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Quality Of Life In Young Patients Taking Oral Anti-Epileptic Drugs In Kgh Outpatient Department.

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ABSTRACT
BACKGROUND. *In addition to increased mortality and physical morbidity risks, epilepsy also has well documented psychosocial squeal.* ***PURPOSE:*** *To evaluate antiepileptic drug usage pattern in our hospital and their influence on quality of life.To study association between quality of life and factors influencing it.* ***METHODS:*** *A Hospital based cross-sectional study was conducted on epileptic patients on follow up. Recruited 98 patients with epilepsy who fulfilled the eligibility criteria from April 2016 to August 2016 from the outpatient department of Neurology,King George hospital. The demographic, clinical and treatment data were collected by personal interview and medical records of patients and the QOLIE-10 questionnaire was used to measure their quality of life scores. The level of statistical significance was declared at -value ≤ 0.05.* ***RESULTS:*** *A total of 98patients were included in the study and mean age was 29.1 ± 11.7 years. Among clinical variables polytherapy (p=0.003) , presence of adverse drug reactions(p=0.0001) were significantly associated with a low QOLIE-10 score. . Except for marital status in which divorced patients had shown significantly poor QOL scores, none of the demographic variables were significantly associated with QOLIE-10 score.* ***CONCLUSION.*** *The patient sample had an optimal overall QOL scores. Appropriate AED selection preferably monotherapy and careful evaluation of drug side effects play a crucial role in achieving the ultimate target .*

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I. Introduction

Epilepsy is an episodic and chronic central nervous system disorder which is characterized by unprovoked, recurrent seizures that can have a psychological and emotional impact on people with this disorder and their caregivers.[(1)]. Epilepsy has a known association with increased risk of suicide, particularly shortly after diagnosis[(2)] and increased risk of suffering from other chronic conditions of ill-health [(3,4)] . In addition to these increased mortality and physical morbidity risks, epilepsy also has well documented psychosocial squeal.

Of the 70 million persons with epilepsy (PWE) worldwide, nearly 12 million PWE are expected to reside in India; which contributes to nearly $1/6^{th}$ of the global burden. The overall prevalence (3.011.9 per 1,000 population) and incidence (0.20.6 per 1,000 population per year) data from recent studies in India on general population are comparable to the rates of high income countries (HICs) despite marked variations in population characteristics.[(5)]

The paucity of medical infrastructure, economic concerns and socio-cultural attitudes prove a hindrance to the optimal care of epilepsy in many developing countries. The threat of recurrent seizures and fear of social rejection are lifelong concerns for patients with epilepsy. Traditionally, the main treatment goals for epilepsy have focussed on seizure control and minimisation of adverse effects of drugs with much less importance rendered to the impact of epilepsy on the everyday life of the patient, particularly in the psychosocial realm. The growing recognition of this importance has led to the need to define and quantify quality of life (QOL) in affected individuals.

Quality of life is an individual perception of their position in life in the context of culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.[(6)] In many studies psychiatric morbidities have been demonstrated to determine QOL more adversely than epilepsy related factors.[(7)]Thus QOL is a crucial component in the clinical care of patients with epilepsy and optimal quality of life is one of the main goals of antiepileptic therapy [(8)]. There are limited Indian studies examining the effect of pharmacotherapy characteristics (type of anti-epileptic drug/monotherapy vs. polytherapy) on overall quality of life.[(9)] The main objective of this study is to examine the pattern and extent of AED use in a tertiary care hospital setting in Visakhapatnam and to assess the quality of life in people with epilepsy. The second objective is to ascertain any association between quality of life and other factors influencing it like pharmacotherapy, clinical and demographic variables.

II. Aims And Objectives

- To evaluate antiepileptic drug usage pattern in our hospital and their influence on quality of life.
- To study association between quality of life and factors influencing it.

1. Pharmacotherapeutic characteristics
- Monotherapy vs. polytherapy
- Adverse event profile.

2. Disease characteristics.(seizure type, seizure frequency)
3. Demographic characteristics (age, gender, socioeconomic characteristics etc.)

III. Review Literature

María E. Ruiz et al Conducted invitro and in vivo studies regarding nanofurmulation preparations of antiepileptic drugs. In their study nearly 70 % of people provisionally responded to treatment, but 20–60 % of patients were resistant to current antiepileptic drugs (AEDs) (WHO 2015, Epilepsy Fact Sheet No. 999). Also, they found a negative social impact of the pathology, since patients and their families suffer stigma and discrimination in many parts of the world. Furthermore, patients who positively respond to the anticonvulsant treatment were subjected to high systemic concentrations of drugs to achieve therapeutically effective levels at the site of action in the central nervous system (CNS), which resulted in undesirable side effects that threaten their quality of life and their adherence to the treatment, and concluded that development of nanoformulations of AEDs is a promising strategy to improve pharmacokinetic profile by increasing the fraction of drug that reaches (and stays in) the CNS, as well as by optimizing the drug's distribution/metabolism and elimination profile.[9]

Rui Quintas et al conducted an observational study on psychosocial difficulties, quality of life, and disability levels in patients with epilepsy using PARADISE 24 instrument: There were 80 patients, 40 females. Mean number of AED was 2.09. Moderate severity rating according to clinicians rating scale, low impact of co morbidities (mean: 2.36, SD: 2.97), high levels of QOL (mean: 30.00, SD: 4.4), medium levels of resilience (mean: 13.56, SD: 2.66), high levels of perceived empathy (mean: 15.05, SD: 4.74), poor or moderate perceived social support, and low levels of disability (mean: 10.85, SD: 10.05) were observed. The most frequently reported PSDs were related to tiredness (80%), emotional problems (73.75%), anxiety (68.75%), depressive mood (66.25%), and driving problems (61.25%). [10]

Saadi et al, assessed the quality of life in epilepsy (QOLIE) among adults in the lower middle-income country of Bhutan and the potential demographic and clinical associations with better QOLIE. The mean Bhutanese QOLIE-31 score among 172 adults (mean age 31.1 years, 93 female) was 48.9/100 ± 17.7. Younger age, lower educational attainment level, and increased self-perceived stigma were each observed to have an independent, negative association with QOLIE ($p < 0.05$), while a patient's wealth quintile, sex, seizure frequency, seizure type and number of antiepileptic drugs were not. Education appeared to be most strongly associated with QOL at the high school and college levels.[11]

Annika Hilgers et al evaluated the tolerability of newer antiepileptic drugs (AEDs), such as topiramate, levetiracetam, zonisamide, pregabalin, extended-release oxcarbazepine, lacosamide and eslicarbazepine, under real-life conditions by means of an assessment of routine clinical data of inpatients. In total, the data of 562 patients were assessed, of which 90 % received up to six different AEDs. Levetiracetam and oxcarbazepine as an extended-release formulation were most commonly used, and levetiracetam showed the best tolerance. By using logistic regression, the occurrence of ADRs was significantly associated with the number of AEDs ($p < 0.001$) as well as the defined daily doses ($p = 0.003$). In total, ADRs of AEDs were documented for 318 patients (56.6 %). The most common referred to electrolyte imbalance, e.g., low sodium ($n = 79$, 14.1 %) and potassium ($n = 25$, 4.4 %) levels, the central nervous system, including dizziness ($n = 61$, 10.9 %), disturbed vision ($n = 47$, 8.4 %), fatigue ($n = 40$, 7.1 %), nystagmus ($n = 36$, 6.4 %) and ataxia ($n = 29$, 5.2 %), or cognitive deficits, especially disturbance of speech ($n = 37$, 6.6 %), memory impairment ($n = 36$, 6.4 %) and mental slowing ($n = 32$, 5.7 %).[12]

Edward Firouztale et al conducted a retrospective study regarding the factors Impacting Quality of Life among 91 Patients with Epilepsy. In their study Depression has a strong negative and statistically significant (r=-0.743, P<0.0001)correlation with overall quality of life. The same is also true for fatigue (r= -0.686, P<0.0001). Cognition (r= +0.831, p<0.0001) and energy level (r=0.665, P<0.0001) have strong positive and statistically significant correlation with quality of life. The number of medications has a negative, although weak, and statistically not significant correlation with quality of life (r=-0.138, P<0.19). Addressing depression and underlying causes and Correcting causes of fatigue can potentially improve the quality of life.[13]

Lidia M.V.R. Moura et al aimed to compare physician encountered documentation with patient perceptions of quality of epilepsy care and examine the association between quality and patient assessment of provider communication. There were 88 patients (36%) who completed the interviews. Fifty-seven (24%) refused to participate, and 100 (40%) could not be contacted. Participants and nonparticipants were comparable in their demographic and clinical characteristics; however, participants were more often seen by epilepsy

specialists than nonparticipants (75% vs. 61.9%, $p < 0.01$). Quality scores based on patient perceptions differed from those determined by assessing the documentation in the medical record for several quality measures, e.g., documentation of side effects of ant seizure therapy ($p = 0.05$), safety counselling ($p < 0.01$), and counselling for women of childbearing potential with epilepsy (McNamara's $p = 0.03$; intraclass correlation coefficient, ICC = 0.07). There was a significant, positive association between patient-reported counselling during the encounter (e.g., personalized safety counselling) and patient-reported scores of provider communication ($p = 0.05$).[14]

Hosseini N et al, studied the effect of motivational interviewing on quality of life in fifty-six patients with epilepsy. Motivational interviewing during 5 sessions was applied for the intervention group, and the control group received health-care services. Quality-of-life questionnaire in epilepsy (QOLIE-89) was applied as pre- and post-test for both groups. Before and two months after intervention, both groups were assessed. The data analysis showed that mean score of the QOLIE-89 was 38.94 ± 8.55 and 70.90 ± 7.99 in the intervention group before and after the intervention, respectfully, and 44.59 ± 12.27 and 36.52 ± 7.16 in the control group sequentially. The intervention group showed a significant score increase in their quality of life ($p < 0.001$), whereas the control group had a score decrease ($p < 0.001$). Hence motivational interviewing approach could be used as an effective intervention method for improving patients' quality of life.[15]

Fatma Karantay Mutluay et al, studied among 30 adult patients with epilepsy regarding Health related quality of life in Turkey. According to their study the mean standard deviation scores for Energy / Vitality (VT), mental health and mental health composite among males and females were 51.2±11.1 and 46.3±10.3, 42.1±11.0 and 38.6±12.0, 41.4±10.0 and 37.5±10.2 respectively. Patients with epilepsy do not perceive impaired physical health status. However, their mental health appears to be vulnerable, especially in women, hence the major burden in epilepsy was in the mental health category[16]

Asha Sureshrao Morge et al, conducted a prospective observational study of drug utilization patterns in a tertiary care hospital for a period of 6 months among 562 patients. All ages, either gender receiving Antiepileptic prescription in epilepsy OPD was considered. The demographic data revealed that number of male and female patients were 53% and 47% respectively. Generalized tonic-clonic seizures accounted for almost 62%, followed by partial seizures, myoclonic seizures and others (traumatic, infectious, systemic disorder, metabolic derangement). Monotherapy was used in majority of patients.[17]

M. Wassenaar et al, studied Anti-epileptic drug changes and quality of life in a cohort of 248 people with epilepsy identified from community pharmacy records from which they retrieved AED dispensing history. Changes in AED and current QOL during a 2 year period prior to the index date were assessed using the validated Dutch QOLIE-31 questionnaire. Thirty-one percent had at least one AED change during the study period, either in drug type or dose. People who changed showed significantly lower QOL (QOLIE score 73 vs. 79), especially those who intensified their treatment. Each additional change was associated with a further reduction of 4.9 points in QOL score. Frequent changes, as objective measure of epilepsy severity, are associated with a progressively lower QOL.[18]

Loanna Rizou et al, studied the extent to which gender, epilepsy severity and illness perceptions predict fatigue and sleep problems by conducting structured interviews among 100 young patients and analyzed data by means of multiple hierarchical regression analyses. Most patients (91%) were well controlled by anti-epileptics; 3% had infrequent seizures and 6% were pharmacoresistant. At a multivariate level it appeared that youngsters with epilepsy who believe that they have less personal control over their illness and who feel that the illness has a high emotional impact on their lives reported higher levels of fatigue. In addition, more sleep problems were reported by youngsters who think they have less personal control over the disease, who believe that treatment controls epilepsy and report that the disease has a high emotional impact on their lives.[19]

Lee SA et al, determined the level of knowledge about epilepsy among 530 PWE participated from 31 secondary or tertiary hospitals in and evaluated whether this is associated with self-efficacy, perceived stigma, anxiety, and depressive mood in these patients. Knowledge about epilepsy was assessed using 34 medical items (EKP-M) of the Epilepsy Knowledge Profile-General. Additional questionnaires included the Epilepsy Self-Efficacy Scale (ESES), Stigma Scale, and Hospital Anxiety and Depression Scale (HADS).The mean EKP-M score was 22.2 (SD: 4.1). By univariate analyses, the EKP-M was related to ESES ($r=0.220$, $p<0.001$) and HADS-D ($r=-0.154$, $p<0.001$) scores but not to the Stigma Scale or HADS-A. By linear regression analyses, after adjusting for the confounding variables, the higher EKP-M scores were independently related to both higher ESES ($p<0.001$) and lower HADS-D scores ($p<0.05$).Korean PWE have a relatively low level of knowledge about their condition. Knowledge about epilepsy is associated with a high level of self-efficacy and less depressive symptoms in affected individuals.[20]

Asif Javed et al Rates and predictors of patient-reported cognitive side effects of antiepileptic drugs: An extended follow-up impact of adverse effects of antiepileptic medications (AEDs) such as cognitive side effects (CSEs) on quality of life can be significant. Of 2860 patients, 15% had intolerable CSEs attributed to at least one AED. On multiple logistic regression analysis, independent predictors of intolerable CSEs were lack of

intellectual disability and polytherapy. In polytherapy, we found that intolerable CSEs were most commonly seen with topiramate (22.8% of 281 patients), significantly more than with almost all other AEDs. This was true in monotherapy as well, with significantly more intolerable CSEs occurring with topiramate (18.5% of 54 patients) than with gabapentin, carbamazepine, lamotrigine, and levetiracetam. AEDs with consistently low rates of ICSEs included gabapentin, pregabalin, lamotrigine, levetiracetam and carbamazepine. in polytherapy, 11.2% with new medication had intolerable cognitive side effects. In monotherapy, 7.6% with new medication had intolerable cognitive side effects.[21]

Jesso George et al studied Antiepileptic Drugs and Quality of Life in Patients with Epilepsy in A Tertiary Care Hospital evaluated patterns of the use of antiepileptic drugs (AEDs) and their impact on quality of life (QOL) in patients with epilepsy. Of 200 patients, 53.5% were males and 60% were younger than 30 years. Seizures were predominantly partial (58%) and of idiopathic origin (61%). Monotherapy to polytherapy ratio was 1:1, with 70% of the patients on one new AED. Clobazam (37%) was used most frequently followed by phenytoin (25.5%), levetiracetam (23%), oxcarbazepine (21.5%), and carbamazepine (21%). Patients on polytherapy experienced a significantly more number of adverse drug reactions than did those on monotherapy ($P < 0.0001$). The mean QOLIE-10 score was 74.58 ± 20.60. There was no significant difference in seizure frequency, number of adverse drug reactions, and QOLIE-10 score among patients receiving old and new AEDs. Multiple linear regression analysis identified increased seizure frequency (standardized β −0.157; $P = 0.003$), more number of AEDs (standardized β 0.107; $P = 0.05$) as well as adverse drug reactions (standardized β −0.692; $P = 0.0001$) as significant predictors of poor QOL. early detection, selection of rational and safer AED treatment options, and regular monitoring for adverse effects play a crucial role in achieving seizure freedom and optimal QOL in patients with epilepsy.[22]

Ravi Paul et al, studied The Psychosocial Impact of Epilepsy among 50 Adult People With Epilepsy Attending Clinics In Lusaka with generalized or partial epileptic seizures aged 18 years or more. The outcome measure was the SF-31(Quality of Life in Epilepsy Inventory-31). 38% of persons with active epilepsy had significantly low QOL due to their condition. Females had lower QOL scores than males. Patients with higher levels of education had higher scores than their counterparts with lesser education. People who had been ill for greater than 5 years had higher scores than those who had been ill for a shorter duration. Those whose caregivers had a high income from salary job had higher scores than those whose caregivers were unemployed.[23]

Carlo Cianchetti et al conducted studies regarding The perceived burden of epilepsy: Impact on the quality of life of children and adolescents and their families among 293 parents of children and adolescents with epilepsy, included in an observational study on treatment satisfaction, to evaluate the impact of the disease on several aspects of the QOL of the whole family using a specifically organized questionnaire (IEQoL). Epilepsy impairs all aspects of QOL, although at different degree, both in children/adolescents and in their families. Parental apprehensiveness appears to have a role on this, and it may not reflect the severity of the disease.[24]

Alan B. Ettinger et al studied The relationship of depression to antiepileptic drug adherence and quality of life in epilepsy in A total of 465 eligible patients were surveted. Survey data were combined with administrative claims data for analysis. They conducted a path analysis to assess the relationships between depression, adherence, seizure severity, and quality of life (QOL). Patients with depression scored significantly worse on measures of seizure severity ($p = .003$), QOL ($p < .001$), and adherence ($p = .001$). On path analysis, depression and QOL and seizure severity and QOL were related, but only the NDDI-E scores(Neurological Disorders Depression Inventory for Epilepsy) had a significant relationship with medication adherence ($p = .001$). Depression as measured by the NDDI-E was correlated with an increased risk of AED no adherence. They concluded that depression or seizure severity adversely impacted QOL.[25]

Shubham Mehta et al evaluated interrelationship between depression, seizure frequency and quality of life in Indian population. They recruited 31 patients suffering from epilepsy in this cross-sectional study. Their clinical profile was recorded. Quality Of Life in Epilepsy (QOLIE-31) was used to assess quality of life of our patients. Depression was screened by Neurological Disorders Depression Inventory in Epilepsy (NDDI-E). Among all the clinical variables, only seizure frequency significantly correlated with seizure worry (P=0.002), emotional well-being (P=0.026) and social functions (P=0.013) subscales of QOLIE-31.[26]

Jamal M. Al-Khateeb[a] reviewed research conducted on the psychological aspects of epilepsy in Arab countries. Fifty-one studies were conducted in 12 Arab states. Social/emotional, employment, and other problems; knowledge and attitudes; and quality of life (QOL) were the most commonly measured parameters of psychosocial aspects of epilepsy in Arab countries. Results revealed elevated levels of depression and anxiety, a decline in cognitive function, various behavioural problems, sexual dysfunction, and underemployment among persons with epilepsy (PWE). Misconceptions about epilepsy were found to be prevalent. While many studies reported limited knowledge of epilepsy, some studies found an average knowledge. Negative attitudes toward epilepsy

were reported in most studies, and moderately positive attitudes were reported in some studies. Finally, PWE showed low overall QOL scores in the majority of studies.[27]

Maja Milovanović et al evaluated Determinants of quality of life in people with epilepsy in Serbia recruited consecutive adults with epilepsy attending our outpatient department. Adult patients (age range: 18–65 years) of normal intelligence and without any progressive neurological disease or psychiatric disorder were included in the study. They completed the following questionnaires: QOLIE-31 Inventory (Serbian version), Beck's Depression Inventory-II, Beck's Anxiety Inventory, Symptom Check List-90, and Neurotoxicity Scale-II. Hierarchical multiple regression analysis was performed to assess the predictive effects of some factors on QOLIE-31 Inventory. The results suggest that seizure severity and aetiology of epilepsy, depressive and anxiety symptoms, and cognitive adverse medication effects are main determinants of quality of life in this population of PWE.[28]

P. B. Adebato et al evaluated the relationship of seizure severity to health-related quality of life of patients with epilepsy being followed up in an outpatient neurology clinic in south-western Nigeria. Eighty-eight consecutive patients with epilepsy who met the recruitment criteria completed the study questionnaire in company of an eyewitness. The study questionnaire comprised of the National Hospital Seizure Severity Scale (NHS3), the Quality of Life Inventory in Epilepsy (QOLIE-31), and the Beck's Depression Inventory-II (BDI-II). Increased seizure severity predicted a worse QOLIE-31 seizure worry ($R^2 = 0.311$, $\beta = -0.289$; $P = 0.003$).[29]

Juri Alexander witt et al reviewed the cognitive effects of antiepileptic pharmacotherapy, approaching the individual patients at Germany and concluded that Cognition is a major aspect of treatment outcome and Cognitive deficits in epilepsy reflect synergistic effects of epilepsy and treatment.[30]

IV. Materials And Methods

1. Study design: Cross sectional study.
2. Sample size: 100
3. Study setting: King George Hospital, Visakhapatnam.
4. Study period: April 2016 to august 2016.

Inclusion Criteria

1. Patients with confirmed diagnosis of epilepsy who have been on treatment for at least 1 year.
2. Age of 18 to 35 years
3. Patients who have consented to participate.

Exclusion Criteria

1. Patients with known significant disability- mental retardation, motor, visual, hearing or speech impairment
2. Patients with known major psychiatric disorders (Schizophrenia/ major depression).
3. Chronic severe medical co morbidity confounding quality of life assessment (Chronic renal failure/Chronic heart failure/Chronic liver disease).

This study was conducted at Department of neurology, King George Hospital under the guidance of Dr. J. Sudha professor and HOD, Department of Pharmacology, KGH. The institutional ethics committee of King George Hospital approved the study protocol. The participants declared their willingness on the details of the study and gave written informed consent. Patients who consented to participate were then interviewed to collect relevant data.

All participants are recruited from department of neurology, who are on anti epileptic drug therapy for a period of at least one year. It was calculated that 92 patients were needed for the study to powered at 90% with alpha error-5% to detect a difference in QOL scores of 10 SD between patients on monotherapy and polytherapy.

Enrolment of patients:

No. of patients screened for enrolment : 103
No. of patients selected in this study : 103
No. of drop outs :5
No. of patients completed the study :98

98 patients with epilepsy who are on antiepileptic drug therapy for a period of at least one year, age ranging from 18 to 35 years were enrolled in this study. The data were collected in a case record form (CRF) consisted of two parts.

A. The data captured in the first part of the CRF were broadly classified into

i. **Demographic data**: Patient name, age, gender, address, background, socioeconomic status. The patient's, occupation, were factored in for assessing the socioeconomic status.

ii. **Disease Data**: Seizure type, aetiology and frequency, age of onset of seizure & duration, family history of epilepsy. Seizure burden was scored according to Engel system that scores seizure frequency and burden in a quasi logarithmic scale ranging from 0-12[31]. Scores less than 5 indicate no seizures or non disabling seizures (aura or brief loss of consciousness). Score 5 denotes 1-3 seizures per year; score 6 indicates 4-11 seizures per year. Seizure frequency of 1 per month is scored 7-12. Seizure freedom was defined as absence of disabling seizures for more than 12 months continuously.

iii. **Treatment Data**: Details of treatment including generic names of drugs, daily doses, duration of treatment, past treatments.

iv. **Adverse event profile**:

side effects with Antiepileptic drugs which was derived from the AEP (Adverse event profile): a 19 item validated questionnaire. (32) were evaluated.

v. **Investigational data**: Some of the key investigations (as available with the patient) were noted. These included EEG, MRI/CT scan, TDM levels of AEDs, haematological and biochemistry measurements.

B. The second questionnaire used was the QOLIE-10 (Quality of Life in Epilepsy Inventory-10) which is an abbreviated quality of life questionnaire consisting of 10 items derived from the more detailed QOLIE-31. (33) It is a self administered questionnaire designed for completion by patients alone. Although designed as a screening tool, it can still be scored and used in research. Studies have suggested that shorter versions such as QOLIE-10 was as effective as its longer counterparts(QOLIE-31) . (34) It comprises of 10 subscales. Below are the ten subscales with the range of scores indicated in brackets.

1. Energy Fatigue. (1-6)
2. Emotional well being. (1-6)
3. Driving difficulty. (1-5)
4. Work limitations. (1-5)
5. Social limitations. (1-5)
6. Cognitive function. (1-5)
7. Physical effects of medication. (1-5)
8. Psychological effects of medication. (1-5)
9. Afraid of seizure recurrence. (1-4)
10. Overall QOL. (1-5)

Patients who were conversant in English completed the questionnaire themselves. The remaining patient population was multilingual (Telugu, Hindi), the questions were explained to the patients in their respective languages and responses elicited. Responses were scored to provide subscale scores .

Methods of Data Analysis

Data collected were entered on Microsoft Office for Windows 2007 excel spread sheet and analyzed in SPSS version 21.0 software. Baseline data (demographic, clinical and treatment) were subjected to descriptive statistical analysis and expressed as mean (±SD), median, interquartile range (IQR), frequencies and percentages. The QOLIE-10 scores categorical variables were compared using Chi-square ($\chi 2$) test. Statistical significance was set at $p< 0.05$.

V. Results And Observation

We recruited 98 patients with epilepsy who fulfilled the eligibility criteria from April 2016 to August 2016 from the outpatient department of Neurology. The demographic, clinical and treatment data were collected by personal interview and medical records of patients and the QOLIE-10 questionnaire was used to measure their quality of life scores. Following is the summarization of the observed results and the association of QOLIE-10 scores with the clinicosocial and pharmacotherapy variables.

1. Patient characteristics and demographic profile

98 young adults between age group 18 to 35 years were taken in this study. Median age of study population was 18. 56.1% were males and 43.9% were females.

Majority of the study group are married (55.1%), there are 11 patients who are not married because of seizures.

60.20% of the study group are residing in rural areas. 20.40% were unemployed out of which there are 5 patients who are unemployed because of seizures. Majority of patients belonged to the poor and lower middle socioeconomic status with 63(64.28%) of them having a per-capita income of Rs 10,000 and below.

Age	n
Median age	25
Mean age	25
Min – max	17-35
Gender	
Male	55
Female	43
Marital status	
Married	54
Unmarried	39
Divorced	5
Employment status	
employed	46
Unemployed	20
House wife	16
Student	16
Residence	
Rural	59
Semi urban	23
Urban	16
Socio economic status	
Poor	63
Lower middle	39
Upper middle	8

Table – 1 Depicts demographic data of study population.

2. Clinical Characteristics of Patients with Epilepsy.

Among 98 patients who presented at the outpatient department 51% are having generalised seizures where as 49% are having partial seizures. Partial seizures with secondary generalization accounted for majority of partial seizures observed(n=27), the other types were simple partial seizures and complex partial seizures. Among generalized seizures, majority of patients presented with generalized tonic-clonic seizures (GTCS) (n= 42). Absence seizures were diagnosed in 1 patient and Myoclonic epilepsy in 7 patients

73.5%patients had either an idiopathic or cryptogenic origin of seizures. The attributable aetiologies for seizures reported in this sample were CNS infections (11.2%), commonly neurocysticercosis; vascular causes like cortical vein thrombosis (1%); and history of trauma (9.2%) Less common were drug/alcohol induced withdrawal seizure, tumours (medial temporal glioma) and calcified granulomas in parietal/frontal regions which were not attributable to Neurocysticercosis (6.10%).

Median age at onset of epilepsy was 18 years and the median duration of epilepsy was 7 years. Majority of patients (40.8%) had a fair control of seizures with a frequency of 1-3 per year (Engel score-5). 28 patients are seizure free which is defined as absence of seizures for more than 12 months continuously(Engel score < 5). 29.6%had an Engel score of 6 and above (>4 seizures per year and above).

27 patients had a family history of epilepsy. 12 patients had associated medical co morbidities like diabetes, tuberculosis, asthma, tension headache. 5 Patients gave history of either having attempted suicide or having suicidal thoughts (Suicidality).

Duration of epilepsy	n
Upto 1 year	7
2-5 years	19
6-10 years	16
11-20 years	24
Over 20 years	32
Age at onset	
Below 10 years	21
11-20 years	38
21-30 years	28
31-40 years	11
Seizure type	
Generalised seizures	50
Partial seizures	48
Seizure frequency	
Absent seizures	28
1-3 per year	40

4-11 per year	16
>1 or more seizure a month	13
Engel category	
<5	28
5	40
>5	29

Table 2 : Representing clinical characteristics of study sample

3. Pharmacotherapy of Epilepsy in the patient sample

55 of patients were on monotherapy. 32 patients were on dual therapy ;11 on triple therapy. The type of AED therapy was categorized into monotherapy, and polytherapy.The old AEDs included 1st generation drugs like Phenytoin (PHT), Carbamazepine controlled release(CBZ CR), Phenobarbitone (PBT) and Sodium Valproate (VA) ; New AEDs included Clobazam (CZ), Oxcarbazepine (OXC), Levetiracetam(LTC).The mean number of AEDs per person was 1.71 ± 0.867, with a range between 1 to 3.

4. Patterns of Use of Antiepileptic Drugs and their Dosages.

Independent of the AED usage profile, valproic acid was the most frequently prescribed AED followed by Carbamazepine Controlled release (CR) formulation, followed by phenytoin. Conventional drugs like Phenobarbitone recorded a lower frequency of use. Newer drugs like Clobazam, Oxcarbazepine and Levetiracetam were used significantly more as adjuvant therapy than monotherapy.

AED Usage	Monotherapy	Polytherapy	Dosage range (mg/day)	Recommended maintenance dose.(mg/day)
VA	14	28	200-1000	500-2500
CBZ	18	25	200-1000	400-1600
PHT	17	23	50-400	200-400
PBT	6	5	30-180	50-200
CZ	-	7	2.5-40	10-40
OXC	-	4	300-1200	600-2400
LTC	-	4	500-4000	1000-3000

Table 3: Proportion of patients on different AEDs with prescribed dosage ranges and the recommended maintenance ranges.

Out of 43 patients on polytherapy, 28 patients were on older AEDs, 15 on combination therapy (old and new AEDs). Valproic acid was most frequently used as polytherapy in 65.11% of cases. The other more commonly employed AEDs in polytherapy regimes were Carbamazepine 58.13%. There were 7 types of 2-drug combinations used by 32 patients. Valproic acid was most commonly used as a 2 drug- combination therapy along with carbamazepine and Phenytoin (10/69) , clobazam(7/69), Oxcarbazepine (4/69) .

Dual therapy used in this study group		
	Type of AED used	N(98)
1	CBZ+VA	10
2	VA+PHT	7
3	PHT+CBZ	7
4	PHT+CZ	4
5	VA+PBT	2
6	PHT+PBT	1
7	VA+LTC	1
	TOTAL	32

Table 4: AED usage pattern in subjects on dual therapy.

There were 7 types of 3- drug combinations prescribed to 11 patients. Again Clobazam along with Phenytoin and valproic acid was the commonly prescribed AEDs in 3-drug regimes for e.g. CBZ+VA+OXC(4 OUT OF 11 PWE)**..**

Triple therapy regimens used in this study		
	Type of AED	N(98)
1	CBZ+VA+OXC	4
2	CBZ+VA+PBT	2
3	PBT+CBZ+PHT	1
4	VA+PHT+CZ	1
5	CBZ+VA+LTC	1
6	PHT+CZ+LTC	1
7	VA+PHT+LTC	1

	TOTAL	11

Table 5: AED usage pattern in subjects on triple therapy

5. Antiepileptic drug therapy and seizure frequency:

In this study better seizure control was observed in patients who are on monotherapy. On performing a chi square test, statistical significance was observed between polytherapy and high seizure frequency with a P-value of 0.024 and chi square value of 9.405.

Seizure frequency	Monotherapy	Polytherapy
I per month & above	2	10
4-11 per year	4	12
1-3 per year	25	15
Absent	24	6
No. of patients who reported ADRs	23	34

Table 6: Relation between type of therapy and seizure frequency.

6.AED dosage range :

Table below shows the dosage range of different AEDs prescribed among patients along with the usual maintenance doses as suggested by Perucca and colleagues.[35] All the drugs were well within the upper limit of the suggested maintenance doses. However lower doses of some drugs Phenytoin, Carbamazepine, clobazam and Oxcarbazepine were noted. The dosage of AEDs as a ratio of Mean Prescribed Daily Dose to Defined Daily Dosage (PDD/DDD) for both monotherapy and polytherapy are shown in Table 7 below. PDD refers to the total dose per day prescribed for a given AED. WHO has defined DDD as the assumed average maintenance dose per day used for its main indication in a reference person of 70 kg body weight.[36] The reference weight for a man and woman in the Indian population according to the Indian Council of Medical Research(ICMR) is 60 kg and 55 kg respectively. [37] Hence the DDD was modified by taking the reference weight as 60 kg. The DDD of AEDs does not vary between monotherapy and polytherapy. The mean PDD/DDD ratio was calculated for each of the AEDs when used as monotherapy and as polytherapy separately. The PDD in monotherapy was lower than polytherapy for most of the drugs except Phenytoin.

#Drug	PDD (mg/ day) Monotherapy	PDD (mg/ day) Polytherapy	DDD (60 kg)	*PDD/DDD Monotherapy	*PDD/DDD Polytherapy
PHT	264.06	238.56	245.56	1.07	0.97
CBZ	532.38	630.05	864.89	0.61	0.72
PBT	70	90	96.68	0.72	0.93
VPA	692.17	712.12	1292.12	0.53	0.55
CLB	13.86	16.28	17.36	0.79	0.93
OXC	650	730.43	857.14	0.76	0.89
LTC	1518.18	1455.9	1285.71	1.18	1.13

Table 7: Mean Prescribed Daily dose/Defined Daily Dose Ratios (PDD/DDD) of the prescribed Antiepileptic Drugs in Mono/Poly therapy.

*: PDD/DDD = 1 : Indicates prescribed doses of AEDs similar to recommended maintenance doses by WHO; PDD/DDD <1 : Prescribed AED doses lower than the recommended maintenance dose.

7. AED use in Partial and Generalized Seizures.

Carbamazepine CR (controlled release formulations) was the most frequently used drug among patients with partial seizures, The other AEDs of choice in partial epilepsy was sodium valproate. Among generalized seizures, the more frequently used drugs were phenytoin and Sodium Valproate,. The utilization of Carbamazepine was significantly increased among patients with partial seizures when compared to generalized seizures. (p=0.003). The use of Sodium valproate and phenytoin were significantly higher among patients with generalized epilepsy when compared to patients with partial seizures. (p=0.041; p=0.0048 respectively). There was no significant difference in the utilization of other antiepileptic drugs between partial and generalized seizures. The other adjunctive AEDs commonly used were Clobazam (7 patients) and Oxcarbazepine (4 patients). There were two women with epilepsy and pregnancy (1 with secondarily generalized seizures and 1 with GTCS) and were on monotherapy with Carbamazepine (400 mg), Phenytoin (200 mg) respectively.

8. Pattern of Adverse Events.

57(58.16%) patients reported to have experienced at least one side effect when queried about specific side effects like drowsiness, tiredness, cognitive impairment, headache, tremors etc. The most common side effects involved the central nervous system(50.5%). Headache(23.40%) was the most common side effect reported among CNS effects followed by drowsiness (19.1%). Memory impairment was reported by 17.02% population of the study group. Next to CNS symptoms were the gastro intestinal related adverse effects(24%). Weight gain is seen in 5 patients of whom 3 are on valproic acid. Side effects observed in other systems include acne, hair loss, etc.. Gingivitis with Phenytoin ,alopecia, menstrual disturbances etc.. Hypersensitivity reactions were observed with Carbamazepine, Phenytoin

CNS	Headache	11
	Drowsiness	9
	Sleep disturbances	5
	Tiredness	4
	Memory impairment	8
	Ataxia	3
	Depression	4
	Tremors	2
Git	Nausea & vomiting	10
	Gastritis	7
	Constipation	4
	Gingivitis	1
Skin	Acne	4
	Hair loss	4
	Rash	2
Others	Weight gain	6
	Gum hypertrophy	3
	Menstrual disturbances	2
	Anemia	1

Table 8: Mean Prescribed Daily dose/Defined Daily Dose Ratios (PDD/DDD) of the prescribed Antiepileptic Drugs in Mono/Poly therapy

62.5% (n=5) of patients who complained of memory problems and 40%(n=9) of patients who complained of gastrointestinal disturbances were on CBZ. 4 out of 6 patients (66.6%) who complained weight gain were on VA. 3 patients who complained of gum hypertrophy were on PHT. Other ADR's were rash menstrual disorders, alopecia, and acne. On doing chi square test statistical significance was found between type of therapy (polytherapy, monotherapy) and the adverse drug effects reported and P-value was 0.036.i.e subjects who are on polytherapy had experienced significantly higher number of adverse drug effects when compared to those who are on monotherapy.

		Adverse drug effects		Total
		yes	no	
Type of therapy	Monotherapy	23	32	55(100%)
	Polytherapy	34	9	43(100%)

Table 9: Relationship between ADRs and Type of therapy.

II. Quality of Life in Epilepsy-10 Inventory (QOLIE-10).

The QOLIE-10 questionnaire was used to measure the overall quality of life in study sample. The overall quality of life score and the scores for each of its subscales are summarized in below Table 10

		Generalised		Partial	
		ES<5	ES>5	ES<5	ES>5
		Therapy-1	Therapy-2	Therapy-1	Therapy-2
Energy	P Value	**0.033***	0.431	0.131	0.851
Low	P Value	**0.034***	0.144	0.536	0.206
Driving	P Value	0.22	0.779	0.07	0.785
Work	P Value	0.988	0.841	**0.048***	0.245
Social	P Value	0.303	0.906	0.138	0.24
Memory	P Value	0.377	0.222	**0.018***	0.459
Physical	P Value	0.313	0.222	**0.014***	0.565
Psychological	P Value	0.545	0.401	0.438	0.436
Afraid_Seizure	P Value	0.783	0.252	0.257	0.205
QOL	P Value	0.311	0.363	**0.037***	0.309

Table 10: Relation between various subscales of QOLIE-10 with Seizure frequency and Type of therapy in patients with Generalized seizures and Partial seizures.

1. Relationship between QOLIE-10 Scores and demographic Variables.

In the Overall quality of life domain, marital status, seizure frequency, type of AED therapy and AED side effects remained significant.

On one-way ANOVA the P value was found to be 0.005. the difference in QOL score among 3 groups based on marital status (married, unmarried, divorced) was found to be statistically significant. On further analysis by doing Post – Hoc tests, significant difference found between married – divorced and unmarried – divorced subjects. The QOLIE -10 scores in subjects with suicidal tendencies was poor when compared to the remaining patients and this difference was found to be statistically significant with a P- value 0.0001.

2. Inference for subscale of QOL - Energy:

Generalized seizures vs. partial seizures

Patients having generalized seizures and low seizure frequency when on monotherapy the energy levels were high when compared to patients on polytherapy and this difference was found to be statistically significant with a P-value of 0.033. Where as if the seizure frequency is high (Engel score > 5) there is no significant difference in energy levels between patients on monotherapy and polytherapy.

Monotherapy vs. polytherapy

20 out of 43 patients on polytherapy expressed low energy levels when compared to 5 out of 55 patients on monotherapy and this difference was statistically significant with a P-value 0.0002.

Engel score <5 vs. Engel score >5

2 out of 28 patients with ES<5 had poor scores in the subscale emotional well-being compared to 23 out of 29 patients with ES>5 and this difference was statistically significant with a P-value 0.0001.

	s.no	**Generalised**							
		ES<5				**ES>5**			
		Monotherapy		**Polytherapy**		Monotherapy		**Polytherapy**	
		N	%	n	%	n	%	n	%
ENERGY	1	6	27.30%	0	0.00%	0	0.00%	0	0.00%
	2	13	59.10%	3	37.50%	0	0.00%	0	0.00%
	3	3	13.60%	4	50.00%	1	50.00%	2	18.20%
	4	0	0.00%	1	12.50%	0	0.00%	3	27.30%
	5	0	0.00%	0	0.00%	1	50.00%	2	18.20%
	6	0	0.00%	0	0.00%	0	0.00%	4	36.40%

Table 11: Depicts scores of QOLIE-10 subscale Energy, among subjects with Generalized seizures.

Energy scores (1 to 6 with 1 representing most positive score and 6 representing most negative score) of PWE having Generalized seizures.

		Partial							
		ES<5				ES>5			
Energy		Monotherapy		**Polytherapy**		Monotherapy		**Polytherapy**	
		N	%	n	%	N	%	N	%
	1	6	23.10%	1	7.70%	0	0.00%	0	0.00%
	2	13	50.00%	4	30.80%	0	0.00%	0	0.00%
	3	7	26.90%	7	53.80%	1	20.00%	2	18.20%
	4	0	0.00%	1	7.70%	3	60.00%	7	63.60%
	5	0	0.00%	0	0.00%	1	20.00%	1	9.10%
	6	0	0.00%	0	0.00%	0	0.00%	1	9.10%

Table 12: Depicts scores of QOLIE-10 subscale Energy, among subjects with Partial seizures.

Energy scores (1 to 6 with 1 representing most positive score and 6 representing most negative score) of PWE having partial seizures.

3. Inference for QOL subscale – Emotional well being:

General seizures vs. partial seizures:-

Patients having generalized seizures and low seizure frequency when on monotherapy the emotional well being was high when compared to patients on polytherapy and this difference was found to be statistically significant with a P-value 0.034.

Monotherapy vs. polytherapy:-

20 out of 43 patients on polytherapy had poor scores in emotional wellbeing when compared to 9 out of 55 patients on monotherapy and this difference was statistically significant with a P-value 0.0002.

Engel score <5 vs. Engel score >5:-

6 out of 28 patients on with ES<5 had poor scores in the subscale emotional well-being compared to 23 out of 29 patients with ES>5 and this difference was statistically significant with a P-value 0.0002.

		Generalised							
		ES<5				ES>5			
		Monotherapy		Polytherapy		Monotherapy		Polytherapy	
	s.no	n	%	n	%	N	%	n	%
Low	1	0	0.00%	0	0.00%	0	0.00%	5	45.50%
	2	0	0.00%	1	12.50%	1	50.00%	0	0.00%
	3	0	0.00%	0	0.00%	1	50.00%	4	36.40%
	4	5	22.70%	5	62.50%	0	0.00%	1	9.10%
	5	10	45.50%	2	25.00%	0	0.00%	1	9.10%
	6	7	31.80%	0	0.00%	0	0.00%	0	0.00%

Table 13: Depicts scores of QOLIE-10 subscale Emotional well being, among subjects with Generalized seizures.

. Scores 1-6 : 1- feeling low all time, 6- feeling low none of the time

Feeling low		**Partial**							
		ES<5				**ES>5**			
		Monotherapy		Polytherapy		Monotherapy		Polytherapy	
		n	**%**	**N**	**%**	**n**	**%**	**N**	**%**
	1	0	0.00%	0	0.00%	1	20.00%	0	0.00%
	2	1	3.80%	0	0.00%	0	0.00%	5	45.50%
	3	2	7.70%	2	15.40%	3	60.00%	3	27.30%
	4	8	30.80%	6	46.20%	1	20.00%	2	18.20%
	5	8	30.80%	4	30.80%	0	0.00%	1	9.10%
	6	7	26.90%	1	7.70%	0	0.00%	0	0.00%

Table 14: Depicts scores of QOLIE-10 subscale Emotional well being, among subjects with Partial seizures

Scores 1-6 : 1- feeling low all time, 6- feeling low none of the time

Inference of driving:

Although there is no statistically significant difference between the comparative groups of this study i.e. patients with partial seizures and generalised seizures; patients on polytherapy and monotherapy, proportionately high number of patients i.e. 19 out of 29 patients who are having high seizure frequency (Engel score >5) are facing difficulty in driving which is significant statistically with P-value 0.025,when compared to patients with low seizure frequency

		Generalized							
		ES<5				ES>5			
		Monotherapy		Polytherapy		Monotherapy		Polytherapy	
		n	%	n	%	n	%	N	%

Driving	1	0	0.00%	0	0.00%	1	50.00%	3	27.30%
	2	1	4.50%	1	12.50%	1	50.00%	4	36.40%
	3	2	9.10%	3	37.50%	0	0.00%	3	27.30%
	4	9	40.90%	2	25.00%	0	0.00%	1	9.10%
	5	10	45.50%	2	25.00%	0	0.00%	0	0.00%

Table 15: Depicts scores of QOLIE-10 subscale difficulty driving, among subjects with Generalized seizures.

Score 1-5, 1- Not at all difficult, 5 - Great deal of difficulty.

		Partial							
		ES<5				**ES>5**			
		Monotherapy		Polytherapy		Monotherapy		Polytherapy	
Driving		**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	1	0	0.00%	2	15.40%	0	0.00%	2	18.20%
	2	0	0.00%	0	0.00%	3	60.00%	5	45.50%
	3	2	7.70%	2	15.40%	1	20.00%	2	18.20%
	4	9	34.60%	6	46.20%	1	20.00%	2	18.20%
	5	15	57.70%	3	23.10%	0	0.00%	0	0.00%

Table 16: Depicts scores of QOLIE-10 subscale difficulty driving, among subjects with Partial seizures.

Score 1-5, 1- Not at all difficult, 5 - Great deal of difficulty.

Inference of work limitations:

General seizures vs. partial seizures:-

In patients with partial seizures with low seizure frequency(Engel score <5) and on monotherapy statistically significant difference in work limitation was seen when compared to patients who are on polytherapy, monotherapy patients had better scores when compared to that of patients on polytherapy(P-value 0.048).

Monotherapy vs. polytherapy:-

Patients on polytherapy 18 out of 43 expressed statistically significant work limitations (P-value 0.0352) when compared to those on monotherapy

Engel score < 5 vs. Engel score > 5:-

18 out of 29 patients with high seizure frequency (Engel score>5) expressed limitation in their work and only 5 out of 28 Patients with low seizure frequency expressed limitations in work. This difference was statistically significant with a P-value 0.042.

		Generalized							
		ES<5				ES>5			
		Monotherapy		Polytherapy		Monotherapy		Polytherapy	
		n	%	n	%	N	%	N	%
Work	1	5	22.70%	2	25.00%	0	0.00%	0	0.00%
	2	11	50.00%	4	50.00%	0	0.00%	1	9.10%
	3	6	27.30%	2	25.00%	1	50.00%	3	27.30%
	4	0	0.00%	0	0.00%	0	0.00%	2	18.20%
	5	0	0.00%	0	0.00%	1	50.00%	5	45.50%

Table 17: Depicts scores of QOLIE-10 subscale – Work limitations, among subjects with generalized seizures.

Score 1-5, 1 – Not at all bothersome, 5 – Extremely bothersome.

		Partial							
		ES<5				**ES>5**			
		Monotherapy		Polytherapy		Monotherapy		Polytherapy	
Work limitation		**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	1	11	42.30%	1	7.70%	0	0.00%	0	0.00%
	2	11	42.30%	7	53.80%	0	0.00%	0	0.00%
	3	4	15.40%	3	23.10%	3	60.00%	2	18.20%
	4	0	0.00%	2	15.40%	1	20.00%	5	45.50%
	5	0	0.00%	0	0.00%	1	20.00%	4	36.40%

Table 18: Depicts scores of QOLIE-10 subscale – Work limitations, among subjects with Partial seizures

Score 1-5, 1 – Not at all bothersome, 5 – Extremely bothersome.

Inference of QOL subscales social limitations:

Social limitations were not statistically significant in this study group.

		Generalized							
		ES<5				ES>5			
		Monotherapy		Polytherapy		Monotherapy		Polytherapy	
		N	%	n	%	N	%	n	%
Social	1	5	22.70%	2	25.00%	1	50.00%	1	9.09%
	2	14	63.60%	3	37.50%	0	0.00%	1	9.09%
	3	3	13.60%	3	37.50%	1	50.00%	6	54.54%
	4	0	0.00%	0	0.00%	0	0.00%	2	18.18%
	5	0	0.00%	0	0.00%	0	00.00%	1	9.09%

Table 19: Depicts scores of QOLIE-10 subscale –Social limitations, among subjects with Generalized seizures

Score 1-5, 1 – Not at all bothersome, 5 – Extremely bothersome.

		Partial							
		ES<5				**ES>5**			
		Monotherapy		Polytherapy		Monotherapy		Polytherapy	
Social limitations		**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	1	11	42.30%	2	15.40%	0	0.00%	0	0.00%
	2	11	42.30%	9	69.20%	0	0.00%	2	18.20%
	3	4	15.40%	1	7.70%	3	60.00%	2	18.20%
	4	0	0.00%	1	7.70%	0	0.00%	3	27.30%
	5	0	0.00%	0	0.00%	2	40.00%	4	36.40%

Table.20; : Depicts scores of QOLIE-10 subscale –Social limitations, among subjects with partial seizures

Score 1-5, 1 – Not at all bothersome, 5 – Extremely bothersome.

Inference of QOL subscales memory difficulties:

Generalized seizures vs. Partial seizures:-

In patients with generalized seizures there is no statistically significant difference between patients who are on monotherapy and polytherapy; in patients having low seizure frequency and high seizure frequency. Patients having partial seizures with low seizure frequency and are on polytherapy had expressed significantly lower cognitive function in the past 4 weeks when compared to that of patients who are on monotherapy and this difference was statistically significant with a P-value 0.018.

Monotherapy vs. polytherapy:-

8 out of 43 patients on polytherapy had significantly lower (P-value0.038) cognitive function when compared to 2 out of 55 patients on monotherapy.

		Generalised							
		ES<5				ES>5			
		Monotherapy		Polytherapy		Monotherapy		Polytherapy	
		n	%	N	%	n	%	n	%
Memory	1	20	90.90%	8	100.00%	0	0.00%	6	54.50%
	2	2	9.10%	0	0.00%	1	50.00%	4	36.40%
	3	0	0.00%	0	0.00%	0	0.00%	0	0.00%
	4	0	0.00%	0	0.00%	1	50.00%	1	9.10%
	5	0	0.00%	0	0.00%	0	0.00%	0	0.00%

Table 21: Depicts scores of QOLIE-10 subscale –Memory difficulty, among subjects with Generalised seizures

Score 1-5, 1 – Not at all bothersome, 5 – Extremely bothersome.

		Partial							
		ES<5				**ES>5**			
		Monotherapy		Polytherapy		Monotherapy		Polytherapy	
Memory difficulties		**n**	**%**	**n**	**%**	**n**	**%**	**N**	**%**
	1	24	92.30%	8	61.50%	3	60.00%	4	36.40%
	2	2	7.70%	5	38.50%	0	0.00%	4	36.40%
	3	0	0.00%	0	0.00%	1	20.00%	2	18.20%
	4	0	0.00%	0	0.00%	1	20.00%	1	9.10%
	5	0	0.00%	0	0.00%	0	0.00%	0	0.00%

Table 22: Depicts scores of QOLIE-10 subscale –Memory difficulty, among subjects with Partial seizures.

Score 1-5, 1 – Not at all bothersome, 5 – Extremely bothersome.

Inference of physical effects of drugs:

Significantly higher number of patients receiving (28 out of 43 PWE) polytherapy experienced AED related physical effects when compared to those on monotherapy and this was found to be statistically significant with a P-value 0.0014.

		Generalised							
		ES<5				ES>5			
		Monotherapy		Polytherapy		Monotherapy		Polytherapy	
		n	%	N	%	N	%	n	%
Physical	1	10	45.50%	1	12.50%	1	50.00%	1	9.10%
	2	7	31.80%	1	12.50%	0	0.00%	0	0.00%
	3	4	18.20%	1	12.50%	1	50.00%	0	0.00%
	4	0	0.00%	3	37.50%	0	0.00%	6	54.50%
	5	1	4.50%	2	25.00%	0	0.00%	4	36.40%

Table 23: Depicts scores of QOLIE-10 subscale –Physical effects of drugs, among subjects with Generalized seizures.

Score 1-5, 1 – Not at all bothersome, 5 – Extremely bothersome.

		Partial							
		ES<5				**ES>5**			
		Monotherapy		Polytherapy		Monotherapy		Polytherapy	
Physical effects of drugs		**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	1	14	61.50%	1	6.66%	2	40.00%	2	18.20%
	2	7	26.90%	4	26.66%	2	40.00%	0	0.00%

	3	3	11.50%	4	26.66%	1	20.00%	1	9.10%
	4	1	0.00%	3	15.00%	0	0.00%	2	18.20%
	5	1	0.00%	3	15.00%	0	0.00%	6	54.50%

Table 24: Depicts scores of QOLIE-10 subscale –Physical effects of drugs, among subjects with Partial seizures.

Score 1-5, 1 – Not at all bothersome, 5 – Extremely bothersome.

Inference of psychological effects of drugs:

Monotherapy vs. polytherapy:-

Patients receiving polytherapy (n=16) had significantly (P-value 0.012) higher number of drug related psychological effects when compared to those on monotherapy (n=6).

Engel score <5 vs. Engel score > 5:-

Statistically significant difference (P-value 0.025) was seen between patients having high seizure frequency and low seizure frequency. Patients with high seizure frequency had very poor scores in QOLIE subscale-pscychological effects.

		Generalised							
		ES<5				ES>5			
		Monotherapy		Polytherapy		Monotherapy		Polytherapy	
		N	%	n	%	n	%	n	%
Psychological	1	19	86.40%	8	100.00%	0	0.00%	2	18.20%
	2	2	9.10%	0	0.00%	0	0.00%	5	45.50%
	3	1	4.50%	0	0.00%	1	50.00%	2	18.20%
	4	0	0.00%	0	0.00%	1	50.00%	1	9.10%
	5	0	0.00%	0	0.00%	0	0.00%	1	9.10%

Table 25: Depicts scores of QOLIE-10 subscale –Psychological effects of drugs, among subjects with Generalized seizures.

Score 1-5, 1 – Not at all bothersome, 5 – Extremely bothersome.

		Partial							
		ES<5				ES>5			
		Monotherapy		Polytherapy		Monotherapy		Polytherapy	
Psychological drug effects		n	%	n	%	N	%	N	%
	1	21	80.80%	9	69.20%	3	60.00%	5	45.50%
	2	4	15.40%	2	15.40%	1	20.00%	3	27.30%
	3	1	3.80%	2	15.40%	0	0.00%	2	18.20%
	4	0	0.00%	0	0.00%	1	20.00%	0	0.00%
	5	0	0.00%	0	0.00%	0	0.00%	1	9.10%

Table 26: Depicts scores of QOLIE-10 subscale –Psychological effects of drugs, among subjects with Partial seizures.

Score 1-5, 1 – Not at all bothersome, 5 – Extremely bothersome.

Inference of afraid of seizure:

Monotherapy vs. polytherapy:-

Higher numbers of patients (30 out of 43 PWE) on polytherapy are afraid of having seizures when compared to those on monotherapy and this difference was statistically significant with a P-value 0.001

Engel score < 5 vs. Engel score > 5:-

There is statistically significant difference between patients who are having low seizure frequency (n=7) when compared to patients having high seizure frequency (n=25) with p-value 0.0001. Patients with high seizure frequency are more afraid of seizure recurrence when compared to those with low seizure frequency.

		Generalised							
		ES<5				ES>5			
		Monotherapy		Polytherapy		Monotherapy		Polytherapy	
		n	%	n	%	n	%	N	%
Afraid Seizure	1	0	0.00%	0	0.00%	1	100.00%	5	36.40%
	2	3	27.30%	2	25.00%	0	0.00%	6	54.50%
	3	11	50.00%	5	62.50%	0	0.00%	1	0.00%
	4	8	22.70%	1	12.50%	0	0.00%	0	0.00%

Table 27: Depicts scores of QOLIE-10 subscale –Afraid of seizures, among subjects with Generalized seizures

Score 1-4, 1 - Very afraid of seizures, 4 - Not at all afraid of seizures.

		Partial							
		ES<5				**ES>5**			
Afraid of seizures		Monotherapy		Polytherapy		Monoherapy		Polytherapy	
		n	**%**	**n**	**%**	**N**	**%**	**n**	**%**
	1	0	0.00%	0	0.00%	2	40.00%	9	63.60%
	2	2	15.40%	5	38.50%	3	60.00%	2	18.20%
	3	18	69.20%	7	53.80%	0	0.00%	0	18.20%
	4	6	15.40%	1	7.70%	0	0.00%	0	0.00%

Table 28: Depicts scores of QOLIE-10 subscale – Afraid of seizures, among subjects with Partial seizures.
Score 1-4, 1 - Very afraid of seizures, 4 - Not at all afraid of seizures

Inference of overall QOL:

Generalized vs. Partial seizures.

Patients with partial seizures who are on polytherapy had significant lower overall QOL with a P-value 0.037.Patients with generalized seizures or partial seizures had shown no significant difference in overall QOL,

Monotherapy vs. Polytherapy

When type of therapy was considered irrespective of type of seizures polytherapy PWE had significantly lower overall QOL (P-value 0.003)

Engel score <5 vs. Engel score >5.

Patients having low seizure frequency had better overall QOL when compared to patients with high seizure frequency and this difference was found to be statistically significant with P-value 0.0002.

		Generalised							
		ES<5				ES>5			
		Monoherapy		Polytherapy		Monoherapy		Polytherapy	
		n	%	n	%	N	%	n	%
QOL	1	2	9.10%	0	0.00%	0	0.00%	0	0.00%
	2	12	54.50%	3	37.50%	0	0.00%	0	0.00%
	3	7	31.80%	3	37.50%	0	0.00%	1	9.10%
	4	1	4.50%	2	25.00%	2	100.00%	5	45.50%
	5	0	0.00%	0	0.00%	0	0.00%	5	45.50%

Table 29: Depicts scores of QOLIE-10 subscale –Overall QOL, among subjects with Generalized seizures

Score 1-5, 1- Very good, 5- Very bad.

		Partial seizures			
		ES<5		ES>5	
		Monotherapy	Polytherapy	Monotherapy	Polytherapy

Overall QOL		n	%	n	%	n	%	n	%
	1	2	7.70%	0	0.00%	0	0.00%	0	0.00%
	2	16	61.50%	3	23.10%	0	0.00%	0	0.00%
	3	7	26.90%	7	53.80%	1	20.00%	2	18.20%
	4	1	3.80%	3	23.10%	2	40.00%	8	72.70%
	5	0	0.00%	0	0.00%	2	40.00%	1	9.10%

Table 30: Depicts scores of QOLIE-10 subscale –Overall QOL, among subjects with Partial seizures.
Score 1-5, 1- Very good, 5- Very bad.

VI. Discussion

Epilepsy is a chronic disease that largely influences the patient's life. It is the most common neurological disorder requiring long-term health care contact. Internalized, interpersonal, and institutional stigma prevents patients with epilepsy from participating in school and employment and reduces their opportunities to establish peer and couple relationships.[38] Especially in India epilepsy is known to have adverse effect on education, employment, marriage, and other essential social opportunities.[39] Therefore the ultimate goal of treatment of epilepsy is no seizures and no side effects with an optimal quality of life. Hence evaluation of quality of life outcomes has been increasingly adopted into the standard management plan for epilepsy along with traditional measures of seizure frequency and adverse effects. The objective of this study was to describe the drug utilization pattern of anti-epileptic drugs in an Indian tertiary care hospital setting and to assess the quality of life (QOL) among adult patients with epilepsy. Further it's needed to identify the various demographic, clinical and pharmacotherapeutic characteristics that would influence QOL.

Demographic and Clinical Profile

The study sample was characterized by its younger age (18-35years).Majority were males(55.10%) though the respective proportions were not significantly different unlike other studies which suggest a gender susceptibility to the development of specific epilepsy subtypes.**[40,41]** In this study majority of population was from rural areas(60.20%). Marriage rate of 59% found in this study was reasonable considering the student number and younger age of the patient sample marriages.[42] In a study done at ethiopia rural dwellers showed more negative attitudes with regard to marriage and working with a person suffering from epilepsy.[43] In another study done in Kanpur, marriage rate was only about 46% among epileptic patients.[44] The divorce rate in this study group was 5.10% which is comparatively low when compared to that of a study done at Hirosaki where the divorce rate was 10.43%[45]. Out of 5 PWE who were divorced 3 patients stated that epilepsy was the reason for their divorce, this could be due to stigma associated with epilepsy among patients and their caregivers.

Compared to many other studies there was a low rate of unemployment (20.4%) in this study group, this could be because most of the patients are self employed like farmers, small scale businesses or unskilled workers. In contrast, in a study conducted at North East England the rate of unemployment was recorded as 59% among patients with epilepsy.[46] Out of 20 patients who were unemployed 9 patients (45%) reported that they could not get a job due to epilepsy or epileptic seizures. Most of these patients reported that they could not perform jobs that had associated risk of injury or driving of a motor vehicle because of the potential for seizures. The percentage of patients who were unemployed due to epilepsy was slightly higher when compared to a study done at Japan where it was only 34%.[47]

In most Indian studies the occurrence of primary generalized seizures account for more than 50% of cases. In a study conducted at a south Indian tertiary care hospital Mysore generalised seizures constituted 81.8%.[48] But a multicentre study in six tertiary level hospitals in three southern states of India reported an equal prevalence of partial and generalized seizures.[49] In another study at omen generalized seizures constituted 51%[50] . In this study partial seizures accounted for 49% and generalized seizures for 51%. The low incidence of absence seizures in this study was probably due to its under detection in developing countries as compared to the developed countries.[51]

Secondary epilepsy accounted for 39% of all seizures and was higher among patients with partial seizures. Neurocysticercosis was reported in 10 patients in this study group. Neurocysticercosis has been recently identified to be the most frequent cause of secondary epilepsy which may be attributable to the higher prevalence of taeniasis in developing countries along with widespread availability of CT/MRI to identify single ring enhancing lesions which correlates with a study conducted at Peru.[52] Central nervous system (CNS) infections have been documented as the main cause of seizures and acquired epilepsy in the developing world.[53] where as in a study done at Mysore trauma was the most common cause of secondary epilepsy.[54] Anti epileptic drugs were the mainstay for control of seizures in neurocysticercosis and can be used as a single

agent therapy.[55] Antihelminthic treatment of Neurocysticercosis results in disappearance of viable cysts in about one-third of patients with parenchymal disease, but a reduction in seizure recurrence has not been demonstrated in randomized controlled trials. Prevention is critical to reduce the burden of seizure and epilepsy related to Neurocysticercosis.[56]

Pharmacotherapy profile

56.1% of the study group were on monotherapy, therefore monotherapy was the preferred treatment regime in this study, which correlates with a study conducted by Dr. S. Vijayarangan et al, in their study group 55% were on monotherapy[57]. Monotherapy with first line drugs was primarily instituted, this treatment pattern correlates with that of study done at Brudwan India[55]. Polytherapy was initiated only if seizure freedom is elusive despite full doses of the first AED and after two monotherapy regimens fail, as chances of seizure control on third monotherapy are slim.[58] Practice of monotherapy improves patient adherence to treatment and hence better seizure control. This practice of monotherapy was supported by clear evidence from studies which highlights many advantages like effective seizure control, fewer adverse effects and drug interactions, better compliance and lower cost. Good adherence may have been hampered by complex medication regimens such as increased frequency of AED intake which may cause confusion and forgetfulness in some of the patients[59]. A cross sectional study in the emergency department of a tertiary care hospital in south India identified non-compliance to AEDs as the most common cause of preventable seizures.[60]

The PDD/DDD ratios noted among our patients on either monotherapy or polytherapy was less than 1 for most of the AEDs. Low PDD/DDD ratios of AEDs were also observed in a study in Kerala.[9]The standard practice is to initiate treatment at lower doses and then titrate if not controlled which probably explains the low ratio. However it also appears that polytherapy was adopted more readily rather than prescribing high defined doses of monotherapy when confronted with poor control. Evidence exists Reducing AED polytherapy to monotherapy frequently reduces the burden of adverse effects and may also improve seizure control[61]. Individualized polytherapy does not increase the burden of adverse events; however the issue of rational polypharmacy in epilepsy remains largely unresolved. Literature supports the efficacy of combinations with different or perhaps multiple mechanisms of action to cover more pharmacological bases e.g. sodium channel blockers with a GABAergic drug (PB/CLB) or valproate.[62] The significantly higher frequency of patients on polytherapy who experienced an ADR warrants the need for more rational prescribing of AED polypharmacy and careful monitoring (TDM) to prevent drug toxicity due to drug-drug interactions.

In this study majority patients n=83 patients were receiving conventional AED's .The use of newer AED's was markedly low(15.30%) and were mainly employed as an add on therapy, probably because of their high cost as most of the patients in this study group belonged to low socio economic group. These findings were not in accordance with the updated NICE guidelines, which recommend the use of Oxcarbazepine, Lamotrigine and Levetiracetam as potential first line drugs in focal/generalized seizures[63]. But the findings in this study correlates with a study conducted at Salem[57]. In our study the limited prescribing of new generation AEDs indicated that these drugs are still relatively under used which correlates with the study done at Coimbatore.[64] where as in a European study the usage of newer AED's was 49%.[65]

CZ was the most used newer AED(31)followed by OXC followed by LTC. The most frequent combinations of CZ were with carbamazepine, valproate, followed by phenytoin. In the present study, clobazam being broad spectrum was selected as add-on AED for patients with epilepsy who were not responding to other AEDs.[66] Oxcarbazepine was the other newer anti epileptic which was used as an add on therapy in this study. Oxcarbazepine represents an important new treatment option indicated for monotherapy and adjunctive therapy in adults with partial seizures[67].

Selection of AED should be primarily guided by evidence of efficacy for the patient's seizure type and tolerability (data from well designed randomized controlled trials) along with patient specific features (age, sex, child bearing potential, and comorbidities and affordability). The use of conventional anti epileptics like sodium valproate(65.11%), CBZ(58.13%) and PHT at higher frequencies is seen in this study which correlates with a study conducted at oman in which sodium valproate (49%) was the most frequently prescribed AED, followed by carbamazepine (44%) followed by phenytoin (12%).[50] In a study regarding Assessment of antiepileptic drugs usage in a South Indian tertiary care teaching hospital, Sodium valproate was the widely prescribed drug[48]. Increased utilization of Phenytoin followed by Sodium valproate was seen in a study done at Hyderabad.[68] In yet another study by dr. S. Vijayarangan Phenytoin was the most commonly prescribed drug as monotherapy[57].

AED usage in generalized seizures and partial seizures:

The choice of AEDs in partial seizures was similar to other South Indian studies with CBZ CR and sodium valproate being used most frequently used.[57] The significantly increased utilization of CBZ in partial seizures when compared to generalized is in accordance with epilepsy treatment guidelines set by the ILAE

which recommends use of Carbamazepine as initial monotherapy in partial seizures with level of evidence A.[69] The vast experience makes it a reasonable first choice drug in focal seizures. Similar to other studies, Sodium Valproate followed by Phenytoin was widely prescribed drugs for generalised seizures. This significantly higher utilization of Valproic acid in generalized seizures is as per the updated NICE guidelines which recommend both as first line drugs in generalized tonic clonic seizures.[69]

The dose of anti epileptic drug varies for every individual patient. For instance the dose range of Phenobarbitone being 50 to 200mg/day, few patients could not tolerate a dose greater than 100mg/day where as some can tolerate a dose of 200mg/day. The same phenomenon was seen with phenytoin as in some can tolerate a dose range of dose of Phenytoin ranged from 50 to 400 mg per day. Some patients could not tolerate more than 200 mg however some could take 400 mg with no unacceptable side effects. Few antiepileptic drugs were recently introduced and were in titration phase where as few anti epileptic drugs were being tapered because of their decreased tolerability and (or) efficacy. This explains the lower doses of anti epileptic drugs in this study. Though the tolerability and clinical profile may partially justify the low PDD/DDD ratio and the use of polytherapy, there is definitely a need to further standardize pattern of monotherapy in our population.

Adverse drug effects of AEDs:

Adverse effects of antiepileptic drugs (AEDs) are common, can have a considerable impact on quality of life and contribute to treatment failure in up to 40% of patients. The proportion of patients who develop AED related adverse events in different studies vary from less than 10% to more than 70%.[70] In this study a total of 78 adverse drug reactions were reported out of which majority are Central nervous system related adverse effects (50.5%) followed by Gastro intestinal related adverse effects (24%). These results correlate with other studies done by Dr. Sourav chakraborthy et al at west Bengal, in their study a Total of 161 ADRs were detected, among which 55.3% were CNS adverse events followed by 15.5% gastrointestinal and 4.3% related to dermatological and allergic manifestations.[71] In a study done at Hyderabad only 13 patients out of a total of 278, reported ADRs (incidence = 4.67%), [68] which is in contrast to our study where 58.16% patients reported ADRs. In this study among CNS related adverse effects majority were sedation and headache. The spectrum of adverse events across systems was largely similar to other studies; however there was a higher frequency of patients who responded positively for memory impairment in contrast to study done at Tamilnadu where most common ADR was memory loss[72]. In this study 62.5%(n=5) of patients who complained of memory problems were on CBZ, (66.6%) who complained weight gain were on VA, these results correlated with a cross sectional study done at Netherlands.[73]

Quality of life in patients with Epilepsy

Demographic profile and QOL:

In this study QOL was evaluated in patients with epilepsy using QOLIE-10, an abbreviated quality of life questionnaire and studied the impact of different variables including demographical and pharmacotherapeutic variables. Other than marital status the other demographical characteristics like socioeconomic status, residence, education etc have not shown any statistically significant association with poor QOL in this study. Being married affords one the social and psychological support and hence reduces on the negative impact of low scores of these aspects on overall QOL, where as in comparative study done at neurology outpatient clinic of Basrah General Hospital, Iraq, patients who were older, from rural areas, and with low education and income levels had lower overall QOL scores.[74]

The general consensus was that suicidality, which encompasses completed suicide, suicide attempt, and suicidal ideation, was significantly more frequent among people with epilepsy than in the general population [75] In this study the QOLIE scores of patients having suicidal tendencies were very poor**.** A recent alert from the FDA, suggested that antiepileptic drugs (AEDs) can be associated with increased suicide risk. [76] In another study it was found that Depression and not seizure factors or self-perceived quality of life was an independent predictor of suicidal ideation.[77] The causes of suicidality for people with epilepsy were multiple, with prior or current psychiatric history and family psychiatric history being the most important risk factors. The degree to which AEDs cause an increased suicidal risk was not yet determined[75]. Therefore caution must be used in patients with epilepsy and current or past psychiatric history.

Type of seizures and QOL:

In this study, patients with generalized seizures, who were on polytherapy though having lower seizure frequency have shown significantly lower energy levels and emotional well being scores when compared to those who are on monotherapy, this could be due to higher association of underlying co morbidities and also associated adverse drug effects. Though psychological co morbidities were not considered in this study, presence of suicidality (3 out of 4 patients had generalized seizures) points to presence of depression. Episodic depression is more prevalent among persons with epilepsy than among those without and it is frequently

overlooked in patients with epilepsy, and accordingly not treated[78,79]. Patients with partial seizures , who were on polytherapy had shown significantly higher adverse medication effects and memory difficulties when compared to patients with generalized seizures who were on polytherapy this could be due to higher number of ADRs associated to CBZ followed by VA, a similar finding which is seen in other studies.[80] CBZ and VA were most frequently used in patients with partial seizures in this study, however there was no significant association between seizure type and overall QOL in this study unlike other studies where QOL was significantly lower in patients with partial seizures.[81]

Pharmacotherapy and QOL:

In this study it was observed that monotherapy was probably underutilized, Similar observations were made in an earlier study also.[9]Patients who were on polytherapy and experiencing 2 or more physical and psychological drug related adverse effects had significantly lower energy levels and emotional wellbeing, where as in other study polytherapy was associated only with poor emotional well being.[82] These patients also experienced increased difficulty with memory when compared to those who were on monotherapy. Therefore patients having antiepileptic drug related adverse effects scored poor QOL scores. There was a significant association between polytherapy and adverse drug effects. Hence as can be inferred, the score in medication effect domain (question in this domain based on side effects of AED) among those on polytherapy was significantly lower compared to those on monotherapy, where as in other similar study no differences were found in overall neurotoxicity between monotherapy and polytherapy.[83] It can be assumed that these patients would have probably not been tolerating the AEDs well due to drug interactions/enzyme induction and hence were started on adjuvant therapy with new AEDs. In this study older AEDs are most commonly used when compared to newer AEDs which probably must have contributed for increased number of drug related cognitive adverse effects as seen in similar other studies where use of older AEDs was associated with impaired cognitive ability when compared to newer AEDs.[84] Therefore adverse effects of AEDs constituted one of the main parameter that influenced QOL among patients with epilepsy in the study group. It should be emphasized that QOLIE-10 contains only general questions about the impact of AEDs on QOL and that this domain comprised relatively a small part of the total calculated QOL score. The increase in number of adverse drug reactions reported and low score in medication effect domain among patients on polytherapy hints at the probability of decreased tolerability and possible drug interactions to AEDs. Thus, where enzyme induction and drug interactions are foreseen as significant problems, especially in patients with other co morbidities, new drugs would be preferable. The ultimate goals in the management of epilepsy are no seizure, no side effects and an optimal quality of life.

Seizure frequency and QOL:

Among clinical characters seizure frequency was the other most relevant determinants of poor QOL scores which had been consistently seen across many studies.[9] In this study patients with high seizure frequency had not shown significant social limitations On a positive note, this is probably because of the decreased disease stigma, social support and increased awareness of their condition among patients attending this tertiary care setup, though attitudes toward people with epilepsy have improved over the years few people with epilepsy stigma continues to adversely impact their psychological wellbeing and quality of life. Stigma can be one of the most distressing consequences of having seizures. High seizure frequency limits usual daily activity and leads to impairment of physical, social and emotional functioning and finally to general deterioration of one's quality of life.[85] When factors influencing on QOL were separately analyzed in this study, increasing seizure frequency was the only clinical variable that was found to be significantly associated with QOL impairment among the patients with epilepsy in almost all the QOL subscales, with seizure frequency being reported as an inverse predictor of QOL among patients with epilepsy, other studies had also shown similar results.[9] Early age at onset of epilepsy or childhood onset epilepsy was another factor significantly associated with higher seizure frequency that also ultimately impaired QOL. Patients with high seizure frequency felt that physical pain prevented them from achieving what they wanted in life and were not satisfied with their capacity for work. Seizure control is essential in improving quality of life as the lower seizure frequency allowed patients to be more productive. Physical functioning and emotional well-being scores were the most affected QOL domains despite PWEs being on AEDs monotherapy and reduced seizure frequency, this could be because many physical activities were usually restricted for fear of seizure occurrence in majority of the patients with epilepsy.[86] In this study medication effects and seizure frequency majorly contributed for low QOL ,in other study medication effect had the least and seizure frequency had the major contribution on QOL, which is in contrast to findings in the study population.[87]

VII. Strengths And Limitations

We evaluated the impact of specific pharmacotherapy characteristics on quality of life in epilepsy. Moreover we attempted to study the effectiveness and tolerability profile of different types of AED therapy in a naturalistic setting. The strengths of our study include an optimal sample size which was adequately powered to detect a clinically meaningful difference in QOLIE scores between groups. We had a fair representation from rural population. The methodology followed along with the patient level interview helped us to get their personal perspectives on factors affecting their life. Robust statistical tests employed enabled us to generate valuable information on variables influencing quality of life.

However there are some limitations. The cross-sectional design of this study makes it difficult to comment with certainty on the differences in efficacy, tolerability and QOLIE scores among the types of AED therapy. Ideally a follow up study with initiation of AED therapy during the same time frame will enable measurement of difference in QOLIE scores from baseline. There is a chance of interviewer bias as patients not conversant with English language had to be explained about various domains in the questionnaire to elicit responses. The exclusion of patients with severe physical or mental limitations may bias our results towards the opinions of people with better general health status.

Concluding Remarks

It's an open label design presence of potential biases might question the evidence obtained from this study. The higher doses of carbamazepine (600 mg/day) used and the immediate release formulations might have biased effectiveness estimates against Carbamazepine by causing undue withdrawals for intolerability. It is also now known that new AEDs are not completely free of severe adverse effects (particularly in case of cognitive and psychiatric adverse effects with Levetiracetam) These facts on new AEDs together with our results raise the question whether their use should be promoted in developing countries where cost is a primary concern. Also the impact of polytherapy on quality of life and the increased number of adverse events reported highlights the need to optimize monotherapy regimes. The key to epilepsy management is to adapt treatment decisions to individual patient characteristics where the AED choice is determined by seizure type, adverse event profile, patient specific features (age, sex, pregnant women) and co morbidities. Undoubtedly, newer AEDs play an important role in refractory epilepsy and in situations where enzyme induction, drug interactions and possible adverse events are foreseen as significant problems. We conclude on the note that appropriate anti-epileptic drug selection, preferably monotherapy and careful recognition and assessment of important factors like AED side effects will move us closer to our ultimate management goals in comprehensive care of epilepsy of achieving a seizure free state and an optimal quality of life.

VIII. Conclusion

This cross-sectional study examined patterns of anti-epileptic drug prescribing and factors affecting quality of life among 98 patients with epilepsy attending a tertiary care hospital in Visakhapatnam.

- Majority were males (55.10%), predominantly young and belonged to poor and lower middle socioeconomic status and resided in rural and semi urban areas.
- The rate of unemployment is low 20.4%, out of which 45% of patients expressed unemployment because of epilepsy in this study.
- Generalized seizures accounted for the dominant seizure type (51%). In which tonic clonic was the commonest type.
- 73% of patients had an idiopathic or cryptogenic aetiology for seizures.
- Secondary epilepsy accounted for 39% of all seizures in which neurocysticercosis was the most common type.
- 56.1% of patients were maintained on monotherapy. Majority of patients were on older AEDs (84.69%).
- Only15.30% of patients had received a newer AED, which were employed as an adjuvant therapy.
- Valproic acid (65.11%) was the most commonly used AED overall and carbamazepine was the most frequently used AED as monotherapy. Clobazam was the most frequently used newer AED.
- The mean PDD/DDD ratios for most AEDs were less than 1 indicating that patients were maintained on lower doses than recommended by WHO.
- The AEDs of choice for the partial and generalized seizures were in accordance with the recommended guidelines.
- 58.16% patients reported having experienced at least one ADR.
- CNS (50.5%) was the most commonly involved organ system followed by gastrointestinal system.
- The proportion of patients on polytherapy who reported an ADR was significantly greater compared to those on monotherapy.(p=0.003)

- Seizure frequency, number of AEDs and number of ADRs were the most important predictors of poor QOL. Patients on monotherapy had a significantly lower medication effect score when compared to old AEDs.

Coping with medical and non medical burden of epilepsy is a difficult task. Optimizing monotherapy use with appropriate AED selection and careful evaluation of drug side effects is a critical component of clinical care and may assist in improving the overall QOL. However, only long term community based follow up studies can establish differences if any on the impact of different types of AED therapy on QOL which is considered to be the most important patient related outcome measure in patients with epilepsy.

IX. Summary

The objective of the present study was to evaluate the patterns of anti-epileptic drug use and to assess the quality of life among patients with epilepsy. This was a hospital based cross-sectional study conducted over a period of 5 months from April 2016 to august 2016. 98 patients with a confirmed diagnosis of epilepsy who met the eligibility criteria were recruited from a random sample of epileptic patients attending the Neurology OPD. Demographic, clinical and treatment details were collected from medical records or by personal interview of patients. QOLIE-10 questionnaire which is an abbreviated quality of life questionnaire for epilepsy was administered to each patient to measure their overall QOLIE-10 score. The median age of our patient sample was 25 with 56.1% males. Majority of patients (80%) were from rural and semi-urban areas and were from a lower socioeconomic background. 51% of patients had generalized seizures. Secondary epilepsy attributed to 39% of causes for seizures, among them neurocysticercosis was the most common cause. The ratio of monotherapy to polytherapy was 1:1.27. Sodium valproate, carbamazepine, phenytoin were the most frequently used AEDs in descending order. Carbamazepine was most commonly used as monotherapy and sodium valproate was the most frequently prescribed as polytherapy. Evidence based choice of AEDs were observed among patients with partial and generalized seizures. Carbamazepine was used significantly more in partial seizure than generalized seizures($p=0.003$) whereas the use of sodium valproate was significantly more in generalized seizures ($p=0.041$).The mean PDD/DDD ratio for majority of the AEDs either in monotherapy or polytherapy were less than 1.The patient sample had an optimal overall QOL scores. Except for marital status in which divorced patients had shown significantly poor QOL scores, none of the demographic variables were significantly associated with QOLIE-10 score. Among clinical variables, increased seizure frequency ($p=0.0002$), polytherapy ($p=0.003$) , presence of adverse drug reactions($p=0.0001$) were significantly associated with a low QOLIE-10 score. A stepwise linear regression analysis model identified increased number of AEDs ($p=0.036$), increased number of adverse drug reactions ($p=0.003$) and increased seizure frequency ($p=0.0002$) as the most important predictors of a poor quality of life. A greater proportion of patients on polytherapy reported adverse drug reactions when compared to monotherapy and had a significantly lower score in medication effects domain ($p=0.03$). Appropriate AED selection preferably monotherapy and careful evaluation of drug side effects play a crucial role in achieving the ultimate target goals of seizure freedom and optimal quality of life among patients with epilepsy.

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