Original Research

Do Anti-Epilepsy Drugs Increase Suicide Ideation Risk in Epilepsy Patients?

Fahmina Ashfaq, Nauman Ismat Butt, Muhammad Bilal Rasheed, Muhammad Sohail Ajmal Ghoauri, Malik Shahzad Tariq, Huma Afzal

ABSTRACT

Objective: To determine the frequency of suicide risk within first six months after starting anti-epilepsy treatment.

Methodology: This Descriptive cross-sectional study conducted at department of Medicine, Jinnah Hospital Allama Iqbal Medical College Lahore Pakistan from January 2019 to January 2020.The Scale of Suicidal Ideation (SCI) consists of 19 items which were used to evaluate patients' suicidal intentions and to monitor patients' response to interventions over time. Patients with diagnosed psychiatric illness such as depression and schizophrenia, past history of suicidal attempts and patients with poor drug compliance were excluded. After informed consent, 140 epileptic patients, who had been recently started on anti-epilepsy medicines, aged 20 to 55 years of both gender were enrolled using non-probability consecutive sampling technique. Demographic information and detailed medical history were noted and patients were assessed for suicide risk using the Scale of Suicidal Ideation (SCI). All data was recorded and analyzed using SPSS version 23.0.

Results: Mean age was 28.9±6.3 years with 104 (74.3%) males and 36 (25.7%) females. Sixty-eight (48.6%) patients belonged to low socio-economic status whereas 29 (20.7%) and 43 (30.7%) patients were from middle and high Socio-economic Status respectively. Sixty-eight (48.6%) patients were illiterate while 42 (30.0%) and 30 (21.4%) patients had educational status of up to matriculation and graduate or above respectively. In the present study, 46 (32.8%) patients had suicidal ideation with low socio-economic status (p-value 0.013) and illiterate educational status (p-value 0.002) having statistically significant association with suicidal ideation.

Conclusion: Suicidal ideation was seen in almost one-third epilepsy patients on anti-epileptic drugs with low socio-economic status and illiterate educational status being significant risk factors.

KEYWORDS: Epilepsy, Anti-Epilepsy Drugs (AEDs), Suicide Risk, Suicide Ideation.

INTODUCTION

Epilepsy is one of the most common and prevalent medical condition with occurrence rate of 8.2 to 12.9 per 1000 population.[1] Epilepsy is not only a neurological but also associated with a wide range of comorbidity which majorly includes psychiatric disorders that constitute a bigger proportion of co morbidity in epilepsy.[1-2] These psychiatric disorders include depression, anxiety and suicidal ideation. Each year nearly 9,00,000 deaths are estimated in the whole world due to suicide which accounts for more deaths than homicides and wars. In Pakistan, there is no official data available however there is accumulating evidence that suicide rates have been alarmingly increased in the past few year.[2] The question of whether people with epilepsy are at significant risk of suicidal behavior has been a debate amongst the medical community for years now.[3,4] There have been some studies that depict presence of psychiatric illnesses like anxiety and depression in various other chronic medical diseases such as chronic liver disease and chronic kidney disease in Pakistan.[5,6]

Antiepileptic drugs (AED) have been linked with suicide related behavior by Food and Drug Administration in 2008. Since then various studies have been conducted which were inconsistent. Some found increased risk with the use of antiepileptic drugs while others found that increased risk with the use of AEDs was primarily due to depression and other factors.[7] People with epilepsy appear to have a significant risk of

Fahmina Ashfaq, *MBBS, MRCP, MCCEE, FCPS*
Consultant Physician,
Jinnah Hospital Allama Iqbal Medical College LHR, Pakistan.
Nauman Ismant Butt, *MBBS, FCPS*
Associate. Professor.
Azra Naheed Medical College Superior University LHR, Pakistan.
Muhammad Bilal Rasheed, *MBBS*
House Physician,
Azra Naheed Medical College Superior University LHR, Pakistan.
Muhammad Sohail Ajmal Ghoauri, *MBBS*
Post Graduate Resident,
Bahawal Victoria Hospital,Quaid-e-Azam Medical College, BHV, Pakistan
Malik Shahzad Tariq, *MBBS, FCPS,*
Consultant Physician
Jinnah Hospital Allama Iqbal Medical College, LHR, Pakistan.
Huma Afzal, *MBBS,*
Senior Medical Officer,
Jinnah Hospital Allama Iqbal Medical College LHR, Pakistan.

Correspondence
Nauman Ismant Butt
Email: Nauman_ib@ yahoo.com

developing suicidality with suicidal ideation than do people without epilepsy.[8] Suicidal ideation in patients with epilepsy has complex etiologies. Various factors have been identified as risk factors which include male gender, young age, temporal lobe epilepsy, frequency of primary generalized seizure, severe epilepsy, psychiatric comorbidity etc.[1] In the literature 3.3% to 14.3% epileptic patients show a lifetime prevalence of suicide as compared to the general population that is 1.4% to 6.9%.[1]

According to an article published in 2011 reviewing various studies to establish a relationship between antiepileptic drug treatment and suicidality show a lack of concordance.[3] Later in 2012 an international study showed the risk of suicidality amongst epileptic patients to be 35%.1 Another study conducted in 2015 found the risk of suicidality to be 30.4% amongst the epileptic patients.[8] Unfortunately in recent times there has been no study conducted in the local settings to study the prevalence of suicidality in epileptic patients. Therefore the present study was aimed to find out the frequency of suicide ideation within first six months after starting anti-epilepsy treatment in patients suffering from epilepsy in Pakistani population.

METHODOLOGY

The present descriptive cross-sectional study was conducted at Department of Medicine, Jinnah Hospital Allama Iqbal Medical College Lahore Pakistan to determine the frequency of suicide risk within first six months after starting anti-epilepsy treatment from January 2019 to January 2020. The Scale of Suicidal Ideation (SCI) consists of 19 items which were used to evaluate patients' suicidal intentions and to monitor patients' response to interventions over time.[9] The minimum score was zero and maximum score 38.9 Based on the score, the patients were ranked having mild risk (score 0-12), moderate risk (score 13-26) or severe risk (score 27-38) of suicidal ideation. The calculated sample size was 140 by taking 95% level of confidence, absolute precision of 0.8% and expected percentage of suicide risk in epileptic patients as 35%.[1] Patient enrollment was from outpatient department of patients with epilepsy who were started on anti-epilepsy medication aged 20-55 years of both sex. All included patients had been seizure-free while taking anti-epilepsy drug treatment. Patients with diagnosed psychiatric illness such as depression and schizophrenia, past history of suicidal attempts and patients with poor drug compliance as assessed by detailed history and examination were excluded from the study.

After approval from Ethical Review Committee, 140 epileptic patients as per operational definitions who had presented to Department of Medicine, Jinnah Hospital Allama Iqbal Medical College Lahore Pakistan were enrolled using non-probability consecutive sampling technique. After taking informed written consent, demographic information and detailed medical history were noted for each patient and assessment for suicide risk was done. The patients were assessed for suicide risk using the scale of suicidal ideations (SCI).

Statistical analysis: All data was recorded and analyzed using SPSS version 23.0. Mean and standard deviation were calculated for quantitative variables. Frequency and percentage were calculated for qualitative variables. To develop a correlation between factors like age, gender, socioeconomic status and educational level, Chi-Square Test was applied between each group and p-value was calculated, p-value less than or equal to 0.05 was considered significant.

RESULTS

A total of 140 patients with epilepsy were included. Age range in this study was from 20 to 55 years with mean age of 28.9±6.3 years. Among 140 patients with epilepsy, 104 (74.3%) patients were male and 36 (25.7%) patients were female. Eighty-five (60.7%) patients were aged 20-30 years while 42 (30.0%) and 13 (9.3%) patients were in 31-40 years and >40 years age group respectively. Sixty-eight (48.6%) patients belonged to low socio-economic status whereas 29 (20.7%) and 43 (30.7%) patients were from middle and high Socio-economic Status respectively. Sixty-eight (48.6%) patients were illiterate while 42 (30.0%) and 30 (21.4%) patients had educational status of up to matriculation and graduate or above respectively. In the present study, 46 (32.8%) patients had suicidal ideation. On stratification it was found that low socio-economic status (p-value= 0.013) and illiterate educational status (p-value = 0.002) were associated with suicidal ideation whereas age (p-value 0.982) and

sex (p-value= 0.416) were not associated as shown in Table 1.

Table 1: Comparison of qualitative clinical parameters according to Suicide Ideation Risk

Clinical Parameters	Suicide Ideation Risk		p-value
	Present	Absent	
Gender:			
Female	08 (22.2%)	28 (77.8%)	0.416
Male	35 (33.7%)	69 (66.3%)	
Age:			
20-30 years	25 (29.4%)	60 (70.6%)	0.982
31-40 years	16 (38.1%)	26 (61.9%)	
>41 years	03 (23.1%)	10 (76.9%)	
Educational Status:			
Illiterate	30 (44.1%)	38 (55.9%)	0.002
Up to Matriculation	09 (21.4%)	33 (78.6%)	
Graduate and above	06 (20.0%)	24 (80.0%)	
Socio-economic status:			
Low	31 (45.6%)	37 (54.4%)	0.013
Middle	06 (20.7%)	23 (79.3%)	
High	08 (18.6%)	35 (81.4%)	

P value≤ 0.05 considered significant

DISCUSSION

In the present study, suicide ideation was seen in 32.8% of the 140 epilepsy patients enrolled who were taking anti-epilepsy drugs (AEDs) with educational status and socio-economic status being significant risk factors. There are numerous studies that depict the effects of epilepsy both as a disease and a social condition on the patient. Correlation of epilepsy with depression has been documented by various studies showing fluctuations from 11% up to 65%.[10,11] Epilepsy, by itself, may lead to an elevated risk of depression. A vicious reinforcing cycle, numerous studies depict a bi-directional cause and effect relationship of epilepsy and depression.[12,13,14] Depression can itself lower the threshold seizures and cause epileptic fits while recurrent or persistent seizure episodes, intra-ictal and post-ictal psychosis can lead to depression. Of the whole spectrum of depression in epilepsy, the most bothersome and crucial component is suicidal ideation which is distressing to the patient causing a poor quality of life and reduction in functional status. Suicidal ideation has been reported in up to 36.7% of epilepsy patients.[15] This is in stark contrast to the prevalence of suicide ideation in general population which ranges from 1.0% to 1.4%.

The type of epilepsy itself also affects the risk of suicide ideation in these patients. Temporal lobe epilepsy elevates suicide risk up to 6-fold.[16] Complex partial seizure increase suicide risk by up to 25 fold.[17] Many epilepsy patients face negative socio-economic stigma, difficulty in finding employment, causing financial difficulties and consequently resulting in poor mental health and suicide ideation. This is more common in Asian countries due to poor support from society rendering patients to feel isolated and depressed. Complications of disease and activity restrictions also increase pressure on the patients, their care-givers and family members. Furthermore, easy access to drugs especially AEDs facilitates suicide by overdosing on prescription drugs causing significant mortality in such patients.[1,16] The most vital risk factor for suicide is presence of mood disorder in epilepsy patients. Depression is a predictor of suicidal ideation in patients with epilepsy in addition to affecting the quality of life.[18,19] Depression has been reported in up to 65% of epilepsy patients.[19,20] Risk factors contributing to depression in epilepsy are variable and include the type of epilepsy, frequency of seizures, social and occupational isolation, economic and financial restrain and the taboo associated with epilepsy itself.[21] In generalized epilepsy, the most common form of epilepsy, suicidal ideation is up to 18.7%.[22,23] This is followed by Complex Partial Epilepsy having suicidal ideation at 12.5%.[22,23] In Malaysia up to 92.0% of epilepsy is due to generalized epilepsy and 14.0% due to partial seizures.[22,23] It should be acknowledged that AEDs (such as benzodiapines, gabapentin, topiramate, phenobarbitone, lamotrigine, levetiracetam)with positive GABA properties lead to decrease in serotonin secretion causing negative psychotropic effect thereby increasing risk of depression and suicide.[1] In the literature 3.3% to 14.3% epileptic patients show a lifetime prevalence of suicide as compared to the general population that is 1.4% to 6.9%.[8] According to an article published in 2011 reviewing various studies to establish a relationship between antiepileptic drug treatment and suicidality show a lack of concordance.[3]

The present study has some limitations as well which need to be considered. Based in a single center, the present study had a relatively small

sample size and enrolled outpatient care patients only. Randomized Controlled Trials and cohort studies are a better option but require more resources and time. Using the results of our study as baseline data, researchers could plan more studies and generate further evidence regarding association of suicide ideation risk in epilepsy patients taking Anti-Epileptic Drugs.

CONCLUSION

We conclude that suicidal ideation was seen in almost one-third of the epilepsy patients in our study. Furthermore, low socio-economic status and illiterate educational status elevate the risk of suicide. Therefore, we recommend that patients of epilepsy should be screened for suicide ideation so that timely intervention may lead to reduction in disease stigma, morbidity and disability. A multidisciplinary approach involving physicians, neurologists, psychiatrists and psychologists is warranted in such patients.

Conflict of Interest: None
Funding Source*:* None

REFERENCES

1. Hamed SA, Elserogy YBE, Abdou MA, Abdellah MM. Risks of suicidality in adult patients with epilepsy. World J Psychiatry. 2012;2(2):33-42. doi: 10.5498/wjp.v2.i2.33.
2. Abbas A. Suicide trends in Pakistan. Pakistan [Internet].Health Watch;2015.Available from healthwatch.pk/2015/09/1167. [Cited 19 Dec 2022]
3. Mula M, Hesdorffer DC. Suicidal behavior and antiepileptic drugs in epilepsy: analysis of the emerging evidence. Drug Healthc Patient Saf. 2011;3:15-20. doi: 10.2147/DHPS.S13070.
4. Habib O, Javed M, Mahmood K, Qureshi MA, Butt NI, Ashaq F. Prevalence of Post-traumatic Stress Disorder in Medical Students. PJMHS.2022;16(11:188-191. doi:https://doi.org/10.53350/pjmhs20221611188.
5. Habib O, Ashaq F, Butt NI, Mahmood K, Khan AA, Qureshi MA. Does Having a Chronic Liver Illness Make One More Likely to Become Melancholic and Anxious? PJMHS. 2022;16(07):227-229. doi:https://doi,org/10.53350/pjmhs22167227.
6. Habib O, Ashaq F, Butt NI, Ashraf HH, Mahmood K, Anser A. Prevalence of depression and anxiety in chronic kidney disease patients. PJMHS.2022;16(06):236-238. doi:https://doi.org/10.53350/pjmhs22166236.
7. Pugh MJV, Hesdorffer D, Wang CP, Amaun ME, Tabares JV, Finley EP et al. Temporal trends in new exposure to antiepileptic drug monotherapy and suicide-related behavior. Neurology.2013;81(22):19001906. doi:10.1212/01.wnl.0000436614.51081.2e.
8. Seo JG, Lee JJ, Cho YW, Lee SJ, Kim JE, Moon HJ et al. Suicidality and Its Risk Factors in Korean People with Epilepsy: A MEPSY Study. J Clin Neurol.2015;11(1):32-41. doi:10.3988/jcn.2015.11.1.32.
9. Beck AT, Kovacs M, Weissman A. Assessment of suicidal intention: the Scale for Suicide Ideation. J Consult Clin Psychol. 1979;47(2):343-352. doi: 10.1037//0022-006x.47.2.343.
10. Yousafzai AU, Yousafzai AW, Taj R. Frequency of depression in epilepsy: a hospital based study. Journal of Ayub Medical College, Abbottabad: JAMC. 2009;(2):73-5.
11. Kalinin VV, Polyanskiy DA. Gender differences in risk factors of suicidal behavior in epilepsy. Epilepsy Behavior 2005; 6(3):424-429. doi: 10.1016/j.yebeh.2005.02.003.
12. Bell GS, Gaitatzis A, Bell CL, Johnson AL, Sander JW. Suicide in people with epilepsy: how great is the risk? Epilepsia 2009;50(8):1933-1942. doi: 10.1111/j.15281167.2009.02106.x.
13. Bell GS, Sander JW. Suicide and epilepsy. Curr Opin Neurol. 2009;22(2):174-78. doi:10.1097/WCO.0b013e328328f8c3.
14. Stefanello S, Marin-Leon L, Fernandes PT, Min LL, Botega NJ. Suicidal thoughts in epilepsy: a community-based study in Brazil. Epilepsy Behav. 2010; 17(10):483-488. doi:10.1016/j.yebeh.2009.12.029.
15. Verrotti A, Cicconetti A, Scorrano B. Epilepsy and suicide: pathogenesis, risk factors, and prevention. Neuropsychiatr Dis Treat. 2008;4(2):365-370. doi: 10.2147/ndt.s2158.
16. Blumer D, Montouris G, Davies K, Wyler A, Phillips B, Hermann B. Suicide in epilepsy: psychopathology, pathogenesis, and prevention. Epilepsy Behav 2002;3(3):232-241. doi: 10.1016/s1525-5050(02)00006-9.
17. Pompili M, Vanacore N, Macone S. Depression, hopelessness and suicide risk among patients suffering from epilepsy. Annali dell'Istituto Superiore di Sanita 2007; 43(4):425-429.
18. Loring DW, Meador KJ, Lee GP. Determinants of quality of life in epilepsy. Epilepsy Behavior 2004;5(1):976-980. doi: 10.1016/j.yebeh.2004.08.019.
19. Senol V, Soyuer F, Arman F, Ozturk A. Influence of fatigue, depression, and demographic, socioeconomic, and clinical variables on quality of life of patients with epilepsy. Epilepsy Behav. 2007; 10(1):96-104.
20. Hesdorffer DC, Hauser WA, Olafsson E, Ludvigsson P, Kjartansson O. Depression and suicide attempt as risk factors for incident unprovoked seizures. Ann Neurol 2006; 59(1):35-41. doi: 10.1002/ana.20685.
21. Mac TL, Tran DS, Quet F, Odermatt P, Preux PM, Tan CT. Epidemiology, aetiology, and clinical management of epilepsy in Asia: a systematic review. Lancet Neurol 2007; 6(6):533-543. doi: 10.1016/S1474-4422(07)70127-8.
22. Win MN. The EEG and epilepsy in Kelantan--a hospital/laboratory-based study. The Med J Malaysia 1993:48 (2):153-159.
23. Machado RA, Espinosa AG, Melendrez D, Gonzalez YR, Garcia VF, Rodriguez YQ. Suicidal risk and suicide attempts in people treated with antiepileptic drugs for epilepsy. Seizure. 2011;20(4):280-284. doi: 10.1016/j.seizure.2010.12.010.

Author's Contribution	
Fahmina Ashfaq	Study design, data collection, data analysis and interpretation revise and approve the article
Nauman Ismat Butt,	Study design, data collection, Data analysis and interpretation, revise all intellectual contents and approve the article
Muhammad Bilal Rasheed	Study design, data collection, manuscript writing, revised and approve the article
Muhammad Sohail Ajmal Ghoauri	Study design, manuscript writing revise and approve the manuscript
Malik Shahzad Tariq	Study design, data collection revise and approve the article
Huma Afzal	Study design, data collection revise and approve the article
All the authors are equally accountable of accuracy, integrity of all aspects of the research work.	

Date of Submission: 30-12-2022
Revised: 7-5-2023
Accepted: 10-5-2023