nm.2011.24039.
37. Sweileh WM, Ihabesheh MS, Jarar IS, Taha AS, Sawalha AF, Zyoud SH, et al. Self-reported medication adherence and treatment satisfaction in patients with epilepsy. *Epilepsy Behav.* 2011 Jul; 21(3):301-5. doi: 10.1016/j.yebeh.2011.04.011. PMID: 21576040.
38. Desai P, Padma MV, Jain S, Maheshwari MC. Knowledge, attitudes and practice of epilepsy: experience at a comprehensive rural health services project. *Seizure.* 1998 Apr; 7(2):133-8. PMID: 9627204.
39. Modi AC, Monahan S, Daniels D, Glauser TA. Development and validation of the Pediatric Epilepsy Medication Self-Management Questionnaire. *Epilepsy Behav.* 2010 May;18(1-2):94-9. doi: 10.1016/j.yebeh.2010.03.009. PMID: 20452831; PMCID: PMC2904867.

40. Tang F, Zhu G, Jiao Z, Ma C, Wang B. Self-reported adherence in patients with epilepsy who missed their medications and reasons for non-adherence in China. *Epilepsy Behav.* 2013 Apr; 27(1):85-9. doi: 10.1016/j.yebeh.2012.12.022. PMID: 23399942.
41. Ramsey RR, Zhang N, Modi AC. The Stability and Influence of Barriers to Medication Adherence on Seizure Outcomes and Adherence in Children with Epilepsy Over 2 Years. *J Pediatr Psychol.* 2018 Mar;43(2):122-32. doi: 10.1093/jpepsy/jsx090. PMID: 29049791; PMCID: PMC5896586.
42. Modi AC, Guilfoyle SM, Rausch J. Preliminary feasibility, acceptability, and efficacy of an innovative adherence intervention for children with newly diagnosed epilepsy. *J Pediatr Psychol.* 2013 Jul; 38(6):605-16. doi: 10.1093/jpepsy/jst021. PMID: 23613481; PMCID: PMC3701128.
43. Modi AC, Guilfoyle SM, Mann KA, Rausch JR. A pilot randomized controlled clinical trial to improve antiepileptic drug adherence in young children with epilepsy. *Epilepsia.* 2016 Mar;57(3):e69-e75. doi: 10.1111/epi.13289. PMID: 26693964; PMCID: PMC4783218.

APPENDICES

Appendix A. Morisky, Green, and Levine Self-reported Medication-taking Scale¹⁸

1. Do you ever forget to take your medicine?	Yes/No
2. Are you careless at times about taking your medicine?	Yes/No
3. When you feel better do you sometimes stop taking your medicine?	Yes/No
4. Sometimes if you feel worse when you take the medicine, do you stop taking it?	Yes/No

Appendix B. Filipino-translated Morisky, Green, and Levine Self-reported Medication-taking Scale

1. Nakakalimutan mo bang uminom ng gamot??	Oo/Hindi
2. Minsan ba ay pabaya ka pagdating sa tamang pag-inom ng iyong gamot?	Oo/Hindi
3. Minsan ba ay tumitigil ka sa pag-inom ng gamot kapag bumubuti ang iyong pakiramdam?	Oo/Hindi
4. Minsan ba ay tumitigil ka sa pag-inom ng gamot kapag mas sumama ang iyong pakiramam matapos inumin ito?	Oo/Hindi

Appendix C. Questionnaire Regarding Factors That Might Affect Adherence

Code Number: _____

Edad: _____

Petsa ng huling followup: _____

1. Kasarian
 - Lalaki
 - Babae
2. Address _____
3. Antas ng pag-aaral
 - Mababang Paaralan/Grade school
 - Antas: _____
 - Mataas na Paaralan/High school
 - Antas: _____
 - Hindi nag-aaral
4. Tagapag-alaga (Piliin lahat ng akma)
 - Nanay
 - Tatay
 - Lolo/Lola
 - Iba pa: _____
5. Trabaho ng tagapag-alaga _____
6. Nakakasagabal ba ang side-effects ng gamot sa pang-araw-araw mong gawain?
 - Oo
 - Hindi
7. Ilarawan ang pakikitungo mo sa iyong Pediatric Neurologist bilang doctor. _____

8. Nararamdaman ko ang suporta ng aking doktor at mga nars sa akin at sa aking sakit.
 - Oo
 - Hindi
9. Alam ng aking pamilya na ako ay may sakit na epilepsy.
 - OoKung oo ang iyong sagot, nararamdaman ko ang suporta ng aking pamilya sa akin at sa aking sakit.
 - Oo
 - Hindi
 - Hindi

Katanungan tungkol sa Epilepsy

1. Anong klaseng epilepsy ang meron ka?
 - Generalized
 - Focal
2. Gaano katagal ka nang mayroong Epilepsy? (pumili ng isa)
 - 1 buwan
 - 2-6 buwan
 - >6 buwan-1 taon
 - 2-3 taon
 - 3-6 taon
 - >6 taon
3. Gaano kadalas ang iyong pagkukumbolsyon? (pumili ng isa)
 - 0
 - <10/taon
 - 1-2/buwan
 - 3-4/buwan
 - >4/buwan
4. Ilan ang gamot na iniinom laban sa epilepsy? (pumili ng isa)
 - 1
 - 2
 - 3 pataas
5. May mga side effects ba ang iyong gamot?
 - MeronKung meron, Ito ay ang mga sumusunod (pakisulat sa patlang): _____

 - Wala
10. Alam ng aking mga kaibigan at ibang tao na ako ay may sakit na epilepsy.
 - OoKung oo ang iyong sagot, nararamdaman ko ang suporta nila sa akin at sa aking sakit.
 - Oo
 - Hindi
 - Hindi
11. May mga bagay na hindi ko nagagawa dahil sa ako ay mayroong epilepsy.
 - OoTulad ng ano? _____

 - Hindi
12. Dahil sa COVID, may mga pagbabago kung paano ako namumuhay bilang isang taong may epilepsy.
 - OoTulad ng ano? _____

 - Hindi