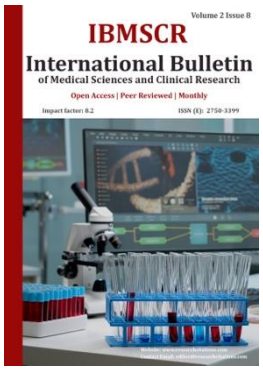

GAUGING THE CLINICAL COURSE OF DRUG-RESISTANT EPILEPSY: A RETROSPECTIVE ANALYSIS OF PROGRESSION FROM SEIZURES TO STATUS EPILEPTICUS

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1. Abstract:-

1.1 Introduction:- Epilepsy is the common neurological condition which effects the people of all age. There are around 50 million people suffering with epilepsy in this world.

1.2 Materials and methods :-The primary aim of this study was to analyze the clinical progression in the individuals with drug-resistant epilepsy (DRE) from status epileptics across different age groups , genders and etiologies. The secondary purpose was to analyze the common cause of epilepsy being drug resistant and also to identify the most frequently affected brain regions with the most occurring factors from congenital to traumatic cases.

1.3 Results:-As clearly shown in the table , 66.66% of cases have developed from focal to bilateral tonic clonic , apart from it we have 16.67 % of the cases with focal and the rest 16.67% with bilateral tonic-clonic from the onset itself.

1.4 Discussion:-MRI findings played a major role in identifying the etiology behind epilepsy. Arachnoid cysts and cystic cerebral arachnoiditis were among the most common findings , they also enhanced a clear correlation with seizure type and clinical presentation.

1.5 Conclusion:-In this study number of patients showed poor response to medical therapy and they required multiple AED's and also surgical intervention in some cases. MRI helps in better treatment and diagnosis. Early MRI evaluation, identification of drug resistance and time management is essential for better treatment and to improve patient outcomes

Keywords:- Drug Resistant Epilepsy, Focal to bilateral tonic-clonic, cystic cerebral arachnoiditis, congenital and structural etiologies.

2. Introduction:-

Epilepsy is the common neurological condition which effects the people of all age. There are around 50 million people suffering with epilepsy in this world. 70% of them live without proper resources for treatment [1] . Epilepsy mainly effects in the form of seizures that occurs without cause. A seizures is odd electrical activity in the brain which causes changes in awareness and it causes temporary loss of consciousness and uncontrolled movements.

There are mainly two types of seizures Generalized seizures and Focal seizures. Generalized seizure occurs in both sides of the brain and causes loss of awareness [2] . In focal seizures it starts in one area of the brain. Half of the people who are suffering from focal seizures caused by any trauma, stroke or meningitis.

This seizures turn into status epilepticus when natural mechanism of brain to stop seizures fail it leads to continuous seizure activity which is greater than 5 minutes. It' physiology is more complex because it involves synaptic and extra-synaptic mechanism [3] .

Around 30% of epilepsy patients affected by this condition. These patients continuously suffer seizures even after taking two or more AEDs in required amount. Drug resistance epilepsy is linked with reduction in quality of life, high medical care and its cost and sudden death [4].

The patients are treated with first line medications (anti-epileptic) drugs were patients responds good to them. But there are more number of patients who continues to experience seizures even after medication. This patients are classified into certain category known as drug resistance epilepsy. DRE is defined when there is failure of two or more anti-epileptic drugs [5].

The alternative treatment and diagnosis options are like pre-surgical evaluation includes MRI EEG and neuropsychological testing to identify the epileptogenic zone. Surgical methods include removing effected part of the brain which has 50-90% success ratio or else usage of microsimulation devices. This device helps to reduce seizures frequency example: VNS, RNS and DBS [6].

These data were collected from medical records of the patients and they include age, gender, onset of disease, seizure type, etiology, EEG, MRI, AEDs used, Surgeries/Therapies and outcomes of the treatments. These data were recorded in a standardized form and then reviewed by us for the reliability and accuracy.

There is proper maintained ethics of handling the patient's cases to maintain confidentiality.

3. Materials and methods:-

3.1 Study design :-

This is a retrospective case study that is based on a set of patient information collected from the Neurosurgery department of Samarkand State Medical University. All the cases were recorded from 2020 to 2026.

3.2 Study objective :-

The primary aim of this study was to analyze the clinical progression in the individuals with drug-resistant epilepsy (DRE) from status epileptics, across different age groups , genders and etiologies. The secondary purpose was to analyze the common cause of epilepsy being drug resistant and also to identify the most frequently affected brain regions with the most occurring factors from congenital to traumatic cases.

3.3 Study population :-

The study is a compilation of a total of 15 cases. The inclusion criteria is based on whether the cases are drug resistant, certain type of epilepsy, distinct anti-epileptic drugs prescribed, onset of seizures , etiology of progression from seizures to status epileptics , and major classification of cases on the basis of post-traumatic , congenital and idiopathic for years, further meeting the guidelines to fall under Drug Resistant Epilepsy (DRE) based on

International League Against Epilepsy (ILAE). In contrast , the exclusion measures are based on whether the key information was unavailable or if diagnostic data were incomplete.

3.4 Data collection :-

Derived from these clinical cases the data obtained was based on age , sex , seizure types , their onsets , AEDs usage, underlying causes, diagnostic tests which include Magnetic Resonance Imaging (MRI), Electrocardiogram (ECG), Electroencephalogram (EEG), Multi-slice Computed tomography (MSCT) and Computed tomography (CT scan) , and lab tests . Some additional information collected was hemoglobin levels and common complaints .

Under the categorization of multiple types of epilepsies the most prevalent type was focal , where in many of which coursed to secondary generalization now specified as bilateral tonic-clonic , and minority were focal impaired aware or were symptomatic according to their etiological reasons . These evolutions can be due to various reasons , like many of the onsets are faint but rapidly deteriorate due to overlying conditions seen in brain injuries , or development defects , AURA patterns , and high or mid amplitude hypersynchronous discharges , hence later spread through transmissible cortical areas or through corpus callosum therefore become secondary generalization.

If we explore the pathogenic factors behind the reason for epilepsy , then comes the divisions as structural (encephalomalacia, gliosis), Infectious (encephalitis), developmental or congenital (tuberous sclerosis) and unknown (due to insufficient data) .

The heterogeneity in the disease course enhances the progression of seizures to epilepsy severity , and resistance towards medications, where DRE is recorded as binary outcome, based on lack of sustained seizure freedom even after undergoing a proper set of anti seizure drugs for enough time .

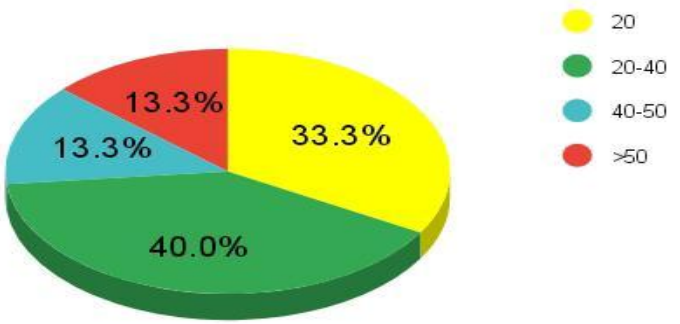
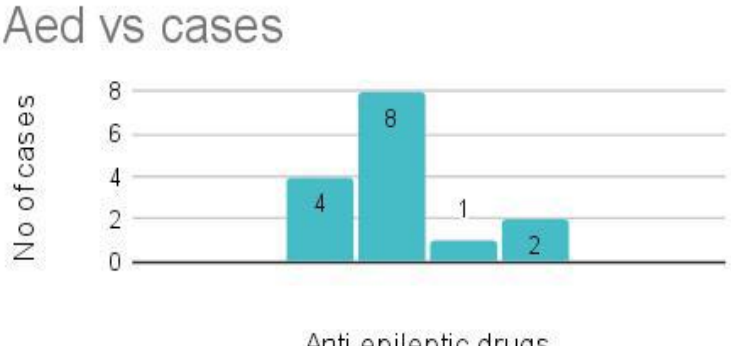


Fig 1.1 Age pie chart.

Fig 1.2 Gender bar graph



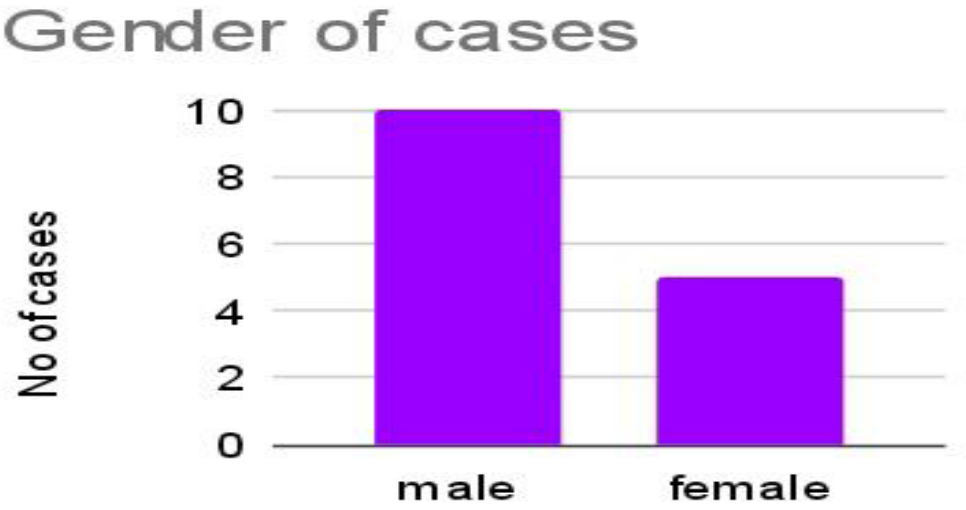


Fig 1.3 Anti-epileptic drugs

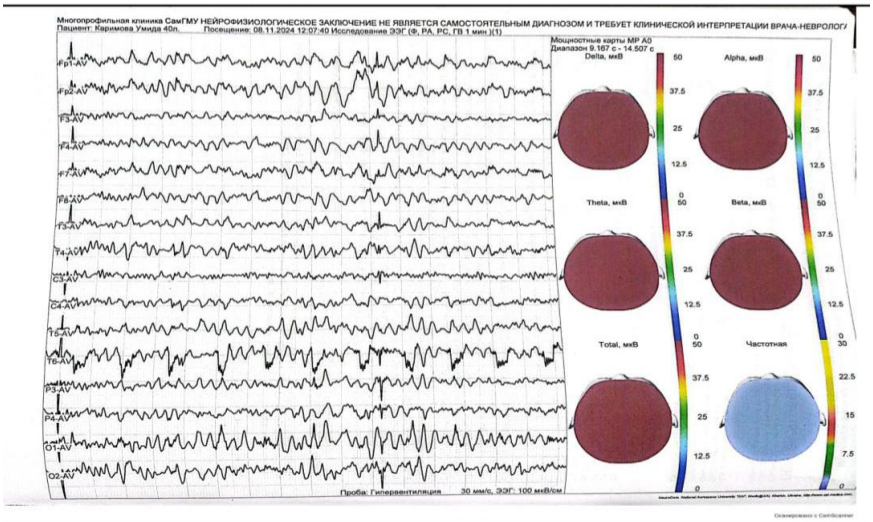


Fig 1.4 EEG report

3.5 Neuroimaging and EEG :-

As required medically, Magnetic Resonance Imaging (MRI), Electroencephalogram (EEG), Multi slice Computed tomography (MSCT) and Computed tomography (CT scan) were used to

diagnose the cause of seizure and defects in around (13/15) 86.6% of all the cases. We also had 13.2% of the cases that received electrocardiogram (ECG) .The major as well as common diagnosis is discussed below.

MRI findings include encephalitis due to multiple focal brain lesions, gliosis focus in left frontal parietal temporal lobe ,discirculatory encephalopathy (DE) with cortical and subcortical changes , lacunar cyst, encephalomalacia, sub atrophic process, Intracranial hypertension (IH) due to increased sub arachnoid space ,arachnoid cyst ,corpus callosum hypoplasia, tuberous sclerosis , perinatal encephalopathy and hydrocephalus. Few had MSCT findings that showed cystic cerebral arachnoiditis and mega cisterna magna. Further, least of them had CT scan showing multi-loculated cyst in left temporal parietal occipital region. EEG has presence of epileptic activity in almost every case and there is mention of diffuse charges with high or mid amplitude hypersynchronous discharges. ECG findings showed echinococcosis of pericardium and another had changes in the anterior wall of myocardium.

3.6 Ethical considerations :-

Personal identifiable information is removed completely to make sure the confidentiality is maintained. Written consents were obtained from the guardians or patients before any surgeries performed.

The studies were approved by the Neurosurgery department of SSMU. The patient's identity is protected by using code alphabets to denote them and not the original names. This article has also focused on bringing forth our ideas on curing the cause of seizure onset, rather than mainly considering treating the seizure completely. There are references also mentioned where we took an idea on how to write the article, so no hint of plagiarism is noticed. There is no clear data on seizure frequency of some patients and hence this is also included. Some data was not completely provided and this is also clearly depicted in the tables and results.

4. Results:-

4.1 Demographics :-

After looking into 15 cases in total, out of which 13 cases were included in study on DRE, 1 had no mention of pharma-co-resistant epilepsy yet was an epileptic case and the other one had only a piece of information regarding the MRI and diagnosis. The age based grouping showed a maximum of young adults and adults ; between ages 10-20 years around 26.67% , from 20-40 years nearly 46.66% , and 40-60 about 26.67%.

The sex stratified group ratio shows 33.33% females over 66.66% males , showing slight male dominance. In fact, it is important to note that gender difference can only change hormonal management towards AEDs , but the core focus is structural lesion or congenital defect seen in individuals.

4.2 Seizure characteristics:-

As clearly shown in the table[1] , 66.66% of cases have developed from focal to bilateral tonic clonic , apart from it we have 16.67 % of the cases with focal and the rest 16.67% with bilateral tonic-clonic from the onset itself.

Regarding the former major cases, the reason lies in their causation like the study of the patient C and E who had encephalomalacia developed from a post traumatic injury , where there is hyper excitability of gliotic border and lacking the inhibitory control , hence allows abnormal firing of signals leading to rapid spread from focal to tonic clonic leading to requirement of high dose AED poly therapy, with progression of worsening symptoms of

aphasia and right sided hemiparesis. Where as in many cases we have noticed cystic cerebral arachnoiditis (due to inflammation)and arachnoid cyst (chronic compression) as a reason for focal being bilateral tonic-clonic, due to structurally abnormal hyper excitable cortex and disrupted inhibitory mechanisms. There is another unique and rare patient H, who has echinococcosis of pericardium and brain, where the cyst in left temporal parietal occipital region acts a chronic lesion inducing gliosis, cortical compressions, hyper excitability allowing the spread far from origin.

And other cases had DE, IH, and DE with focal cortical dysplasia which not only induces seizure but also reduces drug effectiveness.

4.3 Etiology Distribution:-

As per the etiological categorization, there are four groups namely structural, infectious, developmental, post traumatic and unknown . 60% cases like patients with cerebral arachnoiditis, arachnoid cysts, ventriculomegaly, DE, IH , perinatal encephalopathy and diffuse atrophic process are classified under structural. 6.7% cases were classified for infectious due to echinococcosis of brain . 26.67% were grouped to be under developmental or congenital cases that lead to progression of other causes like DE, IH, cerebral arachnoiditis and thinning of corpus callosum, or tuberous sclerosis that were already the factor behind it. 26.67% were post traumatic reports that developed the factors like encephalomalacia, gliosis, arachnoid cyst and cerebral arachnoiditis. The last 6.7% were basically mentioned to be congenital by the patient's guardians though there was no specific proof of diagnostic test, to support it, that is in patient F.

4.4 Diagnostic Findings:-

Magnetic Resonance Imaging (MRI) was conducted on 12 patients (80%). Majority showed dyscirculatory encephalopathy, intracranial hypertension and cerebral arachnoiditis, corpus callosum hypoplasia and hydrocephalus . Computed Tomography (CT scan) and MSCT was available for 5 patients (33.34%) mostly suggestive of mainly showcasing cystic scars and cystic cerebral arachnoiditis, sclerosis of mastoid air cells, multi-loculated cysts and heterogeneous cyst in post section of left frontal lobe .

Electrocardiogram (ECG) was performed on one patient , 6.6% though there was information of findings of ECG in another patient , there was no separate file to validate it. A special factor of low hemoglobin levels was noticed in all the 66.67% cases with only 6.7% had normal and 26.67% had incomplete blood reports.

Patient name	HB levels	Seizure type	Seizure onset	Etiology	DRE	AED	MRI	ECG	Surgery
A	Low	Bilateral Tonic-clonic	Since Childhood	Cerebral arachnoiditis and DE	Yes	Carbamazepine	Lacunar cyst's Vascular encephalopathy Intracranial hypertension	—--	__
B	Low	Focal	Since Childhood	Cystic cerebral arachnoiditis and DE	Yes	Benzonal	__	Changes in anterior wall of myocardium	Endolumbar ozone therapy
C	Low	Focal bilateral tonic-clonic	For 23 years Post trauma	Encephalomalacia and gliosis	Yes	Carbamazepine	Encephalomalacia Gliosis DE	—-	Endolumbar ozone therapy
D	Low	Focal sympto matic to tonic-clonic	For several years	Cystic C.A, diffuse atrophic Process and DE	No	___	Cystic CA Diffuse brain atrophy	—--	Endolumbar ozone therapy
E	_	Focal to bilateral tonic-clonic	Post trauma	Encephalomalacia and gliosis In left frontal lobe	Yes	___	Extensive areas of encephalomalacia and gliosis on right	—--	—-
F	_	Focal	Congenital	___	___	___	__	—--	__
G	Low	Focal to bilateral tonic clonic	Congenital	Congenital Right sided hemispheres is due to left lateral ventriculomegaly	Yes	Valproate Benzonal	Thinning of corpus callosum 2 degree widening of left lateral ventriculomegaly	No abnormality	To treat MRI conditions and DRE
H	Low	Focal to bilateral Tonic clonic	For several years	Cyst in left temporal parietal occipital region Echinococcosis of brain Right side hemiparesis	Yes	Carbamazepine	___	Echinococcosis of pericardium	Re-Trepanation of skull in left parietal temporal region and removal of recurrent echinococcosis

I	Low	Focal impaired aware	Congenital at eight months	Cystic cicatricle degeneration of left temporal lobe CA	Yes	Valproate Carbamazepine	IH	Cardia autonomic dysfunction	Endolumbar ozone therapy
J	Low	Tonic-Clonic	Congenital	DE with focal cortical dysplasia IH	Yes	Carbamazepine	DE IH	_	_
K	Low	Focal to bilateral tonic-clonic	Several years	IH DE Perinatal encephalopathy	Yes	Carbamazepine	Cerebral arachnoiditis	_	Endolumbar ozone therapy
L	Low	Focal Symptomatic	Several years	Post meningoencephalic cerebra arachnoiditis Arachnoid cyst at cerebral poles	Yes	Levetiracetam Carbamazepine	Cystic CA Arachnoid cyst	_	Endolumbar Ozone therapy
M	Normal	Focal	Post trauma for 10years	Cystic -scars-atrophic process Large arachnoid cyst C.A	Yes	Valproate	Large arachnoid cyst in posterior cranial process IH	_	_
N	_	Focal obligate tonic-clonic	Post trauma for 5 years	Perinatal encephalopathy Arachnoid cyst C.A	Yes	Carbamazepine	Ventriculomegaly Arachnoid cyst CA	_	_
O	_	Focal to bilateral tonic-clonic	—	Tuberous sclerosis	—	valporate	Corpus callosum hypoplasia IH	_	_

Table 1. Cases study statistics (CA -cerebral arachnoiditis, DE – discirculatory encephalopathy, IH-intracranial hypertension, and all the dashes denote incomplete or lack of information)

4.6 Treatment Profile:-

The most commonly used Anti epileptic drug in our cases is Carbamazepine (53.34%) which is a tricyclic anticonvulsant works by blocking sodium channels . The second most common is valporate (26.67%) also an anticonvulsant works by GABAergic increase and blocking T-type calcium and sodium channels. 6.67% patients use both these drugs .

Benzobarbitol (13.3%) a barbiturate acts on central nervous system to reduce neuronal excitability is also seen . Levetiracetam (6.7%) seen in patients who also have carbamazepine and adjunctive therapies.

Other treatments pre surgeries , post surgeries, or general medications involve antibiotics like ceftriaxone , Riboxin , potassium chloride , sodium chloride, diclofenac , thiamine , pyridoxines, magnesium sulfates, nootropic drugs for memory improvise, Ascorbic acids, pentocalcinin , heparins, atropine , propofol, diphenhydramine and anesthetics.

5. Discussion:-

This retrospective study included 15 patients with status epileptics associated with brain defects, of total (66.7%) males and females (33.3%). The majority of patients fall under 20–40-year age group (40%), after which above 40 years (26.7%) and those below 20 years (33.3%). Most patients are presented with focal seizures progressed to bilateral tonic-clonic seizures, while a smaller number had isolated focal seizures or tonic-clonic seizures or focal impaired aware. This implies that focal onset seizures with bilateral tonic-clonic was the most common clinical presentation in this study.

Drug-resistant epilepsy (DRE) was observed in nearly all except for one patient. Status Epileptics in particularly among patients with cerebral arachnoid cysts, arachnoiditis, encephalomalacia ,gliosis and diffuse brain atrophy was noticed. Congenital abnormalities such as ventriculomegaly , cortical dysplasia and corpus callosum changes were also observed. In addition, rare causes such as echinococcosis and tuberous sclerosis were noted , showing the diverse spectrum of underlying conditions.

The common complaints or clinical symptoms noticed in these cases include headaches , dizziness, seizures, poor memory , numbness in limbs or extremities, depressed mood, irritability, aphasia, fatigue and hemiparesis.

MRI findings played a major role in identifying the etiology behind epilepsy. Arachnoid cysts and cystic cerebral arachnoiditis were among the most common findings , they also enhanced a clear correlation with seizure type and clinical presentation. High frequency of DRE in this study may be explained by the presence of structural epileptogenic lesions identified on neuroimaging .Electroencephalographic evaluation, where available, supported the diagnosis of seizure disorders and helped in clinical correlation, although imaging findings were more consistently contributory in this study.

To manage the epileptic condition, most patients were treated with antiepileptic drugs. Carbamazepine was the most commonly used AED in this study, with valproate, benzobarbital in Levetiracetam, and combination therapy also involved in treating patients based on their seizure types . Even after the treatments, many patients continued to have seizures, indicating poor seizure control and supporting the diagnosis of DRE.

Poly therapy was frequently required, suggesting inadequate response to monotherapy. This may be due to delayed diagnosis, severity of underlying structural lesions, or chronic progression of epileptogenic changes and ignored or untreated cases. In addition to

Antiepileptic therapy, several patients received supplementary treatments such as nootropic agents and vitamins, endolumbar ozone therapy for better management of symptoms .

Greater proportion of focal seizures progressing to generalized seizures in this study implies about the strong association between structural epilepsy and drug resistance. Patients with congenital abnormalities, traumatic brain injury, and post-infectious squeal often demonstrate poor response to standard AED therapy and may require early surgery.

The ongoing seizure activity even after medical therapy increases the risk of neurological conditions and reduces the quality of life.

Different surgeries were performed in selected patients based on their pathology, like for the management of the cystic lesions and other structural abnormalities. These methods emphasize on the importance of individualized treatment plans in patients with structural epilepsy.

Further the focus shouldn't be just on treating the symptoms but and curing the epilepsy with proper and timely managements.

5. Conclusion:-

This study of 15 patients with epilepsy helps us to find that structural brain abnormalities such as arachnoid cysts, encephalomalacia, congenital malformation and perinatal brain injury became reason for recurrent seizures which is epilepsy and drug resistance epilepsy. Most of the patients presented with focal seizures which progresses to generalized tonic- clonic seizures. Carbamazepine is the most commonly used anti epileptic drug. In this study number of patients showed poor response to medical therapy and they required multiple AED's and also surgical intervention in some cases. MRI helps in better treatment and diagnosis. Early MRI evaluation, identification of drug resistance and time management is essential for better treatment and to improve patient outcomes

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