Research Report

DOES PSYCHIATRIC COMORBIDITY INFLUENCES QUALITY OF LIFE AND DISABILITY AMONG SUBJECTS WITH REFRACTORY FOCAL EPILEPSY- A COMPARATIVE CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Refractory focal epilepsy is a disorder associated with a significant impact on quality of life and disability. Having comorbid psychiatric disorders among these subjects has been well documented. Recently studies have looked at how this impacts the quality of life and disability, but they are few in number. **Methodology:** Subjects were taken from the epilepsy clinic whom neurologist diagnosed as having refractory focal epilepsy. MINI International Neuropsychiatric Interview (MINI) was used to identify psychiatric comorbidity. Two groups of 25 subjects were made based on whether they had or did not have psychiatric comorbidities and further assessed with the World Health Organization Quality of Life (WHOQOL)-BREF for quality of life and World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0) for disability. **Results:** Analysis of the two groups showed quality of life score lesser in the group with psychiatric comorbidities, which was significant ($p<0.001$). Similarly, the disability score was higher in the group with psychiatric comorbidities, which was significant ($p<0.001$). The quality of life was lowest in major depressive disorder (60.80 ± 8.47) and disability was highest in psychosis (105.33 ± 1.53). **Conclusion:** Psychiatric comorbidities in subjects with refractory focal epilepsy significantly impact the quality of life and disability. It is essential to have a good team approach, and liaison between neurology and psychiatry for early detection and treatment of such symptoms will decrease healthcare costs and improve quality of life.

Keywords: refractory epilepsy, psychiatric comorbidity, quality of life, disability

INTRODUCTION

Epilepsy is derived from Greek words meaning "to seize upon", it is generally used to denote recurrent seizures. Seizure is a generic term that embraces a diversity of paroxysmal events due to sudden central nervous system function alteration. Seizures have been classifiedin several ways according to their supposed aetiology (primary or secondary), their site of origin (generalised or focal), their frequency, or their electrophysiologic correlates. Epileptic syndromes are disease constellations that may manifest several seizure types. Over two-thirds of all epileptic seizures begin in childhood, and their persistence into adulthood makes it a chronic illness. It is associated with regular long term drug use and follow-ups to hospitals. In addition to this, 30% of persons with epilepsy are found to have refractory epilepsy. Refractory epilepsy is defined as

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failure of adequate trials of two tolerated, appropriately selected and used antiepileptic drug schedules (whether as monotherapies or in combination) to attain sustained seizure freedom.[1] In studies from India, the prevalence of refractory epilepsy has been around 10-20%.[2] These patients then suffer a lifetime burden of seizures that worsen their quality of life with accompanying alterations in the personal, occupational, family and social spheres of life and provide a sufficient base to give rise to a psychological effect that may lead to associated psychiatric comorbidities. Two studies conducted in South India using standardised interview protocols had shown that significantly increased psychiatric comorbidities were associated with epilepsy compared to patients with another chronic condition-asthma and normal controls, as well as increased lifetime prevalence rates of psychiatric conditions.[3] Partial epilepsy, especially temporal lobe epilepsy was found to be associated with more psychiatric comorbidities. This high prevalence has been considered to be due to a possible common mechanism for both.[4] The psychiatric comorbidities can also lead to non-compliance to therapy and can ultimately worsen epilepsy.[5]

Epilepsy makes up a quarter of the global disability-adjusted life years for neurologic conditions, second to migraine, and ranks 20th overall for years lived with disability.[6] There are only a few reports on patient-centred reports of seizure-related disability, as most studies focus on specific constructs of health-related disability rather than epilepsy.[7] It has been observed in a study in Kenya that disability was higher in persons having secondary epilepsy, which was less responsive to treatment.[8] The frequent association between psychiatric symptoms and disability makes it necessary to measure disability/ functional impairment in addition to psychiatric symptoms when tracking treatment outcomes.[9] The diagnosis of psychiatric illness sometimes fosters rather than alleviates their illness, and so they are frequently invoked and are often a genuine source of suffering and disability.[10]

Comorbidity in epilepsy is a condition that can occur in association with epilepsy. That can be a cause of epilepsy or a consequence and can co-occur, precede, or follow the diagnosis of epilepsy. Most patients with refractory epilepsy would suffer a lifetime burden that seizures deteriorate the quality of life with cognitive, psychiatric and other comorbidities.[11] The psychiatric disorders associated with epilepsy are mainly affective disorders, anxiety disorders, psychosis, dissociative disorders, and somatoform disorders. Amongst these, depression and anxiety are the main psychiatric comorbidities associated with epilepsy.[12] Depression is also believed to be especially common in patients with Temporal Lobe Epilepsy.[13] In a study from Italy, a prevalence rate of psychiatric disorders as high as 80% was reported in a selected subgroup of patients with temporal lobe refractory epilepsy.[14]

The antiepileptic medications themselves cause various psychiatric symptoms, making it more challenging for a physician to manage both conditions. Depressive symptoms in epilepsy have been attributed to the adverse effects of certain antiepileptic drugs (AEDs), particularly GABAergic agents, such as vigabatrin, tiagabine, topiramate and phenobarbital.[15]

Hence, it is essential for early diagnosis of psychiatric comorbidities in patients with refractory epilepsy. Our study aims to determine the psychiatric comorbidities in refractory epilepsy and determine the impact of psychiatric comorbidities on the quality of life and disability.

Objectives

I. Primary objectives:

1. To compare the quality of life among subjects having refractory focal epilepsy with coexisting psychiatric comorbidities and those without.
2. To compare disability among subjects having refractory focal epilepsy with coexisting psychiatric comorbidities and those without.

II. Secondary objective:

To assess whether certain psychiatric comorbid disorders have a higher impact on quality of life and disability among subjects.

MATERIALS AND METHODS

Sample size

Based on the mean values of quality of life in subjects with refractory epilepsy with (n=41) and without psychiatric comorbidity (n=36), i.e. 64.99±15.29 and 77.56±11.70 reported in an earlier publication which was statistically significant $p<0.01$. So with a 95%

confidence interval and 80% power for controlling type 2 error 80%; the minimum sample size comes to 25 in each group.[16]

Study setting

The study was done in Amrita Institute of Medical Sciences & Research Centre, Kochi, a 1450-bed hospital. This study was done in two years, from 2017 to 2019, in the subjects diagnosed with refractory focal epilepsy in the Epilepsy clinic, by a consultant Neurologist, Department of Neurology.

Selection of study participants

Diagnosed cases of refractory focal epilepsy by a consultant neurologist attending epilepsy clinic, fulfilling the inclusion and exclusion criteria, were recruited for the study.

Inclusion Criteria:

1) Subjects included are 18 years and above and diagnosed with refractory focal epilepsy as per the International League Against Epilepsy criteria.
2) Subjects who are willing to participate in the study.
3) Subjects having the ability to read and write English or Malayalam and to understand the informed consent and signed the same.

Exclusion Criteria:

1) Subjects who are not willing to participate in the study.
2) Subjects with seizures secondary to some other disease.
3) Subjects unable to complete the assessments.

Study tools

Semi-structured data collection Pro forma:

A semi-structured pro forma was used to record information regarding the sociodemographic and clinical details of the subjects.

1. MINI International Neuropsychiatric Interview (MINI 5.0)

The MINI International Neuropsychiatric Interview (MINI 5.0) is a short, structured diagnostic interview developed in 1990 by David V. Sheehan. It maps on to diagnostic criteria for DSM IV and ICD-10. The studies showed that MINI has acceptably high validation and reliability scores and can be administered in a shorter reliability scores and can be administered in a shorter period. It has been used reliably for multi-centre clinical trials, epidemiological studies, outcomes research, and non-research clinical settings.

2. The World Health Organization Quality of Life (WHOQOL)-BREF

The World Health Organization Quality of Life (WHOQOL)-BREF instrument comprises 26 items measuring the following broad domains: physical health, psychological health, social relationships, and environment. The domain scores demonstrated good discriminant validity, content validity, internal consistency, and test-retest reliability and correlated at around 0.9 with the WHOQOL-100 domain scores.

3. World Health Organization Disability Assessment Schedule 2.0(WHODAS 2.0)

The World Health Organizations Disability Assessment Schedule 2.0 (WHODAS 2.0) was developed for measuring functioning and disability in accordance with the International Classification of Functioning, Disability and Health. The WHODAS 2.0 meets the need for a robust instrument that can be easily administered to measure the impact of health conditions, monitor the effectiveness of interventions and estimate the burden of both mental and physical disorders across different populations.[17]

Impairments and disabilities are assessed over six domains described over the past 30 days. The various six domains are cognition, mobility, self-care, interacting with others, participation in life and community activities.

Procedure

Fifty subjects who came to the Department of Neurology with a diagnosis of refractory focal epilepsy satisfying the inclusion and exclusion criteria were taken into the study. The ethics committee approved the study. A convenience sampling method was used. Subjects on visits to the epilepsy clinic who have had a diagnosis of refractory epilepsy made by a consultant neurologist according to the diagnostic criteria were taken. After explaining the study procedure, written informed consent was taken from the subjects. MINI 5.0 was administered at any time during patient visits to the Epilepsy clinic to look for any psychiatric comorbidities

and to divide the subjects into two groups, with and without psychiatric comorbidities. Sociodemographic and clinical details were recorded from the subjects using the semi-structured clinical proforma The quality of life of subjects were assessed using the World Health Organization Quality of Life (WHOQOL)-BREF instrument, and disability was assessed using World Health Organization Disability Assessment Schedule 2.0(WHODAS 2.0).

Statistical analysis was done using IBM SPSS version 20.0 (SPSS Inc. Chicago, USA). For all the continuous variables, the results are given in Mean ± SD and categorical variables as percentages. To find the statistical significance of difference in demographic and clinical variables between the two groups (comorbidities present and absent the Chi-square test was applied with a correction factor. Mann Whitney U test was used to compare the mean difference of quality of life (WHOQOL- BREF) and Disability (WHODAS 2.0). A P-value < 0.05 was considered as statistically significant.

RESULTS

Fifty subjects with refractory focal epilepsy were taken up for the study. They were divided into two groups of 25 each, which are with and without psychiatric comorbidities. To get the required number of subjects with psychiatric comorbidities, 57 subjects had to be screened.

Table 1 shows the sociodemographic details of the two groups. The mean age of subjects with Psychiatric comorbidities were 33.44±13.09 and without Psychiatric comorbidities were 28.60±8.05, which was not statistically significant using Mann Whitney U test. The two groups did not differ in gender, marital status and type of family distribution. Both groups had all subjects having at least a high school education. Among subjects with Psychiatry comorbidities, 5 (20%) were Diploma/Graduation, and 20(80%) were high school level. And subjects without Psychiatric comorbidities education status of 12(48%) were Diploma/Graduation, and 13(52%) were high school level. The association of educational status between groups was analysed using Pearson's Chi square test and was statistically significant with a p-value of 0. 037. In both groups majority of subjects were unemployed, 18(72%) and 14(56%) respectively. Association using Pearson chi-square test was statistically not significant for employment status, monthly family income and area of domicile.

Table 1.Comparison of Sociodemographic details in subjects with refractory focal epilepsy with and without Psychiatric comorbidities.

Variable	Co-morbidities present (n=25)	Co-morbidities absent (n=25)
Age	33.44	28.6
Gender		
Males	13 (52%)	14 (56%)
Females	12 (48%)	11 (44%)
Marital status		
Single	15 (60%)	11 (44 %)
Married	10 (40%)	14 (56%)
Type of family		
Nuclear	18 (72%)	18 (72%)
Joint	7 (28%)	7 (28%)
Educational status		
High school	20 (80%)	13 (52%)
Diploma/Graduate	5 (20%)	12 (48%)
Employment status		
Unemployed	18 (72%)	14 (56%)
Employed	7 (28%)	11 (44%)
Monthly family income		
≤30000	5 (20%)	4 (16%)
30000-60000	19 (76%)	15 (60%)
≥ 60000	1 (4%)	6 (24%)
Area of domicile		
Rural	4 (16%)	NIL
Urban	20 (80%)	21 (84%)
Suburban	1 (4%)	4 (16%)

education status of 12(48%) were Diploma/Graduation, and 13(52%) were high school level. The association of educational status between groups was analysed using Pearson's Chi square test and was statistically significant with a p-value of 0. 037. In both groups majority of subjects were unemployed, 18(72%) and 14(56%) respectively. Association using Pearson chi-square test was statistically not significant for employment status, monthly family income and area of domicile.

Table 2 shows the comparison of the two groups based on clinical features. The age of seizure onset and mean duration of illness did not have any significant statistical

Table 2. Association of clinical features in subjects with refractory focal epilepsy with and without Psychiatric comorbidities.

Variable	Groups		P-value
	Comorbidities presentn=25 (%)	Comorbidities absent n=25 (%)	
Age of onset	12.56 (SD 10.28)	14.24 (SD 8.62)	0.382
Mean duration of illness	20.88 (SD 11.59)	14.4 (SD 8.55)	0.085
Type of seizure			
Simple	9 (36%)	7 (28%)	0.762
Complex	16 (64%)	18 (72%)	
Aura			
Present	11 (44%)	16 (66%)	0.256
Absent	14 (56%)	9 (34%)	
Post ictal confusion			
Present	7 (28%)	8 (32%)	1.000
Absent	18 (72%)	17 (68%)	
Status epilepticus			
Present	3 (12%)	3 (12%)	1.000
Absent	22 (88%)	22 (88%)	
No: of AED			
1	1 (4%)	0 (0%)	1.000
>1	24 (96%)	25 (100%)	
Drug compliance			
Present	23 (92%)	24 (96%)	1.000
Absent	2 (8%)	1 (4%)	
EEG compliance			
Present	17 (68%)	20 (80%)	0.519
Absent	8 (32%)	5 (20%)	
Medical comorbidities			
Present	6 (24%)	0 (0%)	0.022*
Absent	19 (76%)	25 (100%)	
previous psychiatric disorders			
Present	3 (12%)	1 (4%)	0.609
Absent	22 (88%)	24 (96%)	
Family history of seizure disorder			
Present	1 (4%)	2 (8%)	1.000
Absent	24 (96%)	23 (92%)	

*P value< 0.05 statistically significant

difference on the Mann Whitney U test. Type of seizure, status epilepticus, EEG correlation, family history ofseizure disorder, and history of psychiatric disorders were not statistically significantly associated with psychiatric comorbidity. Both groups had almost all subjects on multiple antiepileptic drugs, so no statistical difference. Among subjects with Psychiatry comorbidities, medical comorbidities were present in 6(24%). None of the subjects in the other groups had it and so was found to be statistically significant with a p-value of 0.022 on Pearson's chi-square test.

Table 3 compares different components of quality of life and the overall quality of life between groups using the Mann Whitney U test. The mean scores of physical health, psychological factors, social relationships, and environmental factors in subjects with psychiatric comorbidities were lower than those without psychiatric comorbidities. It was statistically significant with p values less than 0.01. The mean score of overall quality of life in subjects with Psychiatric comorbidities was also lower than those without Psychiatric comorbidities, statistically significant with a p-value <0.001.

Table 4 compares different components of disability and the overall disability between groups using Mann Whitney U test. The mean score of understanding and communicating though slightly higher for the subjects with psychiatric comorbidities than those without psychiatric comorbidities, it was statistically not

Table 3. Comparison of Quality of life (WHO-QOL BREF) in subjects with refractory focal epilepsy with and without Psychiatric comorbidities using the Mann Whitney U test.

Quality of Life (QoL)	Comorbidity Present (n=25) Mean±SD	Comorbidity Absent (n=25) Mean±SD	p-value
Physical health	42.48±12.200	51.64±9.160	0.001*
Psychological factors	49.84±9.254	57.32±7.487	0.002*
Social relationships	51.40±13.109	63.48±9.760	0.002*
Environmental factors	43.64±7.680	64.16±5.949	<0.001**
Overall Quality of Life	46.84±8.54	59.15±6.09	<0.001**

* P value< 0.05 statistically significant
**P value<0.001 high statistical significance

significant. The mean score of getting around, self-care, getting along with people, life activities, participation in society in subjects with Psychiatric comorbidities were higher than those without Psychiatric comorbidities and was found to be statistically significant with a p-value <0. 001. The mean overall disability Score in subjects with psychiatric comorbidities was higher than those without Psychiatric comorbidities and was statistically significant with a p-value <0. 001.

Table 5 shows the quality of life and disability for the individual psychiatric disorders present in the subjects. Out of the 25 subjects with Psychiatric comorbidities, 10 had dysthymia, 5 had major depressive disorder, 4 had substance abuse disorder, 3 had psychosis, and 3 had panic disorder. The major Psychiatric comorbidities in our study were dysthymia and major depressive disorder contributing 15 out of 50 subjects with refractory epilepsy. The mean raw score of quality of life was lowest in subjects with MDD. The mean score of disability was highest in subjects with psychosis.

DISCUSSION

This study was undertaken in the background evidence that the prevalence of Psychiatric comorbidities in refractory epilepsy has been gaining more attention worldwide.[1] Although various studies have been conducted in India to assess the psychiatric

Table 4. Comparison of Disability (WHODAS) in subjects with refractory focal epilepsy with and without Psychiatric comorbidities using Mann Whitney U test.

Disability (WHODAS)	Comorbidity Present (n=25) Mean±SD	Comorbidity Absent (n=25) Mean±SD	p-value
Understanding and Communicating	12.64±3.21	10.80±1.91	0.056
Getting Around	14.00±2.14	10.32±1.60	<0.001**
Self-Care	6.76±1.16	5.80±0.71	<0.001**
Getting Along with People	13.12±1.36	11.68±1.57	0.003*
Life Activities	23.36±2.23	19.48±1.58	<0.001**
Participation in Society	24.96±2.30	21.68±2.43	<0.001**
Total disability Score	94.84±9.52	79.76±5.50	<0.001**

*P value< 0.05 statistically significant
**P value<0.001 high statistical significance

comorbidities in epilepsy, not many have portrayed the effects of psychiatric comorbidities on the quality of life and disability in the subjects with refractory epilepsy.

The mean age was not statistically significant between groups that were similar to a previous study.[16] From our study, we found that refractory focal epilepsy is a chronic disease usually occurring at a young age and has a prolonged course. Most of the subjects with psychiatric comorbidities were having lower education levels, and it was statistically significant. An earlier study found that the level of education, psychiatric comorbidities and epilepsy are interlinked.[18] Epilepsy has a negative effect on education by causing dropouts from school, and it affects the financial status and social status of the subjects. Our study observed that most of the subjects in both groups were unemployed, which was not statistically significant, contrary to an earlier

Table 5. Mean quality of life and Mean disability score among subjects with different Psychiatric comorbidities in the study.

Psychiatry Comorbidities	n	Mean QOL (Raw score)	Mean Disability
MDD	5	60.80±8.47	103.20±5.50
Dysthymia	10	63.30±6.27	97.50±6.52
Panic Disorder	3	74.00±3.46	84.33±9.61
Substance Abuse	4	79.25±3.59	83.25±6.75
Psychosis	3	66.67±4.51	105.33±1.53

study that reported that unemployment could be related to probable depression and other psychiatric comorbidities.[19]

The difference in the age of seizure onset between groups was not statistically significant, similar to an earlier study.[20] Comparison of duration of illness between groups was not statistically significant, and it was also was identical to another study.[16] Association of drug compliance with psychiatric morbidity was not statistically significant, unlike a study showing that drug compliance was poor in subjects having psychiatric comorbidities. [21] Since our study was a hospital-based study with fewer study subjects, we could not find any correlation between drug compliance and psychiatric comorbidities. Medical comorbidities were only present in subjects with Psychiatric comorbidities. Another study showed an association between medical comorbidities and psychiatric disorders in epilepsy.[22] A study had found that 44% of epileptic patients had psychiatric disorders, with depression being the most common diagnosis (28%).[23] A study had found out that depression is the most frequent comorbidity in patients with refractory focal epilepsy, which is keeping in with our study.[16]

In the current study, the mean score of WHOQOL-Bref major domains physical health, psychological factors, social relationships, and environmental factors were less in subjects with psychiatric comorbidities than in subjects without psychiatric comorbidities with statistical significance. A study from Spain also had shown that subjects with refractory focal epilepsy having psychiatric comorbidity had poorer quality of life scores.[24] Due to stigma, chronicity, complexity and poor drug response in refractory epilepsy, most subjects have a negative illness perception. Such perceptions are especially high in people with psychiatric comorbidities, and hence this was found as an important link between psychiatric comorbidities and quality of life. The subjects with psychiatric comorbidities probably had greater difficulty conducting their daily activities and had decreased energy levels, thus negatively affecting their physical health. Also, subjects with psychiatric comorbidities possibly have more negative feelings such as low mood, anxiety and despair, significantly affecting the psychological domain.

In the current study, other than comparison of the mean score of understanding and communicating in the two groups, the mean score of the rest of the components of disability like getting around, self-care, getting along with people, life activities and participation in society was higher in subjects with Psychiatric comorbidities than in subjects without Psychiatric comorbidities with statistical significance. An earlier study showed that the epilepsy population had more disability days and limitations in activities and lower annual income than all other groups, including the chronically ill similar to our study.[25] This suggests that refractory focal epilepsy carries a significant burden of illness, reflected in poorer health, psychosocial function, and disability. Another similar study showed a consistent relationship between psychopathology and disability, indicating the compelling personal and socioeconomic impact of common mental illnesses.[26] The above study suggests the importance of impairments of higher-order human capacities (emotion, motivation, and cognition) as determinants of functional disability. In our study, we found that subjects with psychiatric comorbidities have difficulty participating in community activities, have poorer financial resources, hence are unable to contribute to society as expected.

In the current study, we assessed whether any comorbid psychiatric disorders have a higher impact on quality of life and disability by comparing the mean score of

overall quality of life and disability among different psychiatric comorbidities. We have found that the quality of life was lowest in major depressive disorder and disability was highest in psychosis. A study from the USA of refractory focal epilepsy subjects showed that depression had poorer health perception and reported lower QOL in various domains.[27] In another study, common mental disorders significantly affecting disability were PTSD, MDD, Psychosis(BPAD) and GAD.[28] Schizophrenia and affective psychosis had the highest degree of disability; young age of onset, poor medication adherence and failure of symptom remission as strong predictors of disability.[29] This may be because the negative perception of health and overall wellbeing, increased tiredness, poor attention and concentration, pessimistic views of the future etc., in people with MDD might reflect in expressing a poor quality of life. Due to poor reasoning, judgement and lack of awareness, the subjects with psychosis may not appreciate the negative cognitions and instead portray themselves to have more disability.

Limitations

1) The design was a cross-sectional study; therefore, inferences about the direction of the relationship between epilepsy and psychiatric comorbidities cannot be made.
2) A scale of quality of life applicable to any disease and not specific for epilepsy was used.
3) The study has been done in a dedicated centre for epilepsy, and the results may not apply to other settings.

CONCLUSION

This study was an attempt to find out the impact of psychiatric comorbidities on the quality of life and disability in subjects with refractory focal epilepsy and their association with sociodemographic and clinical variables. Our study found that MDD and dysthymia are the most common psychiatric comorbidities in subjects with refractory focal epilepsy.

The association of medical comorbidities in subjects with refractory focal epilepsy has led to an increased chance to develop psychiatric comorbidities. The lower educational status of the subjects was found to have a significant association with the presence of psychiatric comorbidities. While comparing the subjects with and without psychiatric comorbidities, psychiatric comorbidities have a significant association with almost all the domains of quality of life and disability. So it is essential to have a good team approach and liaison between neurology and psychiatry for early detection of such psychiatric symptoms and treatment in these subjects. Future research should look at a longer-term follow-up study to impact psychiatric comorbidities on refractory focal epilepsy and intervention studies to manage psychiatric disorders in these subjects.

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None declared.

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