

## ANTIEPILEPTIC MEDICATION ADHERENCE IN CHILDREN WITH EPILEPSY AT QUEEN RANIA AL-ABDULLAH CHILDREN HOSPITAL

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### Abstract

#### Keywords:

*Non-adherence, Epilepsy,  
Barriers, Pediatric  
patients, antiepileptic  
medication.*

Non-adherence to medication is main cause of unsuccessful drug treatment for epilepsy is due to poor adherence to prescribed medication. This study is determining the percentage of adherence to anti-epileptic medication (AED) in pediatric clinic in Queen Rania Children Hospital (QRCH); and identify the factors that affect adherence. 112 pediatric patients' diagnosis of epilepsy and initiation of antiepileptic drug therapy; age between 2 to 14 years; absence of developmental disorders or comorbid chronic illnesses requiring daily medication. Data was collected from children primary caregiver with epilepsy seen at neurology clinic at QRCH during the period January-August 2015. Medication adherence has been assessed based on self-reporting questionnaire. Utilized 8-item Morisky Medication Adherence Scale (MMAS-8).

**Conclusion:** 79.5 % of the patients display some adherence to antiepileptic medication, while 20.5% of the patients do not display adherence to their antiepileptic medication. 23 patients (20.5%) have low adherence, 56 patients (50%) have medium adherence, and 33 patients (29.4%) have high adherence. The top three reasons for non-adherence are: forget to take medication (52.2%), side effects of medications (33.8%), and being improvement and seizure free for a period (30.4%). The least rated reason for non-adherence is related to child refusal to take medication (13.1%).

### Introduction

Medication adherence is defined as "the extent to which patients follow the instructions they are given for prescribed treatments" (1). Adherence can vary from an occasional missed dose to chronic defaulting on medication regimens (2). Another definition is non-adherence in this perspective is defined as the inclination to forget, avoid, or discontinue medicine or to alter the dose from that prescribed by the healthcare provider (3). Scholars generally considered adherence is a behavioral terms (4), as it is regarded as a health-promoting behavior (2). The negative effects of non-adherence among chronically ill children include: (a) Health consequences such as increased morbidity and mortality; (b) reduced cost-effectiveness of medical care as a result of unused medications, increased clinic and emergency room visits and hospital stays; and (c) bias in clinical trials of promising therapies (5, 6,7,8)

Non-adherence to medication is widespread in chronic disease and is a major problem facing medical practice (9). The non-adherence to medication is one of the common problems that were addressed by physicians since many pediatric patients do not follow their physicians' plan. This problem may lead to many implications concerning medicine use especially in children with acute or chronic diseases. Several researchers indicated that (30%-70%) of

patients with chronic illnesses (e.g., epilepsy, asthma and diabetes) have poor adherence because of extended treatment duration, multiple medications, and periods of symptomatic remission. (1, 10, 11).

The main cause of unsuccessful drug treatment for epilepsy is due to poor adherence to prescribed medication (12,13). Non-adherence in children with epilepsy presents a potential ongoing challenge for achieving a key therapeutic goal of no seizures (14). Non-adherent patients experience an increase in the number and severity of seizures, which leads to more ambulance rides, emergency department visits and hospitalizations (15,16). This reduces the benefits that could be gained from the medication. Poor adherence may be the most important cause of poorly controlled epilepsy (17). Convulsive or tonic - clonic status epilepsy is of major concern as it is associated with a mortality rate of (5 – 15)% (14, 18, 19).

The aim of antiepileptic drug (AED) therapy is to achieve freedom from seizures. Patients fail to achieve their goals and outcomes when they fail to adhere to the drug regimen or when a less-than-adequate drug regimen is prescribed. Much of the treatment of epilepsy is aimed at creating a balance between prevention of seizures and minimization of side-effects to a level that the patient can tolerate (20). Non-adherence to antiepileptic drugs (AED) therapy was associated with a higher incidence of emergency room visits, hospital admissions, motor vehicle injuries, and fractures (21), as well as higher inpatient, outpatient, and total health care costs in adults (22). Non-adherence therefore results directly in an increase in health care costs, and reduced quality of life (23).

Treatment failure, Delayed recovery may happen when the patients discontinued their therapeutic regimen and this may lead to more suffers from illnesses, more costs and hospitalization. Poor compliance places children at risk for problems such as prolonged disease, complicates the physician-patient relationship, and prevents accurate assessment of the quality of care provided (24). because the most common cause of recurrent seizures in children with epilepsy can be traced directly to failure to adhere to the prescribed antiepileptic drug treatment, adherence to the prescribed medication plan is crucial (24). The risks of recurrent seizures include intractable epilepsy, cognitive impairment, physical injury, psychosocial problems and death (20). The treatment of epilepsy in developing countries remains far from satisfactory, mainly because of: the general lack of medical personnel, non-availability of medications; and lack of information and/or education on epilepsy for both patients and medical staff. (25,26,27).

Despite the lack of a gold standard for measuring adherence to medication, both direct and indirect measures are currently used in clinical practice (28). Although current literature reveals that perceived barriers, such as beliefs about undesirable medication effects or socioeconomic status, are associated with adherence behavior, research has not determined dependable predictors, barriers, or interventions that relate to medication adherence (29). A variety of barriers to medication adherence have been identified. Common barriers to medication adherence for children and their parents are stress, daily problems of living, and family tension (30).

Reasons for varying levels of adherence include: (a) parental lack of understanding the disease; (b) worries about the effectiveness of medications; (c) fear of medication side effects; (d) extended treatment duration; (e) multiple medications; and (f) periods of remission. For example, the parent of a child with a well-controlled seizure disorder may discontinue daily medications, hoping to prevent concerning adverse side effects. In addition, adherence to treatment may be affected by socioeconomic status, race, age, and family dynamics (31, 32,33).

The purposes of this study are: (1) determine the percentage of adherence to AED in pediatric clinic in Queen Rania Children Hospital at the Royal Medical Services (RMS) in Jordan; and (2) identify the factors the affect adherence to AED.

## Methodology

The data was collected based on self-reporting questionnaire. The researchers utilized 8-item Morisky Medication Adherence Scale (MMAS-8). The scale is composed of 8 items. Items (1-7), except item 5, are yes/no questions, where no answers receive a score of 1.0. On the other hand, 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, 6-8 is moderate adherence, and less than 6 is low adherence. Respondents who scored less than 6 were regarded as non-adherent.

Data was collected from children primary caregiver with epilepsy seen at neurology clinic at Queen Rania Children Hospital at King Hussein Medical Center (KHMC) during the period January-August 2015. Study inclusion criteria are as follows: (1) children diagnosis of epilepsy and initiation of antiepileptic drug therapy; (2) children 2 to 14 years of age; and (3) absence of developmental disorders (eg, autism, Down syndrome) or comorbid chronic illnesses requiring daily medication (eg, diabetes).

The questionnaire is broken into three parts. The first part collects demographical information about patients and their caregivers. The second part gathers data based on MMAS-8. The third part identifies the barriers for adherence. Before conducting the questionnaire, written informed consent were obtained from caregivers. Both the questionnaire and informed consent were approved by the Ethics Committee at RMS.

### Data analysis

Data was collected from 112 patients. Table (1) shows descriptive statistics for demographical information about patients and their caregivers. The mean and standard deviation of patients' age are 7.3 and 4.0 respectively. Patients were equally divided as males and females. For all patients, caregivers are their mothers. About one-third of families have an income that is less than JD500. Approximately 60% of families carry military insurance, while the remaining families maintain a civilian insurance. As indicated in Table 1, the mean and standard deviation of the duration of the disease for patients is 3.5 years and 2.3 years respectively. About one-third of patients have positive epilepsy family history (EFH), while the remaining patients gave negative family history. Number of medications for patients is as follows: 29.5% (one AED), 42% (two AED), and 28.5% (three AED). 55.4% of patients have more than 2 year's duration of AEDs, while the remaining 44.6% have less than 2 years AEDs duration. In terms of seizure frequency, 59.8% have no seizures, while the remaining 40.2% have more than one seizure during the last 3 months.

**Table 1: Descriptive statistics for demographical information about patients and their caregivers.**

Variable	Descriptive statistics
Age (Mean;SD)	7.3; 4.0
Patient Gender (N, %)	
Male	56 (50%)
female	56 (50%)
Caregiver relationship (N, %)	
Mother	112 (100%)
others	0
Family income per month (N, %)	
< 500 JD	35 (31.3%)
≥ 500 JD	77 (68.7%)
Type of insurance (N, %)	
Military	67 (59.8%)
Civilian	45 (40.2%)
Duration of disease in years (Mean, SD)	3.5; 2.3
Epilepsy Family history ( FHx) (N,%)	
Positive FHx	36 (32.1%)
Negative FHx	76 (67.9%)
Number of medications (N, %):	
1 AED	33 (29.5%)
2 AEDs	47 (42%)
≥ 3 AEDs	32 (28.5%)
Duration of AEDs (N, %):	

$\geq 2$ year	62 (55.4%)
<2 years	50 (44.6%)
Seizure frequency during the last 3 months. (N, %):	67 (59.8%)
0	45 (40.2%)
>1	

The second part of the questionnaire measures level of adherence based on MMAS-8. Out of 112 patients, 23 patients (20.5%) have low adherence, 56 patients (50%) have medium adherence, and 33 patients (29.4%) have high adherence. In total, 79.5 % of the patients display some adherence to antiepileptic medication, while 20.5% of the patients do not display adherence to their antiepileptic medication.

The third part of the questionnaire identifies the reasons for non-adherence within the low adherence group which consists of 23 patients. Table 2 lists reasons of non-adherence along with the percentage of patients. The top three reasons for non-adherence as indicated in Table 2 are: forget to take medication (52.2%), side effects of medications (33.8%), and being improvement and seizure free for a period (30.4%). The least rated reason for non-adherence is related to child refusal to take medication (13.1%). Approximately, 21.7% of non-adherent patients have been started AED 6 month before the investigation was conducted. And 26.1 % (6 patients) of non-adherence group in our study had a seizure in the last 3 months.

*Table 2: Reasons for non-adherence*

No.	Reason for non-adherence within the low adherence group	Number of patients (%)
1	Side effects of the medications.	8 (33.8%)
2	Child does not like the taste of medicine.	6 (26.1%)
3	High cost of medications.	5 (21.7%)
4	The pill is difficult for administration or difficult to swallow.	5 (21.7%)
5	Switching to different brand name makes me confused.	4 (17.4%)
6	Forget to take medication	12 (52.2%)
7	Lack of benefit.	5 (21.7%)
8	Poor medication counseling.	3 (13 %)
9	Improvement and seizure free periods	7 (30.4%)
10	Embarrassed to take medicine in front of friends or family.	5 (21.7%)
11	High frequency of medication	5 (21.7%)
12	Other things, like sport or school, get in the way of taking my medicine.	6 (26.1%)
13	The child refuses to take the medicine.	3 (13.1%)

## Discussion

Adherence to medication is regarded as a major challenge in developing countries as a result of illiteracy, ignorance, and low income. There are few studies that targeted medication adherence in developing countries (34). To fill this gap, this study investigates medication adherence in pediatric population with epilepsy in RMS.

Previous studies have shown that chronic illnesses (e.g., epilepsy, asthma and diabetes) patients who have poor adherence ranged between 30%-70% as a result of lengthy duration of treatment, multiple medications, and remission of symptoms (1, 10,11, 35, 36). Other researchers reported different percentages. For example, Hommel&Baldassano (2009) and Logan et al. (2003) indicated a non-adherence percentage ranged between 50% and 75% (35, 36). Additionally, French (1994) and Hargrave and Remler (1996) reported different ranges of adherence for adult patients (40 - 60%) and children (25 - 75%) (15,37).

In relation to our study, it shows 20.5% of non-adherence. This result is close to the results reported by Hommel&Baldassano (2009) and Logan et al. (2003) for children, which indicated a range of adherence in pediatric patient with epilepsy between 50% and 75%. (35,36). Our results are also consistent with the study conducted by Modi et al. (2011), who indicated that non-adherence rates in pediatric with epilepsy are between 12% and 35% based on cross-sectional studies using self-reporting (38).

Our study reflected that 29.46% of pediatric patient have a high adherence to antiepileptic medication. This result is close to the results of Miner et al. (2013), who showed that only 28% of the respondents reported complete adherence (39).

Approximately, 26.1 % of non-adherence group in our study had a seizure in the last 3 months. This result is close to the work conducted by Stanaway et al. (1985), who found that 31% of seizures were precipitated by non-adherence to AED medication (40)

In our study, we found that only 21.7% of non-adherent patients have been started AED 6 month before the investigation was conducted. This result is different than the one reported by Modi et al. (2011), who found that 58% of the newly diagnose children with epilepsy have demonstrated non-adherence to the AEDs over the first 6 months of therapy (32). Another study by Asato et al. (2009) indicated that 35% of adolescents reported that they were not adherent to antiepileptic medications during the month which precedes the study (41).

This study investigated the top reasons for non-adherence to AED medications. Parents' forgetfulness to give medications to their children is ranked first with 52.2%. This result is close to the one reported by Liu et al (2013), who also found that forgetfulness was the primary cause of non-adherent by 69.6% (42). Another study by Wael M. et al (2015) found that forgetfulness is the most common cause of non-adherence among a group of adolescent patients (43). Additionally, a self-reported study conducted in china by Tang F. et al (2013) indicated that forgetfulness by 54.2% is the main reason for non-adherence (44). However, Nazziwal et al. (2014) reported a lower percentage of 29.7% for forgetfulness (45).

The second ranked reason for non-adherence in our study is fear of medication side effects by 33.5% of patients. This result is close to the one reported by Tang et al. (2013), who indicated 27.5% (45). However, both studies are drastically different in this regard compared to Lin et al. (2013) study, which reflected only 5.4% for medication side effects (46).

The third ranked reason for non-adherence in this study is being seizure free by 21.7% of patients, which is less than half the result reported by Tang et al. (2013), who indicated 48.2% (45).

## Conclusion

Adherence to the prescribed medication plan is crucial in pediatric patient with epilepsy to be seizure free. Our study pediatric groups with epilepsy have shown unacceptable adherence to antiepileptic medication by 79.5 %. The top three barriers that effect the adherence, first parents forgetfulness to give medication to their children, second is the side effects of medications, and third being improvement and seizure free for a period. Parents need more supportive and explore different ways to increase the adherence by using different methods like medication organizer or alarm. A routine and periodic evaluation of medication adherence, identification the barriers for non-adherence in pediatric population, and feedback from parents is essential.

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