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1 **Self-reported attitudes about medication in Lebanese people with epilepsy**

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13
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16 Figure 1: Percentages of 4-MMAS answers and adherence score

17 Table 1: Description of the study population

18 Table 2: Description of health status and history of epilepsy

19 Table 3: Comparison of people with epilepsy with positive and negative attitudes towards
20 medication

21 Table 4: Final results of regression using the status of attitudes as the dependent variable

22 Table 5: Final results of regression using the seizure control as the dependent variable

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31 Abstract

32 Background: Epilepsy is a common worldwide neurological disorder. For people with epilepsy, adherence
33 and attitudes towards medication is a crucial step to improve efficacy of prescribed treatment and to
34 prevent seizures.

35 Objectives: The first aim of this study was to evaluate attitudes towards antiepileptic medications in
36 Lebanese population. Secondary aims were to assess factors affecting attitudes and associated with
37 epilepsy control.

38 Material and Methods: A cross-sectional study was conducted in out-patients neurology clinics located in
39 Beirut-Lebanon. Data was collected using a structured questionnaire. Self-report of medication taking
40 behaviors were assessed using the abbreviated (4-items) Morisky Medication Adherence Scale (MMAS-
41 4). Epilepsy was considered as controlled if the patient had no seizures in the last 6 months.

42 Results: Among 250 people with epilepsy (PWE) recruited in this study, male-to-female ratio was 0.87
43 (116/134), and 50.8% were married. Mean duration of epilepsy was 13.7 ± 12.8 years. Valproate was the
44 most common antiepileptic drug used followed by levetiracetam and carbamazepine. About 60.8% of the
45 population presented partial epilepsy. Uncontrolled epilepsy was present in more than half of participants
46 (55.2%), with only 32.4% had positive attitudes to their medication. Positive attitudes towards
47 antiepileptic increased in people who found their treatment was efficacious (OR=4.9; 95%CI 1.2-20.0;
48 $p=0.03$), who had controlled epilepsy (OR=3.4; 95%CI 1.6-7.1; $p=0.001$), and who were diagnosed as
49 people with epilepsy between the age of 12-20 years (OR=3.1; 95%CI 1.1-8.4; $p=0.03$). Oppositely, these
50 attitudes decreased in participants who felt their treatment as an economic burden (OR=0.2; 95%CI 0.1-
51 0.4; $p<0.001$), and in depressive people (OR=0.4; 95%CI 0.2-0.9; $p=0.04$). Controlled epilepsy was
52 higher in people who contacted a neurologist if seizure occurred, in people with positive attitudes, and
53 after a long duration of disease, but it decreased if patient didn't follow neurologist's instructions in
54 fasting period.

55 Conclusions: Lebanese PWE were less likely to have positive attitudes towards medication, which may
56 lead to poor epilepsy control. Depression and economic burden were the major factors decreased these
57 attitudes. Identifying factors affecting attitudes to medication and leading to controlled epilepsy may help
58 clinicians to elaborate educational programs to optimize medication adherence.

59

60 Keywords: Epilepsy; Attitudes; Behaviors; Antiepileptic drug; Lebanon.

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64

65 1. INTRODUCTION

66 Epilepsy is a neurological chronic disorder that affects almost 70 million people of all ages
67 worldwide, of whom 85% live in developing countries [1]. According to the International League
68 Against Epilepsy (ILAE), epilepsy is a brain disease defined by at least two unprovoked (or
69 reflex) seizures occurring more than 24 hours apart [2]. Epilepsy treatment gap is defined as
70 frequency of people with active epilepsy who need treatment but don't receive it [3,4], exceeded
71 75% in most low-income countries and in rural regions [5,6].

72 Antiepileptic drugs (AED) are essential to control epilepsy, and are able to reduce seizures
73 frequency in almost 67% of people with epilepsy (PWE) [7]. Despite a large number of AED
74 present to date, low adherence and negative attitudes lead to failure of treatment. Studies showed
75 that non-adherence to antiepileptic medication was associated with poor seizure control [8].

76 Many studies showed that worse attitudes and non-adherence proportions among PWE were
77 similar to other chronic diseases and ranged between 30% and 50% [9–13]. Lack of adherence to
78 AED might lead to therapeutic failure, poor quality of life, and increase in the risk of seizures
79 recurrence [8,14,15]. Patients' non-adherent having negative attitudes towards drugs present
80 uncontrolled epilepsy, and are at higher risk of status epilepticus (prolonged seizures) [16]. As a
81 result, number of hospital admissions, healthcare costs, rate of morbidity and mortality increase
82 [17–22]. Furthermore, the risk of sudden unexpected death in epilepsy (SUDEP) is higher in non-
83 adherent PWE [23].

84 Based on these consequences, identifying the barriers to patient's attitudes towards AED is
85 considered essential for clinicians to develop strategies in order to improve attitudes to medication
86 in PWE [11]. Some known factors are unmodifiable by a neurologist in treatment strategy, such as
87 age of disease onset, epilepsy etiology (symptomatic, idiopathic, and cryptogenic), and location of

88 epileptogenic zone (partial or generalized) [10]. The other modifiable factors are socio-economic
89 factors, health care factors, comorbidities, cultural beliefs about epilepsy, frequency of seizures,
90 treatment management, adverse events of AED, type/ frequency of medication use, cost of
91 treatment and forgetfulness [23,24]. These factors can be controlled, and health care providers
92 should resolve these problems to improve patient's attitudes to treatment.

93 A literature review showed that multiple factors that influence medication adherence worldwide.
94 But, very few published studies evaluated attitudes to medication among PWE in Arab countries.
95 Two countries (Saudi Arabia and Palestine) have evaluated adherence to AED [10,25]. More
96 studies are necessary to detect these factors among Arabic people who present some specific
97 habits, attitudes and cultures [10].

98 For this purpose, this study aims firstly to evaluate attitudes towards antiepileptic medications in
99 Lebanese population, and secondary to assess factors affecting attitudes and associated with
100 epilepsy control.

101

102 **2. MATERIAL AND METHODS**

103 **2.1. Study design**

104 A cross-sectional study was conducted in outpatient neurologic clinics of three tertiary care
105 hospitals, two medical centers and ten private neurologic clinics located in Beirut-Lebanon. Beirut
106 is the capital and largest city of Lebanon. Greater Beirut is generally considered as a growth of
107 Beirut city and its peripheral areas (suburbs). These areas are urbanized and considered densely
108 populated

109 This survey was carried out over a period of 6 months from February 1st, 2018 to July 30th, 2018.
110 The clinics included in this study are visited by PWE from different Lebanese regions. The list of
111 neurologists was obtained from Lebanese Order of Physicians.
112 The estimated sample size was 217 patients (with a 95% confidence interval (CI), and a 5%
113 precision error [26]) based on a previous published study using Morisky scale and reporting that
114 only 17% of Lebanese patients with chronic diseases were adherent to their treatment [27].
115 Lebanese outpatients above 18 years of age, diagnosed with epilepsy by a neurologist, and taking
116 at least one AED for at least one month were included in the study.
117 Participants who had mental retardation or intellectual disability, who were newly diagnosed with
118 epilepsy (adherence of patient who didn't take AED for at least 4 weeks can't be evaluated),
119 presented non-epileptic psychogenic seizures, who were taking AED for neuropathic pain, and
120 pregnant women were not included. Also, participants who didn't give written consent to
121 participate in the study were not included.

122

123 **2.2. Data collection**

124 Data was collected using a structured questionnaire prepared at first in English, and then presented
125 in Arabic, the local language, to facilitate comprehension for patients.
126 It was translated into Arabic Language by two independent translators. A back translation to
127 English was done by another bilingual translator, who was not included in developing the initial
128 version. The original Arabic version and the back translated English version were compared to
129 resolve any inconsistency. A pilot study was done with 20 PWE to identify any problem in
130 comprehension. These participants were not included in the final sample of the study.

131 The questionnaire was divided into six sections. Demographic data, natural history of
132 epilepsy/etiology, and treatment were parts used from standardized questionnaire for investigation
133 of epilepsy in tropical countries [28].

134 - Socio-demographic characteristics: age, gender, height and weight, region of residence,
135 education level, occupation, marital status, number of workers/family, presence of medical
136 insurance.

137 - History of epilepsy: duration of epilepsy, age of disease onset, family history, seizures in last 5
138 years, seizure control, seizure type, and etiology.

139 - Treatment: type of AED, number of AED, number of pills/day, frequency of administration,
140 reason for discontinuing treatment, appearance of side effects and its type (such as tiredness,
141 nervousness, headache, skin's problem, hair loss, weight gain/loss, blurred vision, upset stomach,
142 difficulty in concentrating, depression, disturbed sleep)[29], and measure serum level of AED.

143 - Health status: presence of comorbidities (any chronic disease other than epilepsy), and
144 medication history.

145 - Self-report of medication taking behaviors were assessed using the abbreviated (4-items)
146 Morisky Medication Adherence Scale (MMAS-4).

147 - General behaviors and attitudes towards medication: in absence/occurrence of seizures, in
148 fasting/busy periods, if side effects appear, if no money/health coverage, if any neighbor's patient
149 advices to stop medication, if participant forget to take medication, frequency of neurology visits,
150 follow healthcare provider instruction, efficacy of treatment approved by participant, and if a
151 treatment was an economic burden. These variables were not considered by MMAS-4. Data
152 collection was done by a bilingual, Arabic native investigator using a face to face interview with
153 PWE. All PWE attending neurology clinics and fulfilling inclusion criteria were included in this

154 study. The interviewer checked the patient's file to confirm diagnosis and inclusion criteria before
155 taking written informed consent. Data concerning history of epilepsy, medication and health status
156 was extracted from patient's file. The questionnaire was completed for all patients by a unique
157 investigator during a 15 minutes face to face interview, during the patient's visit to the
158 neurologist's clinic. The same questions were asked in the same manner and tone in Arabic to all
159 patients to facilitate direct understanding.

160

161 **2.3. Definition of dependent variables**

162 In this study, seizure control was defined as studies done in Brazil and UK [30,31]. Epilepsy was
163 arbitrarily classified as controlled if the patient had no seizures in the last 6 months and
164 uncontrolled if he/she had at least one seizure in the last 6 months.

165 The MMAS-4 is a standardized validated questionnaire, used in this study to evaluate and reflect
166 general health behaviors toward AED therapy. This structured self-report consists of 4 items with
167 four "yes/no" questions [32,33].

168 Based on previous studies [10,30,34], each item is coded 0 if the answer is "Yes" and 1 if "No". A
169 score can range from 0 to 4. Patients who had a score = 4 were considered adherent having
170 positive attitudes towards AED and who had a score <4 were considered non-adherent having
171 negative attitudes. The adherent state was considered for a patient responding "No" to all 4
172 questions and this reflects positive attitudes. However, if one response was "Yes", a patient was
173 considered non-adherent with negative attitudes. Cronbach's alpha was measured to evaluate
174 reliability of the translated Arabic scale in this study. It was 0.705, which indicates a high level of
175 internal consistency for a scale in this sample.

176

177 **2.4. Data analysis**

178 Statistical analysis was done with the Statistical Package for the Social Sciences (SPSS) software,
179 version 20. Descriptive analysis was used to describe qualitative (by frequency and percentage)
180 and quantitative (by mean and standard deviation) variables. Comparative analysis was carried
181 using Pearson's chi-square test or Fisher's exact test to report significant differences for
182 qualitative variables between PWE with positive and negative attitudes. Student's t-test was used
183 to compare the means between positive and negative attitudes groups. Variables having p-value
184 <0.2 were included in the multivariate model. Backward logistic regression was done to determine
185 predictors affecting attitudes to treatment and controlled epilepsy. The variable "Attitudes towards
186 AED" was dichotomized into a dependent variable as "Positive/ Negative", and seizure control
187 into "Controlled/ Uncontrolled". Statistical tests were considered significant with a p-value <0.05
188 and a confidence interval of 95%.

189

190 **3. RESULTS**

191 **3.1. Socio-demographic and clinical characteristics**

192 Two hundred fifty patients were recruited, with an average age of 40.2 (± 14.8) ranging from 18 to
193 85 years. More than half of PWE (53.6%) were females and lived in Beirut (62.0%). The majority
194 of the participants were unemployed (52.4%). Around quarter of this population (24.8%) have
195 never been to school (Table 1).

196 Of all the participants, 56.8% had comorbidities, where hypertension and heart problems (cardiac
197 insufficiency/ arrhythmia/ atrial fibrillation) were the most common (24.0%) followed by
198 depression and anxiety (12.8%). Seventy-six patients (30.4%) had a family history of epilepsy.
199 The mean duration of epilepsy was 13.7 years (± 12.8). More than half of PWE (55.2%) had an

200 uncontrolled epilepsy. The majority of population (61.6%) presented partial epilepsy, with
201 symptomatic etiology in 57.6% of cases. Monotherapy was prescribed in 60% of PWE; Valproic
202 acid (50.0%), levetiracetam (26.4%), and carbamazepine (23.6%) were the most common AED
203 prescribed. More than half of participants (58.0%) didn't take their medication daily, due to
204 several reasons, including forgetfulness (37.9%), medication cost (13.1%), unavailability of drugs
205 (13.1%), or absence of seizures (13.1%). Side effects of AED affected 57.2% of PWE (Table 2).

206

207 **3.2. Attitudes towards antiepileptic drugs**

208 More than half of the patients (56.0%) said they forgot to take their AED. Thereby, within the
209 remaining some patients were classified non-adherent having negative attitudes because they had
210 stopped taking medication if they felt better (30.4%) or worse (20.4%). However, only 32.4% of
211 the study population were considered having positive attitudes to antiepileptic medication based
212 on the sum of MMAS-4 score (Figure 1).

213

214 **3.3. Comparative analysis between PWE with positive and negative attitudes towards** 215 **medication**

216 Regarding disease history, uncontrolled epilepsy was found in 44.4% of PWE with positive
217 attitudes to AED compared to 60.4% of PWE with negative attitudes ($p=0.02$). Forgetfulness was
218 the main reason for stopping medication in 32.5% of PWE with negative attitudes compare to no
219 PWE having positive attitudes group. Experience of side effects was higher among PWE having
220 negative attitudes (65.1%) than others (40.7%) ($p<0.001$). Measure of the serum level of AED was
221 done by 76.8% of PWE having positive attitudes compare to. 31.3% of PWE with negative

222 attitudes ($p < 0.001$). Depression was significantly higher ($p = 0.04$) among PWE with negative
223 attitudes (27.8%) than in those who had positive attitudes (16%).

224 As for the patient's behaviors, 17.2% of PWE with negative attitudes forgot to take medicine
225 compare to 7.4% of PWE with positive attitudes in a busy period. A proportion of 38.5% of PWE
226 having negative attitudes could not buy treatment compared to 23.5% of PWE having positive
227 attitudes due to a lack of money or no health coverage. In fasting period, 44.4% of PWE with
228 positive attitudes increased time between 2 doses ($>12h$) compare to 26% of others Also,
229 increasing dose when seizure occurs ($p = 0.02$), stopping medication in seizure-free period or when
230 side effects appear ($p < 0.001$), and skipping doses in fasting period ($p = 0.003$) were factors which
231 significantly differed between 2 groups of PWE with positive and negative attitudes (Table 3).

232

233 **3.4. Factors affecting attitudes towards antiepileptic medications**

234 This study showed that seven factors predict patient's attitudes. Efficacy of treatment was an
235 important predictor (OR=4.9; 95%CI 1.2-20.0; $p = 0.03$). Controlled epilepsy also increased the
236 odds of having positive attitudes (OR=3.4; 95%CI 1.6-7.1; $p = 0.001$). Onset of epilepsy at age
237 between 12-20 years was a factor leading to increased positive attitudes, compared to onset at age
238 <12 years (OR=3.1; 95%CI 1.1-8.4; $p = 0.03$).

239 While, patient's positive attitudes decreased in participants who thought that their treatment was
240 an economic burden (OR=0.2; 95%CI 0.1-0.4; $p < 0.001$), depressive PWE (OR=0.4; 95%CI 0.2-
241 0.9; $p = 0.04$), who visited their neurologist clinics every year (OR=0.2; 95%CI 0.04-0.5; $p = 0.002$)
242 or every few years (only when a seizure occurs) (OR=0.2; 95%CI 0.1-0.7; $p = 0.01$), and in older
243 people (OR=0.97; 95%CI 0.94-0.99; $p = 0.02$) (Table 4).

244

245 **3.5. Factors affecting controlled epilepsy**

246 In this study, controlled epilepsy was higher in people who contact a specialist if seizure occurs
247 (OR=2.9; 95%CI 1.3-6.5; p=0.01), in PWE who had positive attitudes towards AED (OR=1.9;
248 95%CI 1.1-3.4; p=0.03), and after a long duration of disease (OR=1.04; 95%CI 1.02-1.07;
249 p<0.001). However, risk of controlled seizures decreased if patient didn't follow neurologist's
250 instructions in fasting period (OR=0.5; 95%CI 0.3-0.9; p=0.03) (Table 5).

251

252 **4. DISCUSSION**

253 Only 32.4% of PWE presented positive attitudes to AED, similar to a study from Ethiopia [9], but
254 lower than findings in other countries such as Palestine (36.0%) [25], England (41.0%) [35], Lao
255 (57.6%) [36], and Saudi Arabia (61.7%) [10]. This variation between countries could be due to
256 different habits, behaviors, cultures between populations [10].

257 Four indirect methods are used to measure medication adherence in the outpatient setting [37]:
258 Self report, electronic medication monitoring, pharmacy refill rates and pill counts.

259 Electronic medication-measurement systems are expensive and rarely available in the outpatient
260 setting. Pharmacy refill rates is not applicable because drugs (AED included) in Lebanon are
261 delivered without prescription and do not require a renewal of prescription at every purchase.
262 Also, it was difficult to count number of pills and to compare with the total number of pills
263 received by a patient because the patient was seen only once, and did not carry his pills during his
264 neurologist's visit. So we chose MMAS-4, a simple and economical self-reporting method.

265 A study conducted in essential hypertension established the concurrent and predictive validity of
266 MMAS-4 regarding blood pressure measurements recorded throughout a 3-year follow-up period

267 [32]. This self-reporting method is used for different chronic diseases, epilepsy included, in
268 several countries and populations [9,10,25,30,35,36].

269 However, a comparison with studies using other methods to evaluate adherence shows that a low
270 percentage of adherence was more present in studies using subjective methods such as MMAS. In
271 studies using MMAS to estimate adherence in PWE, percentage of adherence ranged between
272 20% and 55% [30,35,36,38]. However, objective measures such as a medication possession ratio,
273 which definition and estimation differ between studies, show that adherence varied between 50%
274 and 65% [12,17,19,39,40]. In addition, a therapeutic drug concentration monitoring in prospective
275 studies show that adherence to medication was around 60% [41,42].

276

277 This study identified three key factors that increase positive attitudes in PWE. These attitudes
278 were present in people who had good perception toward AED, and who were correctly motivated
279 [43]. The PWE who were satisfied and felt that treatment was effective had more positive attitudes
280 in this population.

281 Controlled epilepsy is a factor leading to increased positive attitudes in this study. When epilepsy
282 is controlled, adherence and positive health behaviors to AED increased. This is in agreement with
283 other studies [15,30].

284 Attitudes to medication were also associated with age of epilepsy onset. People diagnosed as
285 epileptic at adolescence (12-20 years) had more positive attitudes than those diagnosed during
286 childhood (<12 years). Adolescents were more able to follow instructions of neurologists, and
287 learn more about their disease and treatment. In pediatric patients, parents have a critical role to
288 improve adherence. However, they may tend to be fearful and stressed, this may negatively affect
289 attitudes to AED [44].

290 Oppositely, positive attitudes to medication decreased by four factors. Positive attitudes were
291 lower in PWE who felt that their treatment was an economic burden, similar to another study
292 conducted in Ethiopia [45]. Cost of medications was found to be a big burden due to absence of
293 health coverage for some Lebanese people

294 Depressive PWE were less adherent with negative attitudes to AED. Another study showed also a
295 significant correlation between medication adherence and depressive status [46].

296 PWE who visit neurologist clinic only every year or every few years had less positive attitudes.
297 Patient education about the disease and treatment is essential to resolve patient distress and
298 improve patient's attitudes to medication [15,47].

299 Positive attitudes towards antiepileptic medications decreased in older age. In Ethiopia, older
300 PWE were less adherent with negative attitudes [9], in agreement with another study done in
301 China that reported the same association [8]. Older people present physical difficulties and
302 cognitive problems making it difficult to follow healthcare provider's instructions [48]. However,
303 presence of other comorbidities, complexity of treatment regimen, and multiple daily dosing
304 decreased also adherence [44].

305 The reasons for discontinuation of treatment in this study included forgetfulness, high medication
306 cost, adverse effects, unavailability of drugs, inefficacy of treatment and absence of seizures.

307 Forgetfulness was the main reason for non-adherence and discontinuing treatment in this study.
308 This was reported also in other studies [8,9,49,50], which found that forgetfulness was the key
309 reason for being non-adherent. Most people may forget to take medication when they are busy at
310 work, away from their home or while travelling. High cost of drugs was significantly associated
311 with decreased adherence, similar to a study done in China [8]. PWE who experienced adverse
312 effects of AED had negative attitudes. A common cause for stopping antiepileptic treatment, and

313 limiting adherence without consulting neurologist was adverse effects [8,51]. PWE who stop
314 taking their medication when the drug is not available had negative attitudes than those who
315 didn't. Thus, the inability to obtain treatment in this population leads to decreased adherence and
316 positive attitudes to medication. The Lebanese government should provide and preserve the
317 required drugs in the public sector at any time in a better manner. Participants who had negative
318 beliefs about their treatment were significantly non-adherent to AED. This negative perception
319 was probably due to treatment failure and recurrence of seizures. These results were similar to
320 another study conducted in UK [12].

321

322 Controlled epilepsy was positively associated with adherence and positive attitudes to AED. A
323 reciprocal significant association was found between patient's attitudes and controlled epilepsy,
324 where low medication adherence and negative attitudes showed to be also a cause for uncontrolled
325 epilepsy, similar to results in other studies [14,52,53]. Precisely, PWE who stop treatment are
326 more likely to have uncontrolled epilepsy. This suggests that evaluation of adherence can predict
327 epilepsy outcome.

328 Duration of epilepsy was a factor affecting controlled epilepsy. PWE who were diagnosed as
329 epileptics since long time were more likely to have controlled epilepsy. Seizures may take longer
330 time to become controlled. Long duration leads to adaptation for this disease, and then improved
331 adherence. In Nigeria, PWE were more likely to have controlled epilepsy when they are in older
332 age [54].

333 However, controlled epilepsy decreased if patient didn't follow neurologist's instructions in
334 fasting period. Some research was carried out on PWE during the fasting month. During this
335 period, only two meals are consumed per day, separated by a fasting time of 11 to 18 hours

336 depending on season [55]. A study done in Turkey showed that some of PWE had more seizures
337 during fasting month. This increase was probably due to changes in the way epilepsy medicine
338 were taken, sleep patterns being disturbed, and going for a long time without food [55]. For this,
339 PWE should follow neurologist's instructions in fasting period such as adapting posology and
340 prescribing extended-release drugs taken once a day.

341

342 This study was the first to evaluate attitudes to antiepileptic medications in Lebanese PWE, and
343 one among few studies done in the Arab world which has its specific culture and behaviors.
344 However, due to a lack of studies in Arab countries, we didn't have enough data to compare our
345 findings.

346 With a cross-sectional design, it is impossible to establish causal relationship. Some recall bias
347 may be present due to the fact that self-report was the method used to evaluate behaviors towards
348 medication. Self-report is the most practical method in the outpatient setting, but it tends to
349 overestimate responses compared to the objective methods. In addition to this, the overestimation
350 of acceptable responses may be due to the fact that the questionnaire was completed by the
351 investigator and not privately by the patient. This study evaluated medication problems related to
352 treatment acceptance and patient's attitudes towards medications; all people accepted to take AED
353 but a low level of positive attitudes was found.

354 Participants were recruited from neurology clinics due to necessity of accurate diagnosis, but
355 selection bias may be present. However, to reduce selection bias, and to be more representative,
356 PWE were recruited from different health structures (private clinics, clinics in hospitals, and
357 clinics in medical centers). Those health structures allow people from all economic stages to
358 access neurologists' consultation. Since PWE were recruited from neurologists' clinics, a high

359 level of adherence was expected; however, low adherence was found. This approves diversity of
360 PWE recruited and reduces the risk of recruitment bias.

361 A longitudinal prospective study will be necessary to focused on people who discontinue their
362 medication after a long-time treatment. Persistence of adherence during a follow-up period could
363 be evaluated in future studies.

364

365 **5. CONCLUSIONS**

366 Lebanese PWE were less likely to have positive attitudes towards antiepileptic medications,
367 which may lead to poor epilepsy control. The positive attitudes of PWE are cornerstone to
368 improve epilepsy treatment, prevent recurrence of seizures, reduce the risk of hospitalization and
369 improve quality of life. Diagnoses followed by pharmacological treatment are not enough in
370 epilepsy management. Thus, evaluation of patient's attitudes is essential in clinical practice, and
371 should be a base in treatment management to predict epilepsy control.

372 Depression, economic burden and visiting neurologist's clinic every year or every few years
373 predicted negative attitudes towards antiepileptic medications in our study. Non-respect of
374 recommendations to neurologist leads in turn to uncontrolled epilepsy. Depressive people should
375 be managed effectively by a specialist. Prescribing generic drugs with affordable costs and
376 having access to a better social security systems in Lebanon are needed to provide medication to
377 patients with no health insurance and thereby limit the economic burden felt by PWE. Contact
378 neurologist and follow his recommendations in case of seizure occurrence or during fasting
379 periods were necessary to control epilepsy.

380 Educating PWE and their families about disease and treatment management, adapting simple
381 medication regimens by neurologists (such as monotherapies to reduce number of pills, and

382 extended-release drugs to reduce frequency of dosing), ensuring a good relationship between
383 PWE and healthcare professionals, and attending regularly to appointments, are important for
384 attaining good adherence to treatment. In fact, using easy reminders to take medications (pill
385 reminder boxes, calendars, alarms, watches with beeper alarms, caregivers reminder) is important
386 to optimize medication adherence and enhance positive attitudes for PWE. Educational programs
387 about the disease and treatment are also necessary for attaining good attitudes towards medications
388 for PWE.

389

390 **CONFLICT OF INTEREST**

391 There is no conflict of interest.

392

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396

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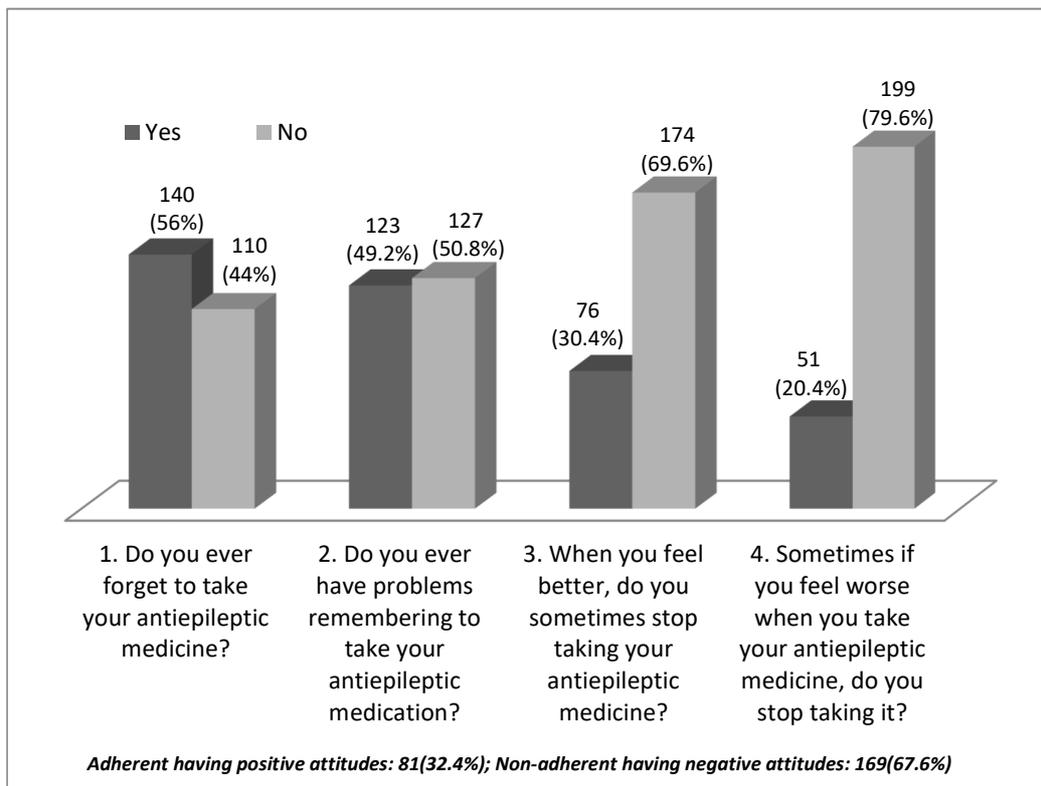


Fig.1. Percentages of 4-MMAS answers and adherence score

Table 1. Description of the study population

Variables		n (%) / Mean \pm SD ¹
Sex	Females	134 (53.6)
Region of residence	Beirut	155 (62.0)
	South	30 (12.0)
	Mount Lebanon	21 (8.4)
	Bekaa	33 (13.2)
	North	7 (2.8)
	Outside Lebanon	4 (1.6)
Body mass index (BMI)²	Underweight (BMI<18.5 kg/m ²)	7 (2.8)
	Normal weight (BMI \geq 18.5 kg/m ²)	105 (42.0)
	Overweight (BMI \geq 25 kg/m ²)	103 (41.2)
	Obese (BMI \geq 30 kg/m ²)	35 (14.0)
Education level	Illiterate	62 (24.8)
	Elementary	60 (24.0)
	Intermediate	41 (16.4)
	Secondary	32 (12.8)
	University	55 (22.0)
Occupation	Unemployed	131 (52.4)
	Employed/Self-employed	97 (38.8)
	Shepherd/ Farmer	3 (1.2)
	Student	19 (7.6)
Marital status	Single lives alone	11 (4.4)
	Single lives with family	75 (30.0)
	Married	127 (50.8)
	Divorced	22 (8.8)
	Widowed	15 (6.0)
Medical Insurance		138 (55.2)
Age		40.2 \pm 14.8
BMI		25.8 \pm 6.0
Number of workers/ family		1.4 \pm 1.1

¹ SD: Standard deviation; ² World Health Organization (WHO). Global Database on Body Mass Index

Table 2. Description of health status and history of epilepsy

Variables	Mean \pm SD ¹ / n (%)
Duration of epilepsy	13.7 \pm 12.8
Age of epilepsy onset	26.5 \pm 18.8
Family history of epilepsy	76 (30.4)
Presence of seizures in last 5 years	195 (78.0)
Seizure control	
Uncontrolled (at least one seizure in last 6 months)	138 (55.2)
Controlled (no seizure in last 6 months)	112 (44.8)
Presence of comorbidities	142 (56.8)
Type of Comorbidities	
Hypertension / Cardiac problems (cardiac insufficiency/ arrhythmia/ atrial fibrillation)	60 (24.0)
Dyslipidemia	29 (11.6)
Respiratory diseases (Asthma or COPD ²)	9 (3.6)
Angina	7 (2.8)
Kidney disease	4 (1.6)
Gastrointestinal disease	24 (9.6)
Diabetes	21 (8.4)
Thyroid disease	19 (7.6)
Cerebrovascular Accident	11 (4.4)
Depression/ Anxiety	60 (24.0)
Psychosis/ Schizophrenia	32 (12.8)
Migraine	13 (5.2)
Cerebral Tumor	7 (2.8)
Other Comorbidities (Parkinson, osteoporosis, rheumatological disease...)	9 (3.6)
Seizure type	
Simple partial	50 (20.0)
Complex partial	73 (29.2)
Secondary generalized	31 (12.4)
Generalized tonic clonic	80 (32.0)
Generalized myoclonic	11 (4.4)
Generalized atonic	3 (1.2)
Absence	28 (11.2)
Others	1 (0.4)
Epilepsy etiology	
Idiopathic	20 (8.0)
Cryptogenic	86 (34.4)
Symptomatic	144 (57.6)
Type of AE³ medication	
Benzodiazepines	36 (14.4)
Phenytoin	19 (7.6)
Phenobarbital	11 (4.4)
Carbamazepine	59 (23.6)
Valproate	125 (50.0)
Lamotrigine	27 (10.8)
Levetiracetam	66 (26.4)
Oxcarbazepine	12 (4.8)
Topiramate	22 (8.8)
Lacosamide	12 (4.8)
Perampanel	1 (0.4)
AE therapy	
Monotherapy	150 (60.0)
Bitherapy	67 (26.8)
>2 antiepileptic medications	33 (13.2)
Taking AED daily	105 (42.0)
Main reason for stopping medication	
Forgetfulness	55 (37.9)
High cost	19 (13.1)
Complexity of treatment regimen	11 (7.6)
Experience of side effects	12 (8.3)
Unavailability of drugs	19 (13.1)
Perception of inefficacy	10 (6.9)
Absence of seizures	19 (13.1)
Experiencing of side effects	143 (57.2)

¹SD: Standard deviation; ²Chronic Obstructive Pulmonary Disease; ³Antiepileptic

Table 3. Comparison of people with epilepsy with positive and negative attitudes towards medication

Variables	n (%)		p-value	
	Negative attitudes	Positive attitudes		
Seizure control	Controlled	67 (39.6)	45 (55.6)	0.02
	Uncontrolled	102 (60.4)	36 (44.4)	
Age onset disease	<12 years	44 (26.0)	16 (19.8)	0.02
	12-20 years	31 (18.3)	27 (33.3)	
	20-40 years	54 (32.0)	15 (18.5)	
	>40 years	40 (23.7)	23 (28.4)	
Measure serum level of AED if specialist prescribe this	No	90 (68.7)	13 (23.2)	< 0.001
	Yes	41 (31.3)	43 (76.8)	
When a seizure occurs	Double a dose	40 (23.7)	8 (9.9)	0.02
	Continue treatment normally	64 (37.9)	31 (38.3)	
	Contact a specialist	65 (38.5)	42 (51.9)	
In stable status (absence of seizures)	Stop medication	49 (29.0)	0	< 0.001
	Reduce a dose	33 (19.5)	2 (2.5)	
	Continue treatment normally	87 (51.5)	79 (97.5)	
In fasting period	Not fasting	61 (36.1)	30 (37.0)	0.003
	Skip or reduce a dose to 2 daily doses instead of 3	33 (19.5)	11 (13.6)	
	Increase the time between 2 doses (>12h)	44 (26.0)	36 (44.4)	
	Take all doses together	31 (18.3)	4 (4.9)	
If side effects appear	Stop medication	47 (27.8)	4 (4.9)	< 0.001
	Continue treatment normally	35 (20.7)	13 (16.0)	
	Contact a specialist	69 (40.8)	62 (76.5)	
	Contact a pharmacist	18 (10.7)	2 (2.5)	
If a patient is in busy period (at work, away from home, in outdoor dinner/ lunch or in travel), he forget his medication	No	140 (82.8)	75 (92.6)	0.04
	Yes	29 (17.2)	6 (7.4)	
If no money/ health coverage, patient buys his medication	No	65 (38.5)	19 (23.5)	0.02
	Yes	104 (61.5)	62 (76.5)	
If a neighbor of patient advices him, he stop medication	No	146 (86.4)	77 (95.1)	0.04
	Yes	23 (13.6)	4 (4.9)	
Frequency of neurologist clinic visits	Every month	24 (14.2)	15 (18.5)	< 0.001
	Every 3-6 months	42 (24.9)	40 (49.4)	
	Every year	50 (29.6)	14 (17.3)	
	Every few years (when a seizure occur)	53 (31.4)	12 (14.8)	
Experience of side effects	No	59 (34.9)	48 (59.3)	< 0.001
	Yes	110 (65.1)	33 (40.7)	
Following healthcare provider instructions	No	63 (37.3)	8 (9.9)	< 0.001
	Yes	106 (62.7)	73 (90.1)	
Main reason for stopping medication	Forgetfulness	55 (42.0)	0	< 0.001
	High cost	18 (13.7)	1 (7.1)	
	Complexity of treatment regimen	11 (8.4)	0	
	Experience of side effects	12 (9.2)	0	
	Unavailability of drugs	9 (6.9)	10 (71.4)	
	Perception of inefficacy	8 (6.1)	2 (14.3)	
	Absence of seizures	18 (13.7)	1 (7.1)	
Participant is satisfied and feels his treatment effective	No	70 (41.4)	3 (3.7)	< 0.001
	Yes	99 (58.6)	78 (96.3)	
Participant feels his treatment is an economic burden	No	66 (39.1)	67 (82.7)	< 0.001
	Yes	103 (60.9)	14 (17.3)	
Presence of depression/ anxiety	No	122 (72.2)	68 (84.0)	0.04
	Yes	47 (27.8)	13 (16.0)	

Non-significant variables:

Gender, Region of residence, Marital Status, Occupation, Education level, Medical insurance, Presence of comorbidities, Family history of epilepsy, Number of AE, Frequency/day, Number of drugs, Number of workers/family, Duration of disease, BMI.

Table 4. Final results of regression using the status of attitudes as the dependent variable

Variables	Adjusted OR	95% CI	p-value	
Age	0.97	0.94 - 0.99	0.02	
Presence of depression/ anxiety	0.4	0.2 - 0.9	0.04	
Participant is satisfied and find his treatment effective	4.9	1.2 - 20	0.03	
Participant feels his treatment is an economic burden	0.2	0.1 - 0.4	<0.001	
Controlled epilepsy (no seizures at least 6 months)	3.4	1.6 - 7.1	0.001	
Age onset disease	<i>Reference: <12 years</i>			
	12-20 years	3.1	1.1 - 8.4	0.03
	20-40 years	0.5	0.2 - 1.4	0.2
	>40 years	2.7	0.9 - 8	0.08
Frequency of neurologist clinic visits	<i>Reference: monthly</i>			
	Every 3-6 months	0.7	0.3 - 2.1	0.6
	Every year	0.2	0.04 - 0.5	0.002
	Every few years (when a seizure occurs)	0.2	0.1 - 0.7	0.01

OR:Odds Ratio; CI: Confidence Interval

Dependent variable: "Positive/ Negative" Attitudes.

Hosmer–Lemeshow test p-value=0.7/ Overall predicted percentage = 79.6%.

Variables excluded from the model following this order:

Family history of epilepsy, in busy period (at work, away from home, in outdoor dinner/ lunch or in travel), Following healthcare provider instructions, Gender, Number of pills/ day, if patient forget to take medication, if no money/ health coverage, if a neighbor of participant advices him to stop medication, Experience of side effects, Occurrence seizures in the last 5 years, Attitude in fasting states.

Table 5. Final results of regression using the seizure control as the dependent variable

Variables	Adjusted OR	95% CI	p-value	
Attitudes status	1.9	1.1 - 3.4	0.03	
Duration of disease	1.04	1.02 - 1.07	<0.001	
Do not follow neurologist's instructions in fasting period	0.5	0.3 - 0.9	0.03	
Attitude if seizure occurs	<i>Reference: Double a dose</i>			
	Continue medication normally	1.2	0.5 - 2.6	0.7
	Contact a neurologist	2.9	1.3 - 6.5	0.01

OR:Odds Ratio; CI: Confidence Interval

Dependent variable: "Controlled epilepsy/ Uncontrolled epilepsy".

Hosmer–Lemeshow test p-value=0.6/ Overall predicted percentage = 67.6%.

Variables excluded from the model following this order:

Participant is satisfied and find his treatment effective, Following healthcare provider instructions, Gender, Number of drugs/day, Presence of tumor.