THE RELATIONSHIP BETWEEN STRESS, ANXIETY, DEPRESSION AND MEDICATION ADHERENCE BEHAVIOR IN PATIENTS WITH EPILEPSY : A SYSTEMATIC REVIEW

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ABSTRACT

Background: *While epilepsy is a disorder characterized by unprovoked seizures, epileptic status refers to recurrent seizures without any improvement in between episodes or seizure activity that does not improve on its own.*

Aims : *This systematic review is to review the association of stress, anxiety, depression and medication adherence behavior in patients with epilepsy.*

Methods: *This study demonstrated compliance with all requirements by means of a comparison with the standards established by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020. Thus, the specialists were able to guarantee that the research was as current as feasible. Publications released between 2014 and 2024 were considered for this search strategy. This was accomplished by utilizing a number of distinct online reference sites, including Pubmed, ScienceDirect, and SagePub. It was determined that reviews, previously published works, and partially completed works would not be included.*

Result: *In the PubMed database, the results of our search brought up 415 articles, whereas the results of our search on SAGEPUB brought up 573 articles, our search on SCIENCE DIRECT brought up 600 articles. The results of the search conducted for the last year of 2014 yielded a total 285 articles for PubMed, 275 articles for SAGEPUB and 391 articles for SCIENCE DIRECT. In the end, we compiled a total of 5 papers, 3 of which came from PubMed, 1 of which came from SAGEPUB and 1 of which came from SCIENCE DIRECT. We included five research that met the criteria.*

Conclusion: *In summary, the anxiety, stress or depression can be the appear at epilepsy patients as the absence of the adherence of epilepsy therapeutic.*

Keyword: *Antiepileptic adherence behavior, anxiety, depression, epilepsy, stress*

INTRODUCTION

While epilepsy is a disorder characterized by unprovoked seizures, epileptic status refers to recurrent seizures without any improvement in between episodes or seizure activity that does not improve on its own. Seizures lasting less than five minutes are classified as prolonged seizures; those lasting five to thirty minutes are classified as prolonged seizures; status epilepticus is defined as seizures lasting longer than thirty minutes or as repeated seizures (two or more) with or without an improvement in awareness during the recurrent episodes.[1]

Recurrent seizures (two or more times) with partial body involuntary movements, typically followed by loss of awareness and control over gastrointestinal or urinary tract function, are the hallmarks of epilepsy, a chronic brain condition. It is estimated that 4–10 per 1000 individuals have active epilepsy with recurrent episodes. Furthermore, a population research on epilepsy in underdeveloped nations revealed a greater prevalence of the condition, with a ratio of 7 to 14 per 1000 individuals.[1]

The primary treatment for epilepsy is the use of anti-epileptic medicines (AEDs), which completely prevent seizures and provide a regimen that is simple to adhere to. With the use of AEDs, 67% of epileptic patients were able to successfully lower or even eliminate their seizure frequency. Consequently, evidence suggests that the drug may regulate epileptic symptoms, as evidenced by seizure-free records spanning at least 18 months. Conversely, a high frequency of symptoms associated with significantly uncontrolled seizures characterizes uncontrolled epilepsy. According to a study, this illness may interfere with or perhaps worsen the patients' quality of life.[2]

It is believed that one of the most crucial elements in managing epileptic seizures is non-adherence. It is recognized as a global health issue that affects social, clinical, and financial results. Missed treatment doses and prescription or delay-related inadequacies are examples of non-adherence. Numerous retrospective investigations have shown the critical consequences of non-adherence to antiemetic therapy. It was determined that non-adherence would result in lower output and higher expenditures from hospitalization. Thus, it's critical to identify barriers to AED adherence so that practitioners may create effective plans to increase adherence. In order to achieve adherence, patients require particular information and assistance.[3,4]

METHODS

Protocol

The author of this study ensured that it complied with the standards by adhering to Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines. This is done to guarantee the accuracy of the results that are derived from the investigation. Thus, the specialists were able to guarantee that the research was as current as feasible. Publications released between 2014 and 2024 were considered for this search strategy. This was accomplished by utilizing a number of distinct online reference sites, including Pubmed, ScienceDirect, and SagePub. It was determined that reviews, previously published works, and partially completed works would not be included.

Criteria for Eligibility

In order to completse this literature evaluation, we looked at published research that discusses the association of stress, anxiety, depression and medication adherence behavior in patients with epilepsy. This is done to enhance the patient's therapy management and to offer an explanation. This paper's primary goal is to demonstrate the applicability of the issues that have been noted overall.

To be eligible to participate in the study, researchers had to meet the following requirements: 1) English must be used to write the paper. The manuscript must fulfill both of these conditions in order to be considered for publication. 2) A few of the examined studies were released after 2013 but prior to the time frame considered relevant by this systematic review. Editorials, submissions without a DOI, already published review articles, and entries that are nearly exact replicas of journal papers that have already been published are a few examples of research that are prohibited.

Search Strategy

We used "antiepileptic adherence", "stress anxiety depression". and "epilepsy" out using the PubMed and SAGEPUB databases by inputting the words: (("stress"[All Fields] OR "stressed"[All Fields] OR "stresses"[All Fields] OR "stressful"[All Fields] OR "stressfulness"[All Fields] OR "stressing"[All Fields]) AND ("anxiety"[MeSH Terms] OR "anxiety"[All Fields] OR "anxieties"[All Fields] OR "anxiety s"[All Fields]) AND ("depressed"[All Fields] OR "depression"[MeSH Terms] OR "depression"[All Fields] OR "depressions"[All Fields] OR "depression s"[All Fields] OR "depressive disorder"[MeSH Terms] OR ("depressive"[All Fields] AND "disorder"[All Fields]) OR "depressive disorder"[All Fields] OR "depressivity"[All Fields] OR "depressive"[All Fields] OR "depressively"[All Fields] OR "depressiveness"[All Fields] OR "depressives"[All Fields]) AND ("epilepsie"[All Fields] OR "epilepsy"[MeSH Terms] OR "epilepsy"[All Fields] OR "epilepsies"[All Fields] OR "epilepsy s"[All Fields]) AND (("medication adherence"[MeSH Terms] OR ("medication"[All Fields] AND "adherence"[All Fields]) OR "medication adherence"[All Fields]) AND ("behavior"[MeSH Terms] OR "behavior"[All Fields] OR "behavioral"[All Fields] OR "behavioural"[All

Fields] OR "behavior s"[All Fields] OR "behaviorally"[All Fields] OR "behaviour"[All Fields] OR "behaviourally"[All Fields] OR "behaviours"[All Fields] OR "behaviors"[All Fields] OR "pattern"[All Fields] OR "pattern s"[All Fields] OR "patternability"[All Fields] OR "patternable"[All Fields] OR "patterned"[All Fields] OR "patterning"[All Fields] OR "patternings"[All Fields] OR "patterns"[All Fields]))) AND ((clinicalstudy[Filter]) AND (2014:2024[pdat])) used in searching the literature.

Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.
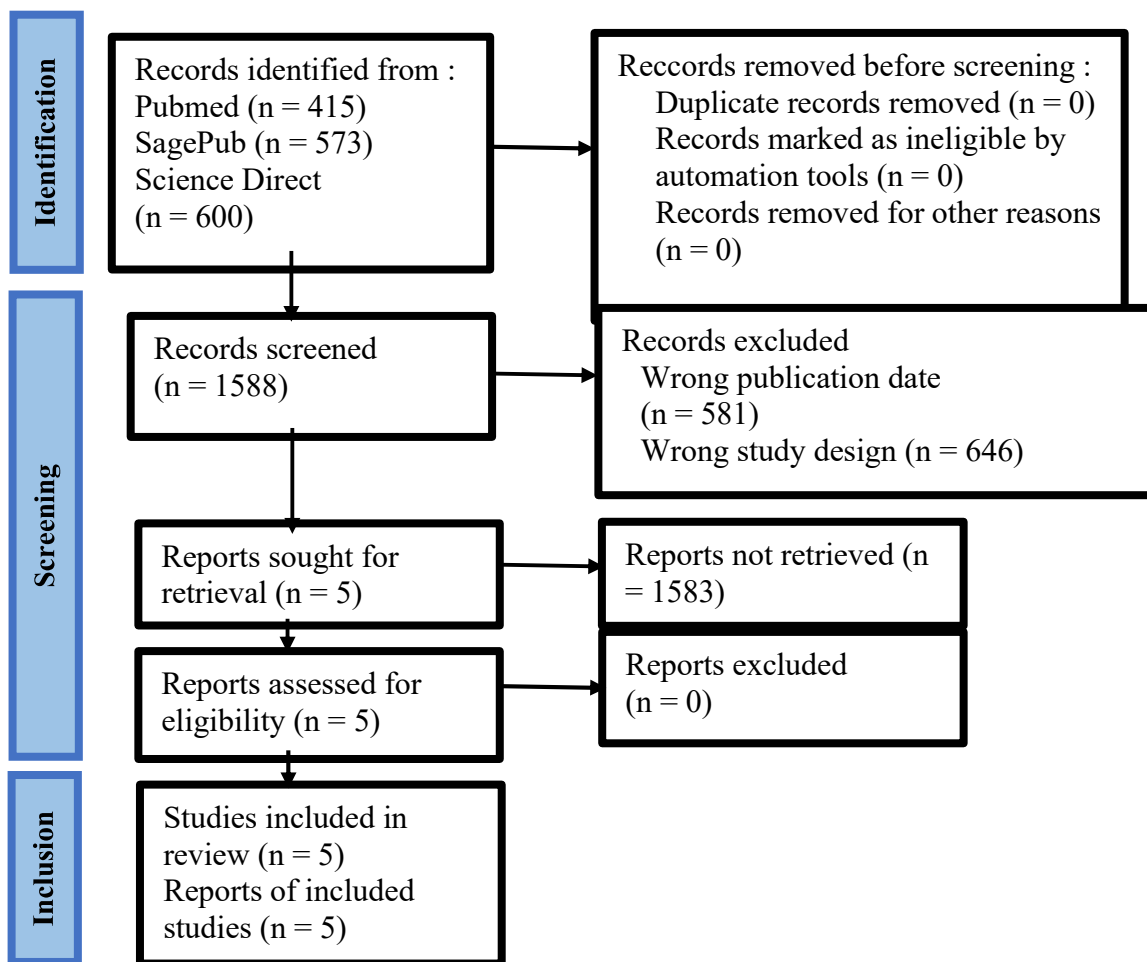

Figure 1. Prisma Flow Diagram

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT

In the PubMed database, the results of our search brought up 415 articles, whereas the results of our search on SAGEPUB brought up 573 articles, our search on SCIENCE DIRECT brought up 600 articles. The results of the search conducted for the last year of 2014 yielded a total 285 articles for PubMed, 275 articles for SAGEPUB and 391 articles for SCIENCE DIRECT. In the end, we compiled a total of 5 papers, 3 of which came from PubMed, 1 of which came from SAGEPUB and 1 of which came from SCIENCE DIRECT. We included five research that met the criteria.

Khatooni, et al[5] (2024) showed that severe and extremely severe anxiety and sadness may be regarded as a significant predictor of non-adherence to antiepileptic therapy.

Zheng, et al[6] (2019) showed that in eastern China, people with epilepsy can improve their quality of life, medication adherence, and mental comorbidities with the help of a 12-month interdisciplinary program.

Losada-Camacho[7] (2022) showed that the most common comorbidity of epilepsy is depression. Both conditions are chronic, complicated illnesses that have an impact on people's quality of life (HRQOL), particularly for women. When a pharmacist is involved in the healthcare team, therapies for women with epilepsy (WWE) may be adjusted and medication-related side effects can be minimized. This means that pharmaceutical care can greatly enhance HRQOL for WE.

Table 1. The litelature include in this study

Author	Origin	Method	Sample	Result
Khatooni et al, 2014[5]	Iran	Cross sectional study	235 patients	Significantly more patients than not reported having mild, moderate, severe, or extremely severe symptoms of stress (158 [67.2%]), anxiety (169 [71.9%]), or depression (177 [75/3%]). 38/3% of the participants reported inadequate medication adherence, compared to 61/8% who adhered to their medications well. According to the adjusted multivariate logistic regression results, there was a greater chance of poor medication adherence ($P < 0.05$) among patients with severe and extremely severe depression and anxiety. Stress levels did not significantly influence adherence to treatment ($P > 0.05$).
Zheng et al, 2019[6]	China	Prospective study	184 patients	The 12-month multidisciplinary program raised the proportion of patients with moderate-to-high AED adherence ($p = 0.006$), decreased the percentage of patients with severe depression ($p = 0.013$) and anxiety ($p = 0.002$), and improved the intervention group's overall QOLIE-31 score ($p < 0.001$). After the 12-month period, there was a substantial rise ($p < 0.001$) in both groups of patients with a low seizure frequency.
Losada-Camacho, 2022[7]	Colombia	Randomized controlled trial	182 patients	Out of the 182 WWE participants, 144 (79.1%) finished the study. In the start

				of the trial, 48.95% of patients had depressive symptoms; for patients in the IG, this percentage dropped to 30.43% (p-value = 0.0238), whereas for patients in the CG, it stayed at 47.30% (p-value = 0.8693). A w = 3138.5 and p-value = 0.01802 were obtained using the Wilcoxon test, which was used to compare the change (Δ) (before-after) in the CES-D scores across groups and demonstrate statistically significant differences.
Loiselle et al, 2015[7]	USA	Longitudinal observational study	91 patients	The study comprised 91 parents and their families who had children with epilepsy (7.3±2.8 years old; 60% male). Early (one month after diagnosis) predictors of two-year adherence trajectories included family communication, socioeconomic level, awareness of epilepsy, and problem-solving techniques within the family. One year after the diagnosis, parent worries and anxieties, parent life stress, and socioeconomic position were significant predictors.
Wang et al, 2017[8]	China	Cross sectional study	123 patients	Poor AED adherence was observed to be 33.3% of the time. Poor adherence to antiepileptic medication was strongly correlated with both moderate-to-severe anxiety (odds ratio (OR) = 2.851, 95% confidence interval (CI) = 1.138–7.144, P = 0.025) and the occurrence of hippocampal sclerosis (OR = 3.098, 95% CI = 1.259–7.620, P = 0.014). Negative adherence was linked to social support (OR = 0.925, 95% CI = 0.863–0.990, P = 0.025). Adherence was not linked to family support or depression.

Loiselle, et al[9] (2015) showed that beyond recognized medical considerations (such as seizures or side effects), modifiable parent and family characteristics can predict two-year adherence trajectories. Providing psychosocial treatments at strategic junctures in the process of treating epilepsy may improve adherence rates.

Wang, et al[8] (2017) showed that AED non-adherence was common in one-third of TLE patients, particularly in those with hippocampal sclerosis. Psychosocial variables should be the primary focus of intervention techniques intended to increase AED adherence in individuals with TLE.

DISCUSSION

AEDs, or anti-epileptic drugs, are the primary treatment for epilepsy that stop seizures. A significant contributing factor to the inability to manage seizures is non-adherence. A situation like this might have several effects on the social, clinical, and financial fronts. Patients with epilepsy are measured for adherence using a variety of techniques, including as direct and indirect assessment. Measuring the amount of medication in hair or bodily fluids like blood or saliva is known as a direct measure. On the other hand, non-biological instruments such as self-report measures, pill counts, appointment attendance, medicine refills, and seizure frequency are used in indirect measures. Age, sex, seizure aetiology, and seizure locations are among the many variables that might impact adherence in epilepsy patients. These characteristics are classified as irreversible and are unlikely to be improved. Nonetheless, a number of variables that are related to treatment and education and are linked to behaviors that are likely to be adhered to may be modified in order to increase adherence, including patient knowledge, medicine, cultural norms, health care providers, and national health policies.[10]

The primary treatment for epilepsy is the use of anti-epileptic medicines (AEDs), which completely prevent seizures and provide a regimen that is simple to adhere to. With the use of AEDs, 67% of epileptic patients were able to successfully lower or even eliminate their seizure frequency. Consequently, evidence suggests that the drug may regulate epileptic symptoms, as evidenced by seizure-free records spanning at least 18 months. Conversely, a high frequency of symptoms associated with significantly uncontrolled seizures characterizes uncontrolled epilepsy. According to a study, this illness may interfere with or perhaps worsen the patients' quality of life.[1]

Adherence in AEDs is the degree to which patients adhere to the predetermined instructions provided by the prescribers and persevere in a regimen of treatment for epilepsy, including the length of time between starting and stopping therapy. The World Health Organization (WHO) has determined that improving adherence may have a bigger influence on population health than improving the efficacy of any particular medical therapy.[11,12]

Patients with epilepsy who do not take their AEDs as prescribed run a higher risk of developing convulsive status epilepticus. The likelihood of unexpected, unexplained death in epilepsy patients is the most devastating effect of non-adherence. Because of such repercussions, it is thought to be crucial for practitioners to recognize the obstacles to AED adherence in order to design effective measures to increase adherence rates.

One of the most complicated neurological conditions is epilepsy, which significantly affects a patient's health-related quality of life (HRQOL) and raises their chance of developing mental health issues. Numerous studies have demonstrated that individuals with epilepsy, particularly women, have a worse HRQOL and have linked it to negative outcomes, depression, using more anticonvulsants, and having seizures more frequently.[13]

The randomized controlled study by Losada-Camacho with 182 women with epilepsy (WWE) and 144 completed it. This study proved that the program significantly decreas sign of depression in women with epilepsy.Khatooni, et al investigate the association of stress, anxiety, and depression and medication adherence behavior in patients with epilepsy. They did cross sectional study with 235 patients with epilepsy with data collection tools of morisky medication adherence scale (MMAS-8). The result of their study showed that depression and anxiety can be appeared severe and extremely and can be the predictor of lack adherence to antiepileptic.[5] This also studied by Zheng, et al in their study of 184 patients with epilepsy, that out of 92 randomized to intervention group and 92 to the control group. This study showed that at their 12 month period of multidisciplinary there is improvement of psychiatric comorbiditiees, medication adherence and quality of life in patients with epilepsy.[6]

Loiselle, et al identify psychosocial predictors the using of two year of antiepileptic drug adherence in 91 parents of youth with epilepsy with age average 7 to 8 year ol and 60% male. Beyond recognized medical considerations (such as seizures or side effects), modifiable parent and family characteristics can predict two-year adherence trajectories. Providing psychosocial treatments at strategic junctures in the process of treating epilepsy may improve adherence rates.[9]

Following an epilepsy diagnosis, the best course of treatment is long-term antiepileptic medication (AED) usage, which allows around 70% of patients to live seizure-free lives. On the other hand, poor adherence to AEDs is common and is thought to be the primary reason why medication therapy fails. Low adherence to AEDs has been observed to vary in severity from 26.0% to 66.2%, with industrialized nations having a lower prevalence of this issue than developing ones. The study by Wang, et al with 123 individuals with temporal lobe epilepsy (TLE) showed that AED non-adherence was common in one-third of TLE patients, particularly in those with hippocampal sclerosis. Psychosocial variables should be the primary focus of intervention techniques intended to increase AED adherence in individuals with TLE.[8]

CONCLUSION

In summary, the anxiety, stress or depression can be the appear at epilepsy patients as the absence of the adherence of epilepsy therapeutic.

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