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A Study To Elucidate The Etiological Profile Of Adult Onset Acute Symptomatic Seizures In Indian Rural Male Population And Compare It With Urban Male Indian Population

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Abstract:
Background*: Men in rural areas presenting with acute symptomatic seizures for the first time compromise a significant component of seizure patients and compared to their urban counterparts, they have a different hierarchy of etiologies and therefore different requirements in terms of evaluation and treatment. A study to elucidate the different etiologies in men of rural areas will not only help the primary care physician to understand the etiologies, differentiate an acute symptomatic seizure from epilepsy, assist in providing appropriate counselling and treatment, but also assist the public health organizations to take appropriate preventive measures.*
Materials and Methods*: A prospective observational cross- sectional study was conducted at Rohilkhand Medical College and Hospital catering to rural population of Bareilly. The first 100 adult men, presenting with new onset symptomatic seizures were recruited.*
Results*: Infective etiology (62%), were most common and neurocysticercosis was commonest, followed by tuberculoma. Alcohol withdrawal was an important cause amongst the miscellaneous causes (18%). Amongst the metabolic causes (11%), hyponatremia was commonest. Cerebrovascular disease (9%) was the least common cause.*
Conclusion:*The etiological hierarchy was different on comparison with studies involving the urban population, where the cerebrovascular disease were the most common single entity responsible, depicting the dominance of lifestyle diseases in urban population leading to cerebrovascular diseases, compared to the poor sanitation and health services of rural population contributing to infections causing acute symptomatic seizures in adult men.*
Key Word*:men, rural India, acute symptomatic seizure (ASS)*

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I. Introduction

As per definition, an epileptic seizure is a transient occurrence of signs and/or symptoms due to an abnormal excessive or synchronous activity in the brain (1). Epilepsy, on the other hand, as per International League against Epilepsy (ILAE), is a disease of the brain which includes a single unprovoked seizure with a high recurrence risk over the next 10 years (at least 60%), therefore epileptic seizures occur in every person with epilepsy, but not everyone who experiences an epileptic seizure suffers from epilepsy (2).

An acute symptomatic seizure (ASS), is described as a seizure that occurs in a close temporal relationship with an acute CNS insult, which may be metabolic, toxic, structural, infectious, or due to inflammation [3,4]. ASS therefore different from unprovoked seizures in many ways. Firstly, unlike in unprovoked seizures, there should always be a clearly identifiable, concomitant acute, causal condition that has occurred close to the time of the seizure. The cause may be an acute disturbance of structural brain such as a brain hemorrhage, or a disturbance of brain function, for example due to alcohol withdrawal. Secondly, ASS usually do not recur once the precipitating factor or condition has been removed or reversed and the functional integrity of the CNS has been restored. This is in contrast to epilepsy where seizures are expected to recur. The absence of a precipitating predisposition, after an acute symptomatic seizure, means epilepsy does not exist. For example, if a patient has two epileptic seizures due to severe hyponatremia, there is no precipitating predisposition once the hyponatremia has resolved. However, the distinction between acute symptomatic seizures and epilepsy is more complicated in persons with acute symptomatic seizures due to destructive brain pathologies, such as stroke or head trauma, because they have an increased risk of developing epilepsy. Thus,

close temporal relationship between a CNS insult and a seizure varies according to the underlying pathology (5). For example, a seizure is considered acute symptomatic if it occurs within the first seven days of a stroke or a traumatic brain injury (2,6).

Seizures that are the manifestation of a neurodegenerative disease, for example Alzheimer's are considered progressive symptomatic seizures. They do not qualify as acute symptomatic seizures as the cause of the seizure is neither transient nor reversible. In such cases, a diagnosis of epilepsy can definitively be made after a second seizure but might be made even after the first seizure, if there is evidence of a recurrence risk greater than 60% and similarly, seizures that arise from most brain tumors are progressive symptomatic seizures (2,5,6).

As far as India is concerned, especially in the rural population, because of lack of knowledge of antiepileptic drugs, poverty, cultural beliefs, stigma, poor health infrastructure, and shortage of trained professionals, there is a large the treatment gap (7) and to further compound the situation, there is a higher prevalence of seizure disorder in rural India (1.9%) compared to urban population (0.6%). Most of the studies conducted in India, are from tertiary care centers in metropolitan cities, catering to urban population (7,8,9,10). There is lack of information concerning the etiological profile of ASS in rural population and we conducted this study with the aim to elucidate the etiology of adult-onset acute symptomatic seizures, that is seizure for the first time, in men more than 18 years of age, in the rural population of India. Understanding the various etiological factors will defiantly assist in taking adequate measures to prevent and thereby decrease the incidence and prevalence of adult-onset acute symptomatic seizures in the men population of our country and be a guiding source for the health authorities and organizations.

II. Material And Methods

This was a prospective observational cross- sectional study conducted in the Medical Emergency department and Medical Intensive Care Unit of Rohilkhand Medical College and Hospital, Bareilly, Utter Pradesh.

Study Design: Prospective observational cross- sectional study

Study Location: Medical Emergency department and Medical Intensive Care Unit of Rohilkhand Medical College and Hospital, Bareilly, Utter Pradesh.

Study DurationAugust 2021 to February 2023
Sample size: 100 patients.

Sample size calculation: The sample size was estimated on the basis of a single proportion design. The target population from which we randomly selected our sample was considered 20,000. We assumed that the confidence interval of 10% and confidencelevel of 95%. The sample size actually obtained for this study was 96 patients, We planned to include 100 patients.

Subjects & selection method: The first 100 men presenting with ASS were included in the study.

Inclusion criteria:
All men more than 18 years of age with no past history of seizures presenting to the medical emergency or in MICU were enrolled in the study

Exclusion criteria:
All the patients who had a history of previous seizure, age less than 18 years, insufficient history for diagnosis of seizures, pseudo- seizures, eclampsia, were excluded from the study.

Procedure methodology

After obtaining approval from the Hospital Ethics Committee and informed consent from all the patients, the first 100 men presenting with ASS, as per the inclusion and exclusion criteria, were enrolled in the study. A detailed history was taken and clinical examination was performed for all the patients. All the patients underwent a routine bio- chemical and hematological profile evaluation, which included complete blood count, liver and renal function tests, blood sugar, electrolytes and EEG. Brain imaging in the form of CT scan was done for all the patients. CSF analysis, X- ray chest PA view, serum anti- cysticercal antibodies, serum anti-tubercular antibodies, CSF and blood culture were done where clinically indicated.

Statistical analysis
Data was analyzed using SPSS version 20 (SPSS Inc., Chicago, IL).

III. Result

Table 1: Demographic data of patients with Acute symptomatic seizures

Age in years	Number of cases	Percentage
>18 <20	5	5
21-30	23	23
31-40	32	32
41-50	19	19
51-60	16	16
61-70	4	4
>71	1	1
Total	100	100

Seizures occurred most commonly in the age group of 31 to 40 years (32%), followed by 21 to 30 years (23%).

Table 2: Type of Seizure

Type of Seizure	Number of Patients	Percentage
Primary Generalized	67	67
Simple Partial	22	22
Complex Partial	4	4
Simple Partial with secondary generalization	7	7

The most common type of seizure observed was primary generalized seizure (67%) followed by simple partial seizures (22%)

Table 3: Etiology of Seizure

Etiology	Number of Patients	Percentage
INFECTIVE CAUSES	62	62
CEREBROVASCULAR DISEASE	9	9
METABOLIC DISORDERS	11	11
MISCELLANEOUS CAUSES	18	18
Total	100	100

Infective etiology was the most common cause of seizures (62%).

Table 4: Infective etiologies

Etiology	Number of Patients	Percentage (n= 62)
INFECTIVE CAUSES	62	
Neurocysticercosis	29	46.78
Tuberculoma	16	25.81
Viral Meningoencephalitis	12	19.36
Bacterial Meningoencephalitis	3	4.83
Cerebral Malaria	2	3.22

Amongst the infective causes, neurocysticercosis was the most common cause (46.78%).

Table 5: Cerebrovascular Diseases

Etiology	Number of Patients	Percentage (n= 9)
CEREBROVASCULAR DISEASE	9	
Arterial Infarct	6	66.67
Intracerebral Hemorrhage	2	22.22
Cerebral Venous Sinus Thrombosis	1	11.11

Arterial infarcts were the most common cerebrovascular causes of acute symptomatic seizures (66.67%).

Table 6: Metabolic Disorders

Etiology	Number of Patients	Percentage (n= 11)
METABOLIC DISORDERS	11	
Uremic encephalitis	2	18.18
Hyponatremia	5	45.45
Hypocalcemia	1	9.09
Hypoglycemia	3	27.27

Hyponatremia was the most common metabolic cause of acute symptomatic seizures (45.45%)

Table 7: Miscellaneous Causes

Etiology	Number of Patients	Percentage (n= 18)
MISCELLANEOUS CAUSES	18	
Tumor	2	11.11
Alcohol withdrawal	12	66.67
Poisoning (Organophosphorus poisoning)	4	22.22

Amongst the miscellaneous causes alcohol withdrawal was the most common cause (66.67%)

Table 8 : Etiology of seizures in relation to Age of the patients

Etiology	Age < 40 years	> 40 to 60 years	> 60 years	Total
	N=60	N=29	N=11	100
INFECTIVE CAUSES	48	13	1	62
Neurocysticercosis	21	8	0	29
Tuberculoma	14	2	0	16
Viral Meningoencephalitis	10	1	1	12
Bacterial Meningoencephalitis	2	1	0	3
Cerebral Malaria	1	1	0	2
CEREBROVASCULAR DISEASE	1	2	6	9
Arterial Infarct	0	1	5	6
Intracerebral Hemorrhage	1	0	1	2
Cerebral Venous Sinus Thrombosis	0	1	0	1
METABOLIC DISORDERS	1	6	3	11
Uremic encephalitis	0	1	1	2
Hyponatremia	1	3	1	5
Hypocalcemia	0	1	0	1
Hypoglycemia	0	2	1	3
MISCELLANEOUS CAUSES	10	7	1	18
Tumor	0	1	1	2
Alcohol withdrawal	8	4	0	12
Poisoning (Organophosphorus poisoning)	2	2	0	4

In the age group of less than 40 years, infective causes were the most common, followed by alcohol withdrawal (miscellaneous causes). In the age group of 41 to 60 years, infective causes were the most common, followed by metabolic disorders. In the age group of more than 60 years cerebrovascular causes were the most common, followed by metabolic causes.

Table 9: Type of Seizure and its relation to etiology

Type of Seizure	INFECTIVE CAUSES (N=62)	CEREBROVASCULAR DISEASE (N=9)	METABOLIC DISORDERS (N=11)	MISCELLANEOUS CAUSES (N=18)
Primary Generalized (N=67)	36	5	10	16
Simple Partial (n=22)	19	2	0	1
Complex Partial (N=4)	2	1	1	0
Simple Partial with secondary generalization (N=7)	5	1	0	1

Amongst all the causes, primary generalized seizure was the most common type of acute symptomatic seizure.

IV. Discussion

Acute onset seizures in adults, in semi-rural India have a very significant clinical and social importance as they are usually linked to an underlying medical condition which could be treatable. Elucidating the etiology, treating the underlying medical condition and then taking preventive measures to control the factors responsible for propagating the causative factor are very important for the primary care physician. Unfortunately, in our country, lot of primary care physicians are not comfortable managing these cases and refer the patients to tertiary care centers for further evaluation and management by a neurophysician. This results in not only overcrowding at the tertiary care centers, but also results in increased financial burden on the patient and their families. Understanding the etiology will assist them to make evidence-based decisions and will not only assist them in evaluating and treating the patients in a better manner, but also will help in guiding the community to take adequate measures to prevent the seizures.

Etiology

In our study the most common etiology was neuroinfections (62%) and amongst it was neurocysticercosis (46.78%), followed by tuberculoma (25.81%), followed by miscellaneous causes (18%), amongst which alcohol withdrawal was the most common cause, followed by metabolic causes (11%) and then by cerebrovascular disease (9%).

Table Number 10: Comparison of etiologies of acute symptomatic seizures

Etiology	Our Study Rural		Vemulapalli*et al* (Bangalore) Urban		Bhatia *et al* (Chandigarh) Urban		Ashwin *et al* (Pondicherry) Urban	
	N=100	%	N=138	%	N=90	%	N=100	%
Infections	62	62	37	26.8%	36	40	17	17
CVA	9	9	45	32.6%	40	43.4	21	21
Metabolic	11	11	18	13%	11	13.3	15	15
Alcohol Withdrawal	12	12	15	10.9%	0	0	5	5
Tumours	2	2	6	4.3%	3	3.3	6	6
Poisoning	4	4	0	0	0	0	1	1

In the study by Vemulapalli*et al* (8), from Bangalore (South India), involving urban population, the most common cause of ASS in their study was cerebrovascular diseases (32.6%), followed by neuroinfections(26.2%). Among the neuroinfections, neurocysticercosis was the most common cause (14.5%), followed by neurotuberculosis (tuberculoma 7.2%, tuberculous meningoencephalitis 1.5%). Bhatia *et al* (9), from Chandigarh (North India), in their study, stroke was the most common cause (40%), followed by infections. Amongst the infective etiologies, tubercular meningitis followed by viral meningoencephalitis were the most common causes overall, with not a single case of neurocysticercoses and no cases of alcohol withdrawal in their study. Ashwin *et al* (10) in their study from a tertiary care center (Pondicherry) reported that the most common cause of seizure was stroke followed by infection followed by metabolic cause. Stroke was leading cause of seizures (21%). Infection was next leading cause of seizures (17%), followed by metabolic cause (15%). They also reported alcohol withdrawal as a cause in 5% of cases and brain tumors in 6%. The study by Bhatia *et al* , which also happens to be from North India , as our study, and Ashwin *et al* , there is a marked difference in the etiological profile which can be explained by the fact that firstly there study population involves urban population, where because of adequate hygiene and sanitary conditions and health measures taken by the community, the factors responsible for propagating the infective etiologies such as neurocysticercosis and tuberculosis have been restrained, also probably because of education and social awareness, there were no or very few cases of alcohol withdrawal.

Table Number 11: Comparison of type of Seizures

Type Of Seizure	Our Study (Bareilly) Rural		Vemulapalli*et al* (Bangalore) Urban		Bhatia *et al* (Chandigarh) Urban		Ashwin *et al* (Pondicherry) Urban	
	N=100	%	N=138	%	N=90	%	N=100	%
Primary Generalized	67	67	97	70.2%	89	98.9%	57	57
Simple Partial	22	22	14	10.1%	0	0	30	30
Complex Partial	4	4	0	0	1	1.1%	4	4
Simple Partial with secondary generalization	7	7	22	15.9%	0	0	9	9

In our study the most common presentation was of generalized tonic- clonic seizures (67%) followed by simple partial seizures (22%) and least common presentation was of complex partial seizures. This can be explained by the etiological factors manifesting as acute symptomatic seizures. In the study by Bhatia *et al*(8), generalized tonic-clonic seizure was also the most common presentation (98.9%), followed by complex partial seizures(1.1%).

In all the study by Vemulapalli*et al* (8), Bhatia *et al* and Ashwin *et al*, generalized tonic-clonic seizure was the most common presentation of acute symptomatic seizures. There were differences in the number of cases presenting with simple partial seizure, complex partial seizure and simple partial with secondary generalization due to differences in the etiological profiles.

V. Conclusion

It is pertinent to understand that the incidence and etiological profile of ASS are different for rural population and urban population and in addition to the geographical distribution of the population under study, urbanization, bringing along with it the changes in education, standard of living, health and hygiene play an important role in determining the hierarchy of the etiological factors, as highlighted in our study. It is indeed saddening that still, infective etiologies are the most common cause of ASS in rural population, compared to cerebrovascular accidents in the urban population. It is the need of the hour that proper steps should be taken to understand and implement appropriate community health measures to eliminate these infective etiologies and also thereby assist the primary care physician to serve the community in a more effective manner.

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