

Title page Letter

Title

Health-Related Quality of life and medication adherence in elderly patients with epilepsy

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Health-Related Quality of life and medication adherence in elderly patients with epilepsy

Abstract

Objective: Considering the high prevalence of epilepsy in the elderly and the importance of their quality of life (QoL), this study aimed to investigate the relationship between medication adherence and QoL, and the mediating effects of medication adherence on the association between serum antiepileptic drug (AED) level and seizure severity with QoL in epileptic elderly.

Methods: In a longitudinal study, 766 elderly patients with epilepsy who were prescribed to minimum one antiepileptic drug were selected by convenience sampling method. Medication Adherence Report Scale (MARS-5) questionnaire was completed at the baseline. Seizure severity and QoL were assessed after 6-month by the Liverpool Seizure Severity Scale (LSSS) and the QoL in Epilepsy (QOLIE-31) questionnaires respectively. Serum level of AED was also measured at 6-month follow-up.

Results: Medication adherence was significantly correlated with both seizure severity ($\beta = -0.33$, $p < 0.0001$) and serum AED level ($\beta = 0.29$, $p < 0.0001$) after adjusting for demographic and clinical characteristics. Neither QoL nor its sub-classes were correlated with seizure severity. In addition, significant correlation was not observed between serum AED level and QoL. However, the medication adherence was significantly correlated with QoL ($\beta = 0.30$, $p < 0.0001$). The mediating effects of medication adherence in the association between serum AED level ($Z = 3.39$, $p < 0.001$) and seizure severity ($Z = -3.47$, $p < 0.001$) with QoL were supported by Sobel test.

Conclusion: This study demonstrates that medication adherence has a beneficial impact on QoL in epileptic elderly. Therefore, adherence to treatment should be monitored to improve the QoL in epileptic elderly.

Keywords: Epilepsy; Medication adherence; Seizure; Quality of life; Elderly

1. Introduction

Epilepsy, a neurological disorder characterized by recurrent unprovoked seizures, is one of the most common chronic brain disorders globally [1]. Despite the advances in understanding the pathophysiological mechanisms of epilepsy and the development of medical treatments in the past decades, people of all ages with this neurological disorder continue to be stigmatized by it [2]. Epilepsy is one of the world's earliest recognized conditions in the history that affects approximately 50 million people worldwide with nearly 80% living in the developing countries [3]. The prevalence of epilepsy in the Iranian population is between 7.8-18/1000 persons or approximately 1.4% of the population [4, 5] which is slightly higher than the reported prevalence of 5.8-8.4/1000 persons in developed countries [1, 6]. This disease affects all ages, ethnicity and socioeconomic groups; however, its prevalence and incidence increase pronouncedly in individuals over the age of 65 years, even higher than the infancy, another high prevalence age; as such, epilepsy is the third most common neurological disease in the elderly, after stroke and dementia [7, 8]. Considering the growth of the world's population of >60 years in the future [9] due to the increase in life expectancy, it is expected that prevalence of epilepsy will dramatically rise over the next few decades.

Medication adherence is a fundamental determinant of effective treatment [10] that is defined by the World Health Organization as "the degree to which the person's behavior corresponds to the agreed recommendations from a health care provider" [11]. The control of epilepsy has been successful with medication adherence, and most people with epilepsy (almost 70% of patients) can become seizure-free by taking one anti-seizure medication daily, called anti-epileptic drug (AED) [12, 13]. Nevertheless, non-adherence to medication is a very common phenomenon in patients with chronic diseases [14-18] including epilepsy [18-23], which not only affects the individual's health but also the health-care system. This leads to uncontrolled symptoms and substantial deleterious effects on the quality of life (QoL) and those patients can become a heavy burden on the society and health-care system [24-26].

Elderly people with epilepsy generally respond well to AED treatment. Up to 80% of patients with late-onset epilepsy can be expected to remain seizure-free with AED treatment [27]; however, only 38-57% (average < 45%) of epileptic elderly patients have good adherence to AEDs [28]. The suggested reasons for poor adherence in this population of patients include patient-physician discordance, complex medication regimen, the frequency of administration of

multiple medications, disturbances of memory, specific beliefs about drugs, being depressed or anxious and unusual time during the day to take the medication [25]. Although the understanding of the optimal care by the patients and improving their QoL are problematic in epileptic treatment, it remains questionable whether adherence to AED can actually effectively improve the QoL in this population. The impact of AED therapy on the QoL in younger groups of patients has been previously reported [10, 29, 30] which have demonstrated both positive and negative effects of AED therapy on QoL [31]. However, the impact with AED treatment on the QoL among the elderly has not been well investigated. Therefore, the primary aim of this study was to assess the QoL and its correlation with AED adherence among elderly patients with epilepsy. In addition, the study aimed to evaluate the mediating effects of medication adherence in the relationship between serum AED level and seizure severity with QoL. To obtain more accurate information on AED adherence, both self-reporting method (Medication Adherence Report Scale, MARS-5) and serum AED level measurement were used. The correlation between MARS-5 score and serum AED level and whether MARS-5 score can be replaced with serum AED level to predict the QoL in the elderly with epilepsy was also examined.

2. Material and methods

2.1. Study design and participants

This longitudinal study was carried out on 766 elderly patients with epilepsy referred to six neurology clinics from March 2014 to December 2015. The patients were recruited through convenience sampling. The subjects included both males and females aged 65 years or above with a confirmed diagnosis of epilepsy according to the International League Against Epilepsy Criteria [32]. The subjects had the ability to perform daily activities, **were prescribed of at least two AED** and had no major cognitive impairment **(a score of 23 or below on the Mental State Examination: MMSE)** or **acute psychiatric disorders (diagnosed by a psychiatrist)**. Exclusion criteria were history of drug abuse, diabetes, cardiovascular diseases, rheumatoid arthritis, malignant tumors, kidney dysfunctions and liver diseases, receiving other medication than AEDs at the time of recruitment or throughout the follow-up period, and unwilling to participate the study.

All the applicants were screened by trained physician for eligibility according to the inclusion and exclusion criteria. All eligible participants were given a full explanation about the objectives and protocol of the study and a written informed consent form was signed prior to the enrolment.

Demographic characteristics, clinical features and medication adherence were then collected from the participants. Six months later, the subjects were invited to attend the clinic to complete the questionnaires evaluating seizure severity and QoL. Then, blood samples were taken on the same day for the measurement of AED level as an objective assessment of AED adherence.

2.2. Instruments

2.2.1. Background information sheet and medical records

Demographic characteristics including age, sex, marital status, educational years, employment and monthly income (*High >1000\$; Intermediate=500-1000\$; Low <500\$*) were collected by face-to-face interviews and recorded in the Background Information Sheet. The clinical features of the participants including the type of epilepsy and the duration of the disease were also collected from their medical records.

2.2.2. Medication Adherence Report Scale (MARS-5)

MARS-5 is a self-reporting and widely applicable questionnaire for the subjective assessment of medication adherence [33]. It consists of five statements of non-adherent behaviors (*I forgot to take my antiepileptic medicine, I altered the dose of my antiepileptic medicine, I stopped taking my antiepileptic medicine for a while, I decided to miss a dose of my antiepileptic medicine, I took less antiepileptic medicines than prescribed*) answered on a 5-point Likert scale (1 = always, 2 = often, 3 = sometimes, 4 = rarely, 5 = never) with the overall score ranged between 5 - 25. According to the threshold, MARS-5 scores equal or greater than 20 was considered as a high adherence [14]. The concurrent validity and internal consistency of the MARS-5 questionnaire has been supported by previous studies [34]. The participants completed the MARS-5 questionnaire at the baseline.

2.2.3. Liverpool Seizure Severity Scale (LSSS)

The participants were asked to complete the LSSS questionnaire if they had reported more than one week from the last seizure. LSSS questionnaire consists of 20 items rated on a Likert scale. A four-point Likert scale was used to respond to each item with higher points indicating greater seizure severity. It has been showed that LSSS is a valid and reliable instrument quantifying seizure severity that may also be used to evaluate the changes in seizure severity over the time [35]. Furthermore, the known-group validity showed subjects with severe seizure symptoms could be distinguished from those with minor seizure symptoms by LSSS [35].

2.2.4. Serum AED level

In order to measure serum **three most commonly used individual AEDs (i.e. Phenytoin, Lamotrigine and carbamazepine)** concentrations at the 6-month follow-up, whole blood samples were taken prior to the next daily routine dose of drug. The serum was then separated and AED concentrations were measured by a microparticle enzyme immunostimulatory assay kit (Abbott AxSYM®, Abbott Laboratories, Abbott Park, IL, USA). The therapeutic dose range of AED which can prevent seizures effectively without toxic effects has been reported in detail previously [36]. The serum concentrations of AEDs were categorized into three groups based on the reference as “below the therapeutic range”, “within the therapeutic range” and “above the therapeutic range”.

2.2.5. Quality of Life in Epilepsy (QOLIE-31)

The QoL was evaluated using QOLIE-31 questionnaire, which was designed exclusively to assess epileptic patient's QoL at the 6-month follow-up. It consists of 31 items in seven subclasses: seizure concerns, cognitive function, energy/fatigue, emotional wellbeing, social function, medication efficacy, and overall QoL [37]. The subscale scores ranges from 0 - 100 points, with higher scores representing better QoL. The overall score of the QOLIE-31 could be calculated by weighting and summarizing seven-dimension scores. The Persian version of QOLIE-31 was a reliable instrument for assessing QoL in patients with epilepsy [38].

2.3. Statistical analysis

The results were expressed as mean \pm standard deviation (SD) for quantitative data with normal distribution, and frequency (percent) for qualitative data. The analyses were performed in several steps. Firstly, Pearson correlation analysis was used to investigate the relationships between serum AED level, MARS-5 score, LSSS score, and overall QOLIE-31 score. The relationships between serum AED level and LSSS score with the MARS-5 score were then evaluated by linear regression after adjusting for potential confounders (age, sex, marital status, education years, employment status, monthly income, type of epilepsy and disease duration). The relationships between independent variables (serum AED level, LSSS and MARS-5 score) and dependent variable (each sub-class of QoL and the overall score of the QoL) were also evaluated using multiple linear regression analysis, after controlling for potential confounders. Based on the Bonferroni correction, $p < 0.00625$ ($0.05/8$) is considered as significant for multiple comparisons between the eight regression models.

Lastly, structural equation modeling (SEM) was used to test the model and investigate whether seizure severity and serum AED level directly correlated with the QoL or being mediated through other factors. Several fit indices including chi-square statistics, Comparative Fit Index (CFI), Goodness-of-Fit Index (GFI), Tucker–Lewis Index (TLI), Normed Fit Index (NFI) and Root Mean Square Error of Approximation (RMSEA) were evaluated to determine the model fit. To interpret these indices, the following criteria were used: χ^2/df ratio < 2 (excellent); $\chi^2/\text{df} < 3$ (good); $\chi^2/\text{df} < 5$ (acceptable); ≥ 0.90 as good fit for CFI, GFI, TLI, and NFI; ≤ 0.08 as good fit for RMSEA[39]. Sobel test was also used to examine the significance of mediation effects. The descriptive analyses and regression models were performed using IBM SPSS version 21.0 software; SEM was conducted using AMOS 21.

3. Results

The Demographic and clinical characteristics of the participants are shown in Table 1. The average age of the participants was 73.9 ± 5.7 years and more than half were female (54.7%). Most participants were married and had low levels of education. All patients received polytherapy with a minimum of two AEDs. Therefore, it is not possible to assess the effect of each type of AEDs on adherence. As shown in Table 1, nearly about two-third of participants had focal epilepsy (70.2%). Of the patients with focal epilepsy, 97 (18%) reported focal seizures without impairment of consciousness, and sixty-eight (13%) patients reported focal seizures with impairment of consciousness. All patients with generalized epilepsy reported convulsive seizures.

The mean overall score of the QOLIE-31 among the participants was 67.8 ± 20.5 with energy/fatigue the worst domain (59.3 ± 18.6) and medication efficacy the best domain (78.7 ± 24.1) (Table 1). Furthermore, nearly half of the participants (48.7%) had serum AED levels below the therapeutic range (*i.e.* non-adherent).

In the first step, we investigated the relationship between the variables. All of the correlation coefficients were statistically significant. In particular, MARS-5 score was positively correlated with serum AED level ($r=0.36, p < 0.001$), and inversely correlated with LSSS score ($r = -0.39, p < 0.001$). In addition, positive correlation was observed between QOLEI-31 score and MARS-5 score ($r= 0.33, p < 0.001$).

The relationships between the variables were then evaluated by multiple linear regression after adjusting for potential confounders. Table 2 shows the results from the regression models that

evaluated the association between MARS-5 score with LSSS score and serum AED level. As shown in Table 2, MARS-5 score was significantly correlated with both LSSS ($\beta = -0.33$, $p < 0.0001$) and serum AED level ($\beta = 0.29$, $p < 0.0001$) after adjusting for confounders. In other words, LSSS and serum AED level were significant predictors of MARS-5 score and accounted for almost a fourth of the variation in the MARS-5 score.

The relationships between LSSS score, MARS-5 score and serum AED level with overall QOLIE-31 score and its domains are shown in Table 3. Neither overall QOLIE-31 score nor its sub-classes were correlated with LSSS score. Similarly, no significant correlation was observed between serum AED level and overall QOLIE-31 score and the scores in QOLIE-31 domains after adjusting for demographic and clinical confounders. However, MARS-5 score was significantly correlated with the overall score of QOLIE-31 ($\beta = 0.30$, $p < 0.0001$) and its domains.

After the confirmation of the correlation between MARS-5 score and QOLIE-31 score, we tried to examine the proxy effects of MARS-5 on QoL using the SEM. The SEM analysis is graphically described in Fig. 1. This model showed an acceptable fit. According to SEM analysis, all the goodness-of-fit indices indicated an acceptable fit, except for the χ^2 which was statistically significant ($p < 0.001$). However, the values of χ^2/df ratio was good ($3.105 < 5$). The rest of the fit indices showed an acceptable fit, with CFI, GFI, TLI and NFI above 0.9, and RMSEA less than 0.08 (CFI = 0.974, GFI = 0.978, TLI = 0.957, NFI = 0.963, RMSEA = 0.052). The standardized coefficients of LSSS score on QOLIE-31 score (-0.015) and serum AED level on QOLIE-31 (0.021) were not significant, while the standardized coefficients of LSSS score on MARS-5 score (-0.316) and serum AED level on MARS-5 score (0.268) were significant. Furthermore, the mediating effects of MARS-5 score was investigated using Sobel test. According to the Sobel test, LSSS ($Z = -3.47$, $p < 0.001$) and the serum AED level ($Z = 3.39$, $p < 0.001$) showed indirect effects on QoL score. This means that MARS-5 score can mediate the relationship between LSSS and QOLIE-31, as well as the relationship between AED level and QOLIE-31 (Fig.1). However, LSSS score and serum AED level did not directly affect the QoL.

4. Discussion

This study examined the associations among several variables that have influence on QoL in the elderly with epilepsy. We suggested a model for the effect of MARS-5 not only on the relation between seizure severity and QoL, but also on the relation between AED level and

QoL. Our findings revealed that serum AED level, medication adherence, and QoL positively correlate with each other in elderly patients with epilepsy. Furthermore, we also found that increased seizure severity as determined by LSSS score was associated with decreased medication adherence among epileptic elderly patients.

The positive correlation between the medication adherence and AED level suggests that the self-reported MARS-5 score could be suitable to assess AED adherence in the elderly with epilepsy, which is consistent with previous studies on epilepsy treatment [25, 37]. Given that serum level measurement is invasive and costly, a MARS questionnaire may be used to evaluate the adherence to patient treatment. However, in contrast to our findings, several studies on patients with chronic obstructive pulmonary disease (COPD) and children with asthma have suggested that the MARS-5 score is not an accurate self-reporting instrument to measure drug adherence in those patient cohorts [15, 16]. Furthermore, it has been reported that MARS-5 score is not an accurate instrument to measure drug adherence in hypertensive patients [14]. The controversial findings observed between our results and those in abovementioned studies might be due to the type of disease and the difference in clinical characteristics, as well as the efficacy of the medication to control medical symptoms.

Our study also indicated that medication adherence was inversely correlated with seizure severity. However, this finding may be confounded by several clinical and demographic characteristics of the participants. Therefore, we adjusted our analyses for several confounders like age, sex, marital status, educational years, employment status, income level, epilepsy type and duration of the disease. Interestingly, we observed that seizure severity and serum drug level were both independently related to the medication adherence after adjusting those confounders. Therefore, our findings show that seizure severity and serum AED level are strong predictors of medication adherence in patients with epilepsy.

In this study, we evaluated the association between medication adherence, seizure severity and serum AED level of the patients with their QoL as well. In particular, we found that, after controlling clinical and demographic characteristics, medication adherence was directly associated with the overall score of QoL and all its domains, while seizure severity and serum AED level did not have a significant correlation with the QoL. Serum AEDs level are not necessarily associated with QoL in patients with epilepsy. That's it, it does not provide details information on patients' level of adherence over time. Moreover, Serum AEDs level is only

possible to be assessed in patients who taking second generation AEDs [40]. Moreover, the interpretation of serum AED level depends on the time of sampling and duration of AED therapy. These problems limit using the information of serum AEDs level in real clinical practice.

Although our findings did not confirm a significant correlation between seizure severity and the QoL, there were a number of studies that have confirmed the inverse relationship between seizure severity and the QoL in epileptic patients. For example, Harden *et al.* [41] examined a group of woman aged 18-45 with refractory epilepsy and found that even when controlling for depression, seizure severity was inversely correlated with multiple domains of the QoL. Bautista *et al.* [42] indicated that quality of life of patients with epilepsy adversely affected by seizure severity. Furthermore, Sancho *et al.* [43] indicated that the QoL in patients with severe seizure has been consistently shown to be worse than those with mild and moderate seizure.

Moreover, our study indicated that medication adherence was positively correlated with the QoL. Indeed, AED non-adherence impacted negatively on QoL as a result of poor seizure control. There is a number of studies that examined the relationship between medication adherence and the QoL. However, the findings remain controversial. Consistent with our findings, several studies have previously demonstrated the beneficial effects of medication adherence on the improvement of the QoL in epileptic patients [10, 44, 45] and other diseases [46, 47]. Loon *et al.* [47] found that adherence to glaucoma medications was associated with better QoL. Moreover, medication adherence has been reported to be associated with increased QoL in patients with epilepsy [44, 45]. However, Martinez *et al.* [48] could not find any significant association between medication adherence and QoL in patients with type 2 diabetic. In the study by Saleem *et al.* [21], no relationship was found between medication adherence and QoL in hypertensive patients. However, due to the conflicting results, the question of whether increased seizure severity or decreased QoL is the primary event, remains debatable.

Despite the evidence that medication adherence can improves the QoL, it is uncertain whether seizure severity and serum AED level can be replaced by medication adherence to predict the QoL. Our hypothesis was that the medication adherence may mediate the correlation between seizure severity and QoL, as well as serum AED level and QoL. Sobel test was used to test the hypothesis, which revealed that medication adherence did mediate the correlation between seizure severity and QoL. This indicates that lower seizure severity may be due to increase

medication adherence and eventually increase the QoL. Moreover, Sobel test revealed the mediation effect of medication adherence on AED level and QoL, suggesting that higher AED level can be due to increased medication adherence resulting in improved QoL. In addition, these results were supported by the SEM model, which confirmed the proxy effect of the medication adherence on the latent score of QoL.

This study revealed that neither seizure severity nor serum AED level had a direct effect on the QoL; however, there was an indirect effect between these variables via medication adherence. Therefore, medication adherence is very important to improve the QoL in elderly patients with epilepsy and should be strongly emphasized by the physicians.

According to the findings in this study, elderly people with epilepsy who are concerned about the impact of epilepsy on their independency and QoL could potentially control their seizure symptoms through medication adherence. Furthermore, there is the need to pay more attention to medication management and adherence to improve the QoL among the elderly with epilepsy. As the elderly are prone to multiple comorbidity they are at higher risk of polypharmacy, and therefore may present with higher risk of non-adherence to medication compared to the younger population. This results in decreased therapeutic benefits for the patient, increased health care expenditure.

There are several strengths in this study, including serum AED level measurement to assess medication adherence, a relatively large sample size and longitudinal design, which can yield firm conclusions. However, some cautions should be considered to interpret our findings. Firstly, it is likely that the associations between the variables may also be partially explained by the other confounders that were not controlled for in this study, e.g. unhealthy lifestyle. Secondly, we did not assess serum AED level and the QoL at the beginning of the study. Therefore, we are unable to discuss the association between the changes of medical adherence and quality of life throughout the study. Thirdly, major cognitive and acute psychiatric disorders such as depression and anxiety could be key factors affecting both medication adherence and QoL, which were excluded in the current study.

5. Conclusion

In elderly patients with epilepsy, medication adherence significantly correlates with the QoL, and with proper medication management, the QoL these patients can be improved. Therefore, health-

care providers need to provide appropriate level of support by frequently reviewing drug management and monitoring adherence in elderly patients with epilepsy.

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Table 1: Demographic and clinical characteristics of the participants (n=766)

Age (years)	73.94 ± 5.77
Male, n (%)	347 (45.3%)
Married, n (%)	582 (76.0%)
Education (years)	8.91 ± 5.10
Employed, n (%)	276 (36.0%)
Monthly income, n (%)	
High (>\$1000)	162 (21.2%)
Intermediate (\$500-1000)	461 (60.2%)
Low (<\$500)	143 (18.7%)
Epilepsy type, n (%)	
Generalized	228 (29.8%)
Focal	538 (70.2%)
Etiology, n (%)	
Vascular	214 (28.0%)
Trauma	122 (15.9%)
Idiopathic/cryptogenic	430 (56.1%)
Type of medication, n (%)	
Phenytoin	506 (66.0%)
Lamotrigine	333 (43.5%)
Carbamazepine	305 (39.8%)
Oxcarbazepine	204 (26.6%)
Phenobarbital	148 (19.3%)
Topiramate	73 (9.5%)
Primidone	42 (5.5%)
Zonisamide	33 (4.3%)
Gabapentin	28 (3.7%)
Seizure frequency	3.4 ± 3.2
Disease duration (years)	17.71 ± 4.56
QOLIE-31score	
Seizure concerns	77.16 ± 35.05
Cognitive function	66.45 ± 42.93
Energy/fatigue	59.33 ± 18.63
Emotional wellbeing	61.27 ± 18.92
Social function	78.00 ± 21.61
Medication efficacy	78.72 ± 24.12
Overall quality of life	61.77 ± 19.99
Overall score	67.81 ± 20.50
LSSS score	54.91 ± 23.46
MARS-5 score	13.32 ± 6.48
Serum AED level, n (%)	
Below therapeutic range	373 (48.7%)
Within therapeutic range	295 (38.5%)
Above therapeutic range	98 (12.8%)

QOLIE-31, Quality of Life in Epilepsy Inventory-31; LSSS, Liverpool Seizure Severity Scale; MARS-5, Medication Adherence Report Scale

The data is expressed as mean ± SD unless specifically indicated.

Seizure frequency was defined as the mean frequency of complex partial seizures per month during 6 months of follow-up.

Table 2: The association between MARS-5 score and LSSS score as well as serum AED level

	B	SE	β	p^*
LSSS score	-0.09	0.009	-0.33	<0.0001
Serum AED level	2.68	0.302	0.29	<0.0001

AED, Antiepileptic drug; LSSS, Liverpool Seizure Severity Scale; MARS-5, Medication Adherence Report Scale; SE, standard error.

The results were analyzed by Multiple Linear Regression method after adjusting for age, sex, marital status, educational years, employment, income, epilepsy type and disease duration; * $p < 0.05$ was considered as statistically significant.

Table 3: Results from multiple linear Regression analysis that evaluated the association between dependent (QOLIE-31 score and its domains) and independent (LSSS score, MARS-5 score and serum AED level) variables

Variables	LSSS		serum AED level		MARS-5	
	B (SE)	β	B (SE)	β	B (SE)	β
Seizure concern	0.07 (0.06)	0.05	-1.33 (1.84)	-0.03	1.37 (0.21)	0.25 *
Cognitive function	-0.05 (0.07)	-0.03	4.61 (2.29)	0.07	1.58 (0.26)	0.24 *
Energy/fatigue	-0.07 (0.03)	-0.08	0.57 (0.98)	0.02	0.57 (0.11)	0.20 *
Emotional well being	-0.04 (0.03)	-0.06	-0.90 (1.01)	-0.03	0.57 (0.12)	0.20*
Social function	-0.05 (0.03)	-0.05	-0.06 (1.16)	-0.01	0.75 (0.13)	0.23*
Medication efficacy	-0.05 (0.04)	-0.05	0.91 (1.28)	0.03	0.64 (0.15)	0.17*
Overall QoL	-0.01 (0.03)	-0.02	0.70 (1.05)	0.02	0.46 (0.12)	0.15*
Overall score	-0.04 (0.03)	-0.04	1.19 (1.05)	0.04	0.93 (0.12)	0.30*

QOLIE-31, Quality of Life in Epilepsy Inventory-31; LSSS, Liverpool Seizure Severity Scale; MARS-5, Medication Adherence Report Scale; AED, Antiepileptic drug; QoL, Quality of Life; SE, standard error.

The results were analyzed by Multiple Linear Regression method adjusted for age, sex, marital status, educational years, employment, income, epilepsy type and Disease duration. * $p < 0.00625$ ((Bonferroni correction with eight comparisons; $0.05/8=0.00625$) was considered as statistically significant.

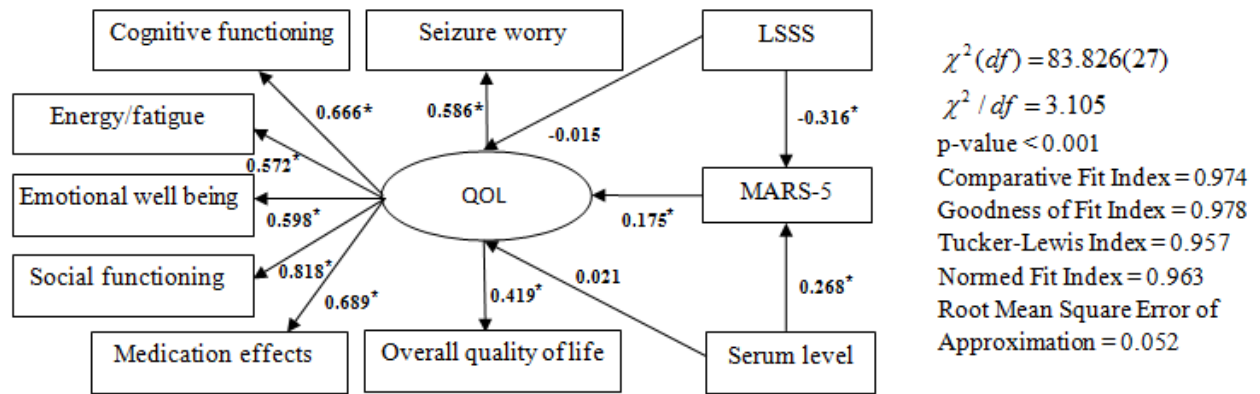


Fig. 1: The proxy effects of MARS-5 score on the quality of life (QoL) in elderly patients with epilepsy; * $p < 0.001$
 LSSS, Liverpool Seizure Severity Scale; MARS-5, Medication Adherence Report Scale; QoL, Quality of life