Antiseizure medication adherence and epilepsy surgery attitude in people with epilepsy in Morocco: A cross-sectional study

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ABSTRACT

We determine the proportion of non-Antiseizure Medication Adherence (non-AMA) and refusal attitude towards Epilepsy Surgery (ES) and their associated factors in Moroccan People With Epilepsy (PWE). A cross-sectional study was conducted (December 2021-December 2022) among adult Moroccan PWE. PWE were interviewed for their reactions to AMA and the ES attitude. Their medical files were processed to complete their socio-demographic and clinical data. Data were analyzed by the Statistical Package for Social Sciences (SPSS) software 21.0. A Chi-square test was performed to compare variables and multivariate logistic regression was used to highlight associations. Statistical tests were considered significant at a p-value ≤ 0.05 for a Confidence Interval (CI) of 95 %. The median age of our sample (n = 294) was 38 years (IQR: 25.00–55.00). Non-AMA was noted in 24.5 % with indifference as the main reason (55.6 %). ES refusal was found in 33.3 %, attributed mostly to apprehension (61.2 %). In the multivariate analysis, male sex (aOR = 1.94; 95 %CI: 1.03–3.64) and the existence of a family history of epilepsy (aOR = 1.96; 95 %CI: 1.02–3.75) were the factors associated with the non-AMA, whereas the use of allopathic treatments (aOR = 2.32; 95 %CI: 1.20–4.51), exclusively focal or generalized (not combined) seizures (aOR = 2.66; 95 %CI: 1.36–5.21) and the combination of a generic with the originator ASM (aOR = 2.64; 95 %CI: 1.12–6.18) were the predictive factors with the ES refusal attitude. The proportions found of non-AMA and ES refusal were relatively low compared to other studies, which may indicate the effort that medical staff have devoted recently to raising awareness of the importance of PWE's therapeutic involvement.

1. Introduction

Epilepsy is one of the most problematic neurological disorders [1]. According to the World Health Organization (WHO), around 50 million people of all ages are affected by epilepsy worldwide, which makes it one of the most common neurological disorders [2]. Its prevalence is 7.60/1000, with an incidence reaching 67.77/100,000 [3]. Nearly 80 % of people with epilepsy (PWE) worldwide belong to middle-and low-income countries [4], with higher prevalence and incidence [3]. This disparity makes epilepsy a real public health problem in these countries [5]. The management of epilepsy requires a proper diagnosis, followed by the prescription of appropriate antiseizure medication (ASM) at an adequate dosage [6]. However, proper therapeutic follow-up and treatment efficacy depend in large part on the involvement of PWE. This involvement is represented by good antiseizure medication adherence (AMA) [7]. The poor or non-AMA can mimic drug-resistant epilepsy

(DRE) and expose the PWE to many complications [8]. However, epilepsy may be refractory to ASDs in about 30–40 % of PWEs, which may suggest surgical treatment to control seizures and improve PWEs' quality of life [9,10]. In addition to the lack and underestimation of epilepsy surgery (ES) in developing countries [11], the attitude of PWE towards this surgical alternative tends to influence their consent and, consequently, their proper management of their DRE [12].

In this context, our study aims to evaluate the level of collaboration in epilepsy management in PWE, through the study of the proportion of non-AMA and poor attitudes towards ES and their promoting factors.

2. Materials and methods

2.1. Desing and study area

We conducted a cross-sectional study for 12 months (December 2021 to December 2022) among PWE in the Casablanca-Settat region of Morocco.

2.2. Population

- **Inclusion/exclusion criteria**

Our inclusion criteria are a medical diagnosis of epilepsy conforming to the definition of the International League Against Epilepsy (ILAE), adult age (>18 years), and a period of ASM > 12 months.

We excluded PWE aged under 18, PWE suffering from non-epileptic seizures, and PWE who are deaf or suffer from severe cognitive impairment.

2.3. Sampling and procedure

The study was cross-sectional following a simple random sampling, among adult PWE received in the consultations of neurology, neurosurgery, and psychiatry of the different public hospitals and private doctor's offices randomly selected in the "Casablanca-Settat" region.

We defined the region's different cities and excluded those without regional or provincial hospitals. Casablanca, Settat, and El Jadida are the selected cities with more public hospitals and private doctor's offices for the targeted specialties. These are the most representative cities because they receive the most PWE from all the other cities of the region.

Among the different provinces of Casablanca (the largest city), we selected the province of "Casablanca Anfa" which seats the University Hospital Center, the Regional Hospital Center, and a large percentage of private doctor's offices. We conducted a random selection of the different private doctor's offices, prioritizing specialties that receive the most PWE: neurology, neurosurgery, then psychiatry. For each doctor declining to participate, we replaced him with the one next on the draw list.

2.4. Variables and measures

2.4.1. Main variables

Our study evaluates poor AMA and refusal attitude toward ES as two main dependent variables:

- **Antiseizure Medication Adherence (AMA)**

The AMA was verified by asking the PWE if he or she is taking his/her treatment continuously.

For PWE who claimed adherence to their ASM, AMA was checked by comparing the reported dosage with that mentioned in the medical prescription.

The AMA was judged to be poor for each PWE who confirmed that they had forgotten, voluntarily stopped, or reduced his or her ASM, and for each PWE who reported a dosage that did not comply with the medical prescription.

- **Epilepsy Surgery (ES)**

For PWE with DRE, we asked directly whether they would accept ES as an alternative approach to ASM treatment. For drug-responsive PWE, we asked each whether he or she would accept or refuse surgical treatment should his or her epilepsy prove to be drug-resistant.

Patients who refused ES were asked to state the reasons for their refusal: distrust of ES itself and its complications (apprehension), confidence and/or ignorance about its success (confidence), and the belief that they would not be able to stand it (presumed fragility).

2.4.2. Secondary variables

Our two dependent variables are analyzed depending on sociodemographics (age, sex, city, area, education, economic level, medical sector (private offices or public hospitals), treatment-seeking behavior (use of allopathic treatments), and clinical, paraclinical data relating to epilepsy.

2.5. Instrument and data collection

During the consultations, a questionnaire was completed for each PWE to collect sociodemographic, clinical, and paraclinical data. The investigator assessed the AMA of PWE and their attitude towards ES.

The details of clinical and paraclinical data were subsequently discussed and confirmed by reviewing medical files with the attending physicians.

2.6. Data processing and statistical analysis

The data are analyzed using the Statistical Package for Social Sciences (SPSS) software (IBM SPSS Statistics 21.0). Frequencies and percentages present qualitative variables, while quantitative variables are presented by means ± standard deviation (SD) or medians with an interquartile range (IQR). The different variables are compared using the Chi-square test and any significant associations via the logistic regression model. The association of the independent variables with the dependent ones was highlighted by univariate analysis for determining the crude odds ratio (OR). A multivariate analysis was performed to adjust the risk found, generating an adjusted OR (aOR) for each associated independent variable. Statistical tests are considered significant at a p-value < 0.05 for a 95 % confidence interval (CI).

3. Results

3.1. Sociodemographic and clinical characteristics

In our sample (n = 294), the median age was 38 years (IQR: 25.00—55.00), with a slight predominance of the female sex (51.0 %, n = 150). The majority of PWE live in the city of Casablanca (63.6 %, n = 187) and belong to urban areas (76.9 %, n = 226). A large proportion of PWE have no education (33.7 %, n = 99), and the majority have a low economic level (66.6 %, n = 187). More than half of our PWE used an allopathic treatment for their epilepsy (56.1 %, n = 165) (Table 1).

Clinically, 156 (53.1 %) of our PWE have epilepsy associated with concomitant conditions. Anxiety (45.2 %, n = 133) and depression (38.1 %, n = 112) are the most pronounced psychiatric comorbidities. About half of the epileptic seizures are generalized (49.7 %, n = 146), with a predominance of structural etiology (44.6 %, n = 131). Most paraclinical explorations revealed radiological (MRI) (54.1 %, n = 80) and electrophysiological (EEG) (68.7 %, n = 182) abnormalities. Most PWE has been on treatment for more than 5 years (73.5 %, n = 216). A DRE is noted in 74 (25.2 %) of our PWE (Table 2).

Table 1

Sociodemographic characteristics of included PWE.

Sociodemographic factors	N (%)
Age (years)	
Median (IQR)	**38 (25.00 – 55.00)**
[18 – 28]	99 (33.7)
[29 – 39]	56 (19.0)
[40 – 50]	53 (18.0)
> 50	86 (29.3)
Sex	
Men	144 (49.0)
Women	150 (51.0)
Marital status	
Single	166 (56.5)
Married	118 (40.1)
Divorced/widowed	10 (3.4)
City	
Casablanca	187 (63.6)
Settat	35 (11.9)
El Jadida	44 (15.0)
Others (*)	28 (9.5)
Area	
Urban	226 (76.9)
Rural	68 (23.1)
Education level	
Without	99 (33.7)
Primary	69 (23.5)
Middle or high school	98 (33.3)
University	28 (9.5)
Socioeconomic level	
Low/limited	187 (66.6)
Medium/high	107 (36.4)
Allopathic treatment users	165 (56.1)
Medical consultation sector	
Public	146 (49.7)
Private	148 (50.3)

(*): Mohammedia, Berrechid, Marrakech, Sidi Slimane, Benslimane, Safi, Agadir, Ouarzazate, Khouribga, Khenifra, Tanger.

3.2. Rates of non-AMA and poor attitude toward ES

In our sample, 72 (24.5 %) of PWE are non-AMA. Among them, the main reasons are indifference (55.6 %, n = 40), financial constraints (38.9 %, n = 28), and the problem of ASD tolerance (5.6 %, n = 4). On the other hand, poor attitude towards ES is mainly presented by refusal in 98 (33.3 %) of PWE. Apprehension (61.2 %, n = 60), trust (24.5 %, n = 24), and presumed fragility (14.3 %, n = 14) are the main causes (Fig. 1). Of the 98 (33.3 %) PWEs who refused the ES, 23 (23.5 %) have DRE.

3.3. Associated factors with non-AMA and poor attitude toward ES

In the multivariate analysis, male sex (aOR = 1.94; 95 %CI: 1.03——3.64) and the existence of a family history of epilepsy (aOR = 1.96; 95 %CI: 1.02——3.75) are the factors associated with non-AMA (Table 3). On the other hand, the use of traditional allopathic treatment for epilepsy (aOR = 2.32; 95 %CI: 1.20——4.51), exclusively focal or generalized (not combined) types of seizures (aOR = 2.66; 95 %CI: 1.36——5.21), and the combination of a generic with the originator ASM (aOR = 2.64; 95 %CI: 1.12——6.18) are the factors associated with the poor attitude (refusal) of ES (Table 4).

4. Discussion

4.1. Non-AMA

We report non-AMA in 24.5 % of our PWE. This proportion appears relatively similar to that observed in China (25.2 %) [13] and Pakistan (26.6 %) [14]. On the other hand, our percentage of non-AMA is higher compared to what is reported in Norway (22 %) [15] while it is lower

Table 2

Clinical, paraclinical, and pharmacological features of PWE.

| Variable	N (%)
Concomitant disorders with epilepsy	**156 (53.1)**
Psychiatric comorbidity	
Anxiety	133 (45.2)
Depression	112 (38.1)
Family history of epilepsy	**81 (27.6)**
Personal antecedents	**176 (59.9)**
Seizure type	
Focal	28 (9.5)
Generalized	146 (49.7)
Combined	120 (40.8)
Seizure symptomatology	
Convulsive	272 (92.5)
Non-convulsive	22 (7.5)
Seizure frequency	34 (23.2)
None	128 (43.5)
Low	50 (17.0)
Medium	81 (27.6)
High	35 (11.9)
Epilepsy etiology	
Structural	131 (44.6)
Genetic	97 (33.0)
Unknown	27 (9.2)
Unclassifiable	39 (13.3)
EEG abnormalities	**182 (68.7)**
MRI abnormalities	**80 (54.1)**
Antiseizure medication combination	
Monotherapy	126 (42.9)
Polytherapy	168 (57.1)
ASM nature	
Originator	238 (81.0)
Generic	20 (6.8)
Both	36 (12.2)
Antiseizure medication duration (years)	
Median (IQR)	**2 (1.00 – 2.00)**
≤5	78 (26.5)
>5	216 (73.5)
Epilepsy responsiveness	
Drug-responsive	220 (74.8)
Drug-resistant	74 (25.2)
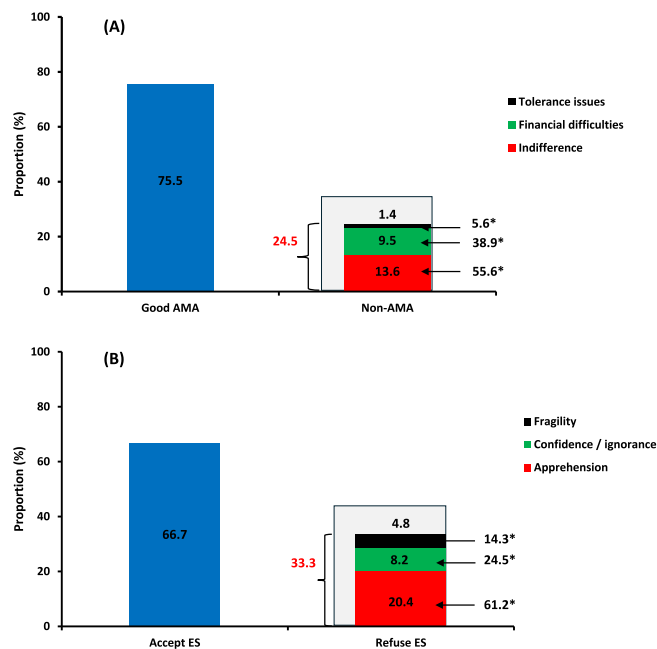
Fig. 1. Proportions (%) of non-AMA (A) and poor attitude towards ES and its reasons (B).* Valid percentage.

Table 3
Multivariate analysis of factors associated with non-AMA.

Predictive factors	Category	Adherence n (%)		aOR (95 % CI)	p-value*
		Good	Poor		
Sex					
	Men	168 (78.1)	47 (21.9)	1.94 (1.03 – 3.64)	0.039
	Women	193 (83.5)	38 (16.5)	1	
Education					
	Without	74 (74.7)	25 (25.3)	1	
	Primary	59 (85.5)	10 (14.5)	0.43 (0,16 – 1.11)	0.082
	Secondary	72 (73.5)	26 (26.5)	1,23 (0,56 – 2.68)	0.594
	University	17 (60.7)	11 (39.3)	2.63 (0.91 – 7.60)	0.073
Economic level					
	Low/limited	133 (71.1)	54 (28.9)	1.95 (0.95 – 4.00)	0.068
	Medium/high	89 (83.2)	18 (16.8)	1	
Familial history of epilepsy					
	Yes	53 (65.4)	28 (34.6)	1.96 (1.02 – 3.75)	0.042
	No	169 (79.3)	44 (20.7)	1	
Seizure frequency					
	None	100 (87.1)	28 (21.9)	1	
	Low	35 (70.0)	15 (30.0)	1.65 (0.73 – 3.74)	0.225
	Medium	66 (81.5)	15 (18.5)	0.60 (0.26 – 1.37)	0.232
	High	21 (60.0)	14 (40.0)	2.41 (0.94 – 6.17)	0.065

*p-value of Wald test.

compared to that reported in Brazil (66.2 %) [16] and Saudi Arabia (48.7 %) [17]. Taking all these studies, we report a relatively average proportion of non-AMA among our PWE. This rate can be explained by the efforts of the health professionals in Morocco to educate and raise awareness among PWE during consultations about the importance of systematic follow-up of treatment and the dangerousness of non-AMA [18]. However, the inability to measure serum doses of ASDs and not using a standardized scale to measure adherence obliged us to consider only the direct responses of PWE to their AMA. This approach would tend to mask an even higher proportion of non-AMA by failing to include elderly people classified as adherent through the consideration of their incorrect responses. This hypothesis is considered based on the unfavorable conception, attitude, and habits that a large percentage of the Moroccan population adopts toward epilepsy [19,20]. Furthermore, the disparities observed in non-AMA in the different studies could be mainly due to the methodologies and AMA definitions opted for by each study and the sociocultural profiles concerning each country [21].

The main reasons for the non-AMA in our PWE are indifference (55.6 %), financial constraints (38.9 %), and intolerance to ASDs (5.6 %). In our study, indifference manifested itself as forgetfulness and/or despair to achieve seizure freedom. These reasons underline the need to improve communication between the physician and his PWE and raise awareness of the importance of his assumption of responsibility for completing his treatment.

Regarding predictive factors, male sex, and the presence of a family history of epilepsy increase the risk of non-AMA in our study. The association of male sex was also detected in Brazil [16] and Ethiopia [22], whereas the predictive value of a family history of epilepsy is exclusive to our study. In the absence of a relevant explanation in the literature, we can attribute the association of the male sex to the burden of epilepsy disease [23] and to embarrassment and stigma [24] which affect men more than women, making it more difficult for them to monitor their ASM. In addition, the disparities between men's and women's family roles in developing countries mean that men are busier and more caught up in daily professional challenges than women, making it more complicated for them to monitor their antiseizure medication carefully [22]. The association of the presence of a family history of epilepsy with non-AMA may be explained by the familiarity that PWE may have with their epilepsy, which is sometimes pharmacosensitive, of a genetic etiology [25] and is characterized by a low seizure frequency and a relatively long period of seizure-freedom. For PWE, this context could simulate the non-necessity of their ASM and therefore encourage non-AMA.

4.2. Refusal attitude of ES

A refusal attitude is reported in 33.3 % of our PWEs. Among a few studies, we note that our proportion is relatively comparable to that noted in the United States (30 %) [26] and low compared to that observed in Colombia (60 %) [12] and Italy (53.5 %) [27]. These

Table 4
Multivariate analysis of factors associated with refusal attitude towards ES.

Predictive factors	Category	Attitude towards ES n (%)		aOR (95 %CI)	p-value*
		Accept	Refuse		
Allopathic methods					
	Users	102 (61.8)	63 (38.2)	2.32 (1.20–4.51)	0.012
	Non-users	94 (72.9)	35 (27.1)	1	
Depressive comorbidity					
	Depressed	66 (58.9)	46 (41.1)	1.73 (0.91–3.28)	0.089
	Not depressed	100 (70.4)	42 (29.6)	1	
Seizure type					
	Focale/Generalized	108 (62.1)	66 (37.9)	2.66 (1.36–5.21)	0.004
	Combined	88 (73.3)	32 (26.7)	1	
Seizure symptomatology					
	Convulsive	185 (68.0)	87 (32.0)	1	
	Non-convulsive	11 (50.0)	11 (50.0)	3.09 (0.97–9.78)	0.055
EEG					
	Abnormal	128 (70.3)	54 (29.7)	1	
	Normal	48 (57.8)	35 (42.2)	1.90 (0.98–3.68)	0.055
ASD nature					
	Originator	166 (69.7)	72 (30.3)	1	
	Generic	8 (40.0)	12 (60.0)	2.89 (0.82–10.08)	0.096
	Both	18 (50.0)	18 (50.0)	2.64 (1.12–6.18)	0.025

*p-value of Wald test.

differences in percentages are mainly due to the methodological approach chosen for each study. However, the lower percentage of refusal attitudes toward ES in our study could be attributed to the result of PWEs' raising awareness efforts that fit into the program of ES development previously recommended in Morocco [28]. The nature of the doctor-patient relationship that characterizes our population gives total authority to the physician in therapeutic decisions and ethically instills the importance of absolute trust in the patient [29]. This context seems to make the Moroccan PWE less involved in his therapeutic decisions and necessarily accept the proposal of the ES, which could underestimate the proportion of the refusal attitude of the ES in our study.

The rejection of SE in our study is due to apprehension (61.2 %), confidence (24.5 %), and alleged fragility (14.3 %). The proportion of apprehension about ES is comparable to that observed in Colombia (60 %) [12] while 86 % of PWE believe in the dangerousness of ES in the United States [30]. In addition to some characteristics linked to epilepsy, fear of surgery and its difficult consequences was a determining reason for attitudes towards ES in the United States [31] and Colombia [32]. All these reasons for refusing ES stem from ignorance of the principle of this therapeutic alternative, which requires education and awareness efforts on the part of PWE.

The use of allopathic methods (religious clergymen, herbalists, and marabouts), having only focal or generalized (not mixed) seizures, and the introduction of a generic ASD to antiseizure combination medication are the factors associated with the refusal attitude of ES in our study. Apart from the association between seizure duration, frequency, and severity in the United States [31] we did not find in the literature any cross-sectional studies similar to ours, evaluating sociodemographic and clinical factors associated with the SE attitude. Thus, these factors identified in our study, for the first time, increase the risk of ES refusal by PWE. We explain the association between the use of allopathic methods and low treatment-seeking behavior, which signifies an altered socio-cultural context regarding epilepsy. This context could reflect the presence of non-scientific knowledge about epilepsy, including ignorance of surgery as a therapeutic approach [19]. Consequently, this ignorance tends to increase fear and doubt towards ES. Exclusively focal or generalized seizures (including absences) are usually associated with drug-sensitive or drug-dependent epilepsies [33]. After treatment, PWE with these types of seizures have a relatively normal quality of life with good seizure control, which allows them to avoid a rather frightening approach such as SE and therefore encourages them to refuse it. In the context of an ASM combination, the addition of a generic ASD to originator ones could mean reduced efficacy [34] reinforcing the lack of confidence in PWE in medical indications, including ES.

Finally, among all PWE refusing ES, 23.5 % have DRE. This proportion reflects the importance of making drug-resistant PWE (primarily concerned) towards this therapeutic approach, encouraging their consent, and offering them more chances of recovery.

4.3. Strengths and limitations

We can consider the representativeness of our results through several parameters: (i) the size of our sample, which exceeds that of many studies; (ii) the detailed definition of our dependent variables; (iii) the careful choice of the possible associated independent variables; (iv) the detailed study of the PWEs' files in consultation with the treating physicians; and (v) the choice of the target population from the most densely populated region of Morocco. Furthermore, limiting the study to direct responses from PWE and not measuring serum ASD concentrations tends to underestimate the proportion of non-AMA in our study. The number of ASDs and the number of times a day they are taken can have an impact on patient adherence. However, the variability of dosage (number of tablets taken per day) and of the number of antiepileptic drugs updated in the same patient according to his or her clinical condition at each consultation (decrease or increase in dose, addition or withdrawal of a molecule on prescription) made it difficult to take into account the number of ASDs and the number taken per day in data collection and analysis. We believe that this type of analysis requires a cohort study, which is also one of the limitations of our study. The factors found should have an association rather than a causal value, given the cross-sectional nature of this study.

5. Conclusion

This is a cross-sectional study assessing the collaborative value of PWE in the follow-up of ASM. The non-AMA and refusal attitude of ES have considerable proportions in our study but remain relatively low compared to other studies. Our results may reflect the recent efforts of the medical staff to educate and sensitize PWE during consultations, to the importance of their AMA on the one hand, and the therapeutic value of ES in DRE on the other. Associated socio-demographic and clinical factors must be taken into consideration when prescribing and monitoring the therapeutic management of PWE. The non-AMA and refusal attitude of the ES found in our study calls for intensified efforts to reduce the cases of pseudo-DRE, to develop the Doctor-PWE relationship, and to improve the involvement of the PWE in the finality of their ASM.

Ethical consideration and consent

Our study received approval from the Ethics Committee for Biomedical Research of Casablanca. This decision was then approved by the National Commission for the Control of Personal Data Protection (CNDP) under the authorization: A-RS-22/2022. For each PWE, the participation was strictly and systematically conditioned by the signing of informed consent. At the end of the participation, each PWE received a bilingual information letter mentioning the investigators' contact and a simplified description of the study. We note that the investigators have preserved the anonymity of the participating PWE.

CRediT authorship contribution statement

El Bachir Hajji: Writing – original draft, Visualization, Software, Project administration, Investigation, Formal analysis, Data curation. **Boubacar Traore:** Writing – review & editing, Visualization, Validation, Software, Resources, Formal analysis, Data curation. **Samira Hassoune:** Writing – review & editing, Validation, Supervision, Methodology. **Salma Bellakhdar:** Writing – review & editing, Supervision, Project administration, Investigation, Conceptualization. **Mohammed Abdoh Rafai:** Writing – review & editing, Validation, Supervision, Project administration, Conceptualization. **Abdelhakim Lakhdar:** Writing – review & editing, Validation, Supervision, Project administration, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.

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