Original Article　　　　　　　　　　　　　　　　　　　　　**www.wjahr.com**

LATE ONSET EPILEPSY

Rhadwan Hammadi Thanon*

Specialist of Neurology, Al Salam Hospital, Department of Medicine, Neurology unit, Mosul, Iraq.

*Corresponding Author: Rhadwan Hammadi Thanon

Specialist of Neurology, Al Salam Hospital, Department of Medicine, Neurology unit, Mosul, Iraq.

ABSTRACT

Background: Epilepsy with late onset (LOE) is becoming a more widespread global public health concern. Aging itself carries the risk of neurological diseases that can cause epilepsy and significant cognitive impairment such as acute focused damage. the clinical setting, clinical and instrumental examinations are performed on patients who have LOE, which in most cases leads to the identification of the disease's origin. **Objective:** To obtain an easy and effective tool supporting the routine activity of the clinicians facing LOE. **Methods:** A hospital-based cross-sectional study. It was from the period of January to June in the year 2024. The study is conducted at Al Salam Teaching hospital. The questionnaire, is comprised of three sections. The First section for sociodemographic information, the second section for epilepsy types and clinical manifestations. The third section for EEG and CT-scan findings. **Results:** The study included 200 participants, 103 (51.5%) were males and 97 (48.5%) were females, with male : female ratio of 1.06:1. Late onset epilepsy are more prevalent among the age group of 25 to less than 35 years while males are more likely to be affected among the age group of 45 to less than 55 years, among different etiologies, brain tumor is prevalent among 77 (38.5%), cerebrovascular accident among 46 (23%), idiopathic among 39 (19.5%), miscellaneous cerebral lesion among 14 (7%), trauma among 13 (6.5%), brain abscess among 7 (3.5%) and alcohol among 4 (2%). Moreover; the study shows males have more cerebrovascular etiology (30 males versus 16 females) and more alcohol (all are males) while females have more brain tumor (45 females versus 32 males) and among the group of idiopathic etiology (23 females versus 16 males). The study shows that generalized seizure is more prevalent among idiopathic etiology group (64.1%), while partial simple seizure without secondary generalization is more prevalent among CVA (32.6%) but partial simple seizure with secondary generalization is more prevalent among brain tumor patients (41.5%). **Conclusion:** Brain tumor and CVA are the commonest cause of LOE. EEG and CT-scan sometimes are useful in diagnosis of LOE, prospective future studies are needed to confirm the exact etiology of LOE and it contributing factors.

KEYWORDS: Late onset epilepsy, Mosul, Iraq.

1- INTRODUCTION

Epilepsy with late onset (LOE) is becoming a more widespread global public health concern.[1] Notably, LOE differs from those who acquire epilepsy at an earlier age in several ways, indicating that it is a distinct entity.[2] The fact that epilepsy is the third most frequent neurological disease in older persons after dementia and stroke highlights the inadequacy of current prevention efforts, which could have serious ramifications for health systems.[3] The brain's propensity to develop epilepsy increases with age for a number of reasons, such as decreased cerebral perfusion, a decrease in the lymphatic system's ability to eliminate waste, neurodegenerative changes, and the release of pro-inflammatory factors by senescent cells.[4-6] These factors can exacerbate a variety of age-related pathologies, such as immune system suppression and altered astrocytic function. It is also

necessary to take into account a higher genetic risk of stroke and cardiovascular diseases.[7]

Patients with late-onset epilepsies (LOE) and those who are aging with epilepsy pose a challenge to the management of epilepsy in an aging society. Aging itself carries the risk of neurological diseases that can cause epilepsy and significant cognitive impairment such as acute focused damage (for example stroke or slowly increasing degenerative damage).[8-10] Studies about LOE is concluded that cognitive deficits exist from the moment epilepsy manifests itself, even before treatment ever begins.[11] In fact, seizures and cognitive deficits may serve as early warning signs of illnesses that cause mental deterioration.[12] Cognitive and behavioral issues are frequently associated with epilepsy, a condition marked by frequent, unprovoked seizures.[13] In addition

to the underlying causes and therapeutic considerations, the degree and kind of these impairments are determined by the epileptic dysfunction, or the brain disturbance manifested by epileptic activity. As a result, neuropsychological diagnosis is crucial for managing quality and outcomes, monitoring the progression of the illness and its treatment, and making differential diagnoses.[14-15]

In the clinical setting, clinical and instrumental examinations are performed on patients who have LOE, which in most cases leads to the identification of the disease's origin. Specifically, the majority of patients' phenotype can be adequately defined through medical histories, neuroradiological exams, electroencephalography (EEG), and hematochemical testing. But for a subgroup, these first assessments are insufficient, and additional extensive study is required to increase the diagnostic precision. Applying this second-level strategy should be logically specific on a case-by-case basis, taking the patient's particular orientation into consideration. Furthermore, in a variable percentage of patients, the causes of the disease remain unknown even after thorough phenotypic characterization.[16]

The aim of this study is to obtain an easy and effective tool supporting the routine activity of the clinicians facing LOE.

2-　PATIENT AND METHODS
This is a hospital-based cross-sectional study. This study was conducted in Mosul city, Iraq, from the period of January to June in the year 2024. A total of 200 study participants were included in the study. The study was conducted in the left bank of Mosul. Inclusion criteria include Iraqi national, age $\geq$ 25 years, which were admitted to in patient department. In contrast, exclusion criteria include non-Iraqi, age <25 years, individuals who are unwilling to participate in the study. Data were collected using structured, self-administered questionnaire, which comprised of five sections. The First section includes patient age, age at onset. The second section for details of epileptic attacks: either generalized or focal fit, presence and absence of aura and loss of consciousness, the third section for the neurological examination findings. Section four for CT-scan and Electroencephalography findings, lastly section five for Blood investigation results which are includes fasting blood suger, serum calcium, serum electrolytes, complete blood picture, blood urea, serum creatinine to exclude metabolic causes of epilepsy. SPSS (Statistical Package for the Social Sciences) version 30 was used to examine the data. The questionnaire information was kept confidential and did not include any information that might be used to identify a specific individual.

3- RESULTS
The study included 200 participants, 103 (51.5%) were males and 97 (48.5%) were females, with male : female ratio of 1.06:1. As shown in figure 1.
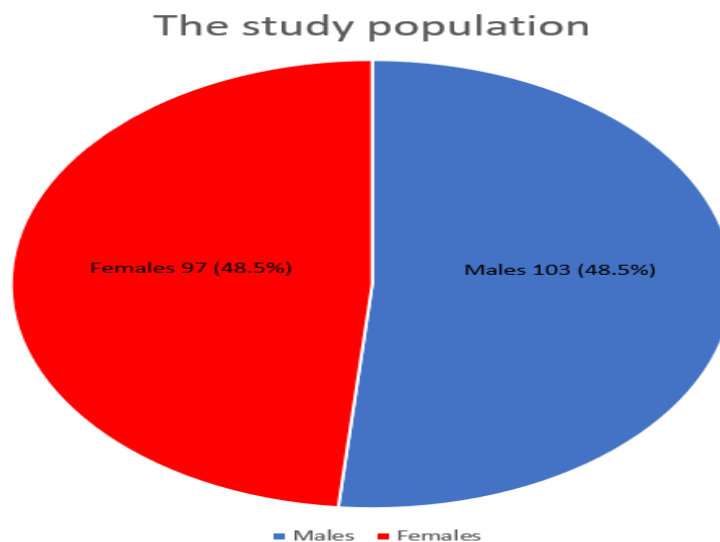

Figure 1: The study population.

Table 1 shows distribution of study population according to their ages, it's evident that the age group of 25 to less than 35 years having 33 (16.5%) females and 30 (15%) males, while the group age of 35 to less than 45 years included 29 (14.5%) females and 25 (12.5%) males.

Moreover; the group age of 45 to less than 55 years included 23 (11.5%) females and 31 (15.5%) males and lastly the group age of more than 55 included 12 (6%) females and 17 (8.5%) males.

Table 1: Distribution of study population according to their ages.

Ages	Female		Male		Total	
25-less than 35	33	16.5	30	15	63	31.5
35 - less than 45	29	14.5	25	12.5	54	27
45 – less than 55	23	11.5	31	15.5	54	27
More than 55	12	6	17	8.5	29	14.5

Figure 2 shows distribution of study population according to their etiology, the study is divided into 7 groups; brain tumor 77 (38.5%), cerebrovascular accident 46 (23%), idiopathic 39 (19.5%), miscellaneous cerebral lesion 14 (7%), trauma 13 (6.5%), brain abscess 7 (3.5%) and alcohol 4 (2%). Moreover; the study shows males have more cerebrovascular etiology (30 males versus 16 females) and more alcohol (all are males) while females have more brain tumor (45 females versus 32 males) and among the group of idiopathic etiology (23 females versus 16 males).

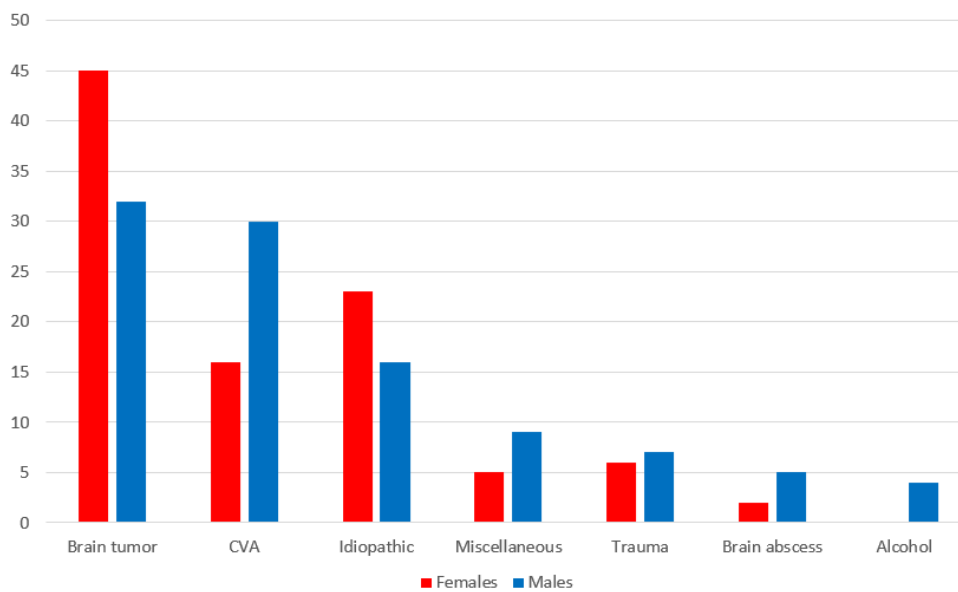Distribution of study population according to their etiology

Table 2 shows the distribution of seizure types according to different etiology, it's evident that generalized seizure is more prevalent among idiopathic etiology group (64.1%), while partial simple seizure without secondary generalization is more prevalent among CVA (32.6%) but partial simple seizure with secondary generalization is more prevalent among brain tumor patients (41.5%). Moreover; partial complex seizure without and with secondary generalization is more prevalent among head trauma patient (23% and 30.7%) respectively. From the other hand; different etiology presented more commonly with different type of seizures as the following: brain tumor and brain abscess presented more commonly with partial simple seizure with secondary generalization, CVA with simple seizure without secondary generalization, idiopathic, miscellaneous trauma and alcohol with generalized seizure.

Table 2: Distribution of seizure types among patients with late onset epilepsy.

Etiology	No.	Generalized	Partial simple seizure		Partial complex seizure	
			Without secondary generaliza-tion	With secondary generaliza-tion	Without secondary generaliza-tion	With secondary generalization
Brain tumor	77	11	17	32	8	9
CVA	46	10	15	9	4	8
Idiopathic	39	25	3	4	3	4
Miscellaneous	14	7	1	2	2	2
Trauma	13	3	1	2	3	4
Brain Abscess	7	2	1	3	---	1
Alcohol	4	4	---	---	---	---
Total	200	62	38	52	20	28

Table 3 illustrates distribution of study population according to EEG abnormalities, according to the most common findings; brain tumor, CVA, trauma and brain abscess patients are linked with focal slowing EEG findings, idiopathic with Diffuse slowing, miscellaneous with diffuse and focal slowing EEG findings, lastly alcohol was linked with normal EEG findings.

Table 3: Distribution of study population according to EEG findings.

Etiology	No.	Diffuse slowing	Focal slowing	Focal spike	Bilateral spike	Normal
Brain tumor	77	4	49	12	2	10
CVA	46	5	29	3	2	7
Idiopathic	39	18	8	3	---	10
Miscellaneous	14	4	4	---	---	6
Trauma	13	---	5	1	---	7
Brain Abscess	7	---	5	1	---	1
Alcohol	4	---	---	---	---	4

Table 4 shows CT-scan findings; from focal, atrophy and normal CT-scan findings, all cases of brain tumor, CVA and brain abscess had focal CT insult versus half of the patient of miscellaneous etiology have it. Moreover, idiopathic cases have mostly atrophy in CT-scanning. Trauma patients had different CT-scan results while all of alcohol patients have normal results.

Table 4: Distribution of study population according to CT-scan findings.

Etiology	No.	Focal CT	Atrophy	Normal
Brain tumor	77	77	---	---
CVA	46	46	---	---
Idiopathic	39	---	17	---
Miscellaneous	14	7	2	5
Trauma	13	5	4	4
Brain Abscess	7	7	---	---
Alcohol	4	---	---	4

4- DISCUSSION

The study explores late onset epilepsy among both gender groups with little bit male predominance, which is consistent with Elena Tartara et al study findings.[17] Moreover; the study shows that females with late onset epilepsy are more prevalent among the age group of 25 to less than 35 years while males are more likely to be affected among the age group of 45 to less than 55 years, however; these results are depended on inpatient department admission rate. Kaur et al had comparable results Tao Shan et al had a global study about the epilepsy burden showing that the global prevalence of epilepsy was increase with age.[18] Brain tumor and CVA are shown to be the commonest cause of late onset epilepsy which is runs with Heidrun Potschka et al findings.[19]

Regarding epilepsy types, table 6 shows each type of epilepsy with its most common related etiology with comparable studies' findings.

Table 5: Types of epilepsy and its most common related etiology.

Type of Epilepsy	Etiological groups	Comparable findings
Generalized seizure	Idiopathic etiology group	Emanuele Cerulli Irelli.[20]
Partial simple seizure without secondary generalization	CVA	Suzy Davenport.[21]
Partial simple seizure with secondary generalization	Brain tumor	Özdem Ertürk Çetin.[22]
Partial complex seizure with and without secondary generalization	Head trauma	Hassan Reza Mohammadi.[23]

The study shows EEG finding with different causes of late onset epilepsy, brain tumor, CVA, head trauma and brain abscess patients are linked most probably with focal slowing EEG findings, idiopathic epilepsy is linked frequently with diffuse slowing, while miscellaneous epilepsy is linked with both diffuse and focal slowing EEG findings, lastly alcohol was linked with normal EEG findings. Comparable studies are shown in table 7.

Table 6: Types of epilepsy and its most likely EEG findings.

Etiology	EEG findings	Comparable study
Brain tumor	focal slowing EEG findings	Cansu Ayvacioglu Cagan.[24]
CVA	focal slowing EEG findings	Maenia Scarpino.[25]
Idiopathic	Diffuse slowing	Emanuele Cerulli Irelli.[26]
Miscellaneous	diffuse and focal slowing EEG findings	Meritam Larsen Pirgit.[27]

Trauma	focal slowing EEG findings	Cheng-Che Chou.[28]
Brain Abscess	focal slowing EEG findings	Chiara Davassi.[29]
Alcohol	Normal	Palaniappan R.[30]

Lastly; the study shows the role of CT-scan in diagnosis of LOE. 100% of the study participants with brain tumor and CVA had focal CT-scan findings, while no patient with alcohol etiology had Ct-scan results, moreover the other groups had variable results between focal, atrophied and normal results, which is parallel to D., Itanyi Ukamaka et al findings.[31]

The study has limitations as this is hospital based (single-center), observational study with limited sample in resource-poor setting.

CONCLUSION AND RECOMMENDATION
Patients with LOE, are of heterogenous etiologies, however; brain tumor and CVA are the commonest ones. EEG and CT-scan sometimes are useful in diagnosis of LOE, prospective future studies are needed to confirm the exact etiology of LOE and it contributing factors.

REFERENCES
1. Punia V, Bhansali S, Tsai C. Late-onset epilepsy clinic: From clinical diagnostics to biomarkers. Seizure: European Journal of Epilepsy, 2024 Jun 26.
2. Balestrini S, Arzimanoglou A, Blümcke I, Scheffer IE, Wiebe S, Zelano J, Walker MC. The aetiologies of epilepsy. Epileptic Disorders, 2021 Feb; 23(1): 1-6.
3. Huang Y, Li Y, Pan H, Han L. Global, regional, and national burden of neurological disorders in 204 countries and territories worldwide. Journal of global health, 2023; 13.
4. Sazgar M, Young MG, Sazgar M, Young MG. Seizures and epilepsy. Absolute epilepsy and EEG rotation review: essentials for trainees, 2019; 9-46.
5. Phan J, Ramos M, Soares T, Parmar MS. Poststroke seizure and epilepsy: a review of incidence, risk factors, diagnosis, pathophysiology, and pharmacological therapies. Oxidative medicine and cellular longevity, 2022; 2022(1): 7692215.
6. Baruah J, Vasudevan A, Köhling R. Vascular integrity and signaling determining brain development, network excitability, and epileptogenesis. Frontiers in physiology, 2020 Jan 22; 10: 1583.
7. Vicente M, Addo-Osafo K, Vossel K. Latest advances in mechanisms of epileptic activity in Alzheimer's disease and dementia with Lewy Bodies. Frontiers in neurology, 2024 Feb 8; 15: 1277613.
8. Torzillo E, Sen A, Schachter SC. Epilepsy in older people. Comorbidities and Social Complications of Epilepsy and Seizures: The cognitive, psychological and psychosocial impact of epilepsy. 2024 Aug 7: 189.
9. Stefan H, Michelson G. Late Onset Epilepsy and Stroke: Diagnosis, Pathogenesis and Prevention. Seizure: European Journal of Epilepsy. 2024 Jun 12.
10. Helmstaedter C, Tailby C, Witt JA. Neuropsychology of late-onset epilepsies. Seizure: European Journal of Epilepsy. 2024 Mar 26.
11. GABRIEL M, OLLEY B. PSYCHOSOCIAL AND SEIZURE-RELATED FACTORS AS PREDICTORS OF COGNITIVE FUNCTIONING CHANGES AMONG NEWLY CLINICALLY DIAGNOSED CHILDREN AND ADOLESCENTS WITH SEIZURE DISORDER IN LAGOS, NIGERIA. AFRICAN JOURNAL FOR THE PSYCHOLOGICAL STUDIES OF SOCIAL ISSUES, 2024 Sep 10; 27(3).
12. Horvath AA, Csernus EA, Lality S, Kaminski RM, Kamondi A. Inhibiting epileptiform activity in cognitive disorders: possibilities for a novel therapeutic approach. Frontiers in Neuroscience, 2020 Oct 15; 14: 557416.
13. Sazgar M, Young MG, Sazgar M, Young MG. Seizures and epilepsy. Absolute epilepsy and EEG rotation review: essentials for trainees, 2019; 9-46.
14. Anwar H, Khan QU, Nadeem N, Pervaiz I, Ali M, Cheema FF. Epileptic seizures. Discoveries, 2020 Apr; 8(2).
15. Scheffer IE, Zuberi S, Mefford HC, Guerrini R, McTague A. Developmental and epileptic encephalopathies. Nature Reviews Disease Primers, 2024 Sep 5; 10(1): 61.
16. DiFrancesco JC, Labate A, Romoli M, Chipi E, Salvadori N, Galimberti CA, Perani D, Ferrarese C, Costa C. Clinical and instrumental characterization of patients with late-onset epilepsy. Frontiers in Neurology, 2022 Feb 25; 13: 851897.
17. Tartara E, Micalizzi E, Scanziani S, Ballante E, Paoletti M, Galimberti CA. Late-onset focal epilepsy: electroclinical features and prognostic role of leukoaraiosis. Frontiers in Neurology, 2022 Feb 23; 13: 828493.
18. Kaur S, Garg R, Aggarwal S, Chawla SP, Pal R. Adult onset seizures: Clinical, etiological, and radiological profile. Journal of family medicine and primary care, 2018 Jan 1; 7(1): 191-7.
19. Potschka H. The aging brain and late onset drug-refractory epilepsies. Seizure: European Journal of Epilepsy. 2024 Aug 28.
20. Irelli EC, Orlando B, Salamone EM, Fisco G, Barone FA, Morano A, Fanella M, Fattouch J, Manfredi M, Giallonardo AT, Di Bonaventura C. High rates of early remission pattern in adult-onset compared with earlier-onset idiopathic generalized epilepsy: A long-term follow-up study. Seizure, 2022 Jan 1; 94: 52-6.
21. Suzy Davenport, Seizure after stroke: What to know, MedicalNewToday, October 28 2022.

22. Çetin ÖE, İşler C, Uzan M, Özkara Ç. Epilepsy-related brain tumors. Seizure, 2017 Jan 1; 44: 93-7.

23. Mohammadi HR, Hatefi M, Rahmatian A, Sadeghi S. Risk Factors for Post-traumatic Epilepsy in Patients with Traumatic Brain Injuries. Archives of Neuroscience, 2024 Jan 31; 11(1).

24. Ayvacioglu Cagan C, Demirel Ozbek E, Dericioglu N. Spectrum of EEG findings in patients with leptomeningeal carcinomatosis and seizures: correlation with neurodiagnostic results and outcome. Clinical EEG and Neuroscience, 2023 Sep; 54(5): 549-55.

25. Scarpino M, Grippo A, Campagnini S, Hakiki B, Maiorelli A, Sodero A, Guolo E, Mannini A, Macchi C, Cecchi F. Stroke-related epilepsy in the rehabilitation setting: Insights from the inpatient post-stroke rehabilitation study–RIPS. Epilepsy & Behavior Reports, 2024 Sep 23: 100713.

26. Cerulli Irelli E, Leodori G, Morano A, Di Bonaventura C. Eeg markers of treatment resistance in idiopathic generalized epilepsy: From standard eeg findings to advanced signal analysis. Biomedicines, 2022 Sep 28; 10(10): 2428.

27. Pirgit ML, Beniczky S. EEG and semiology in the elderly: A systematic review. Seizure-European Journal of Epilepsy.

28. Chou CC, Hou JY, Chou IJ, Lan SY, Kong SS, Huang MH, Weng YC, Lin YY, Kuo CY, Hsieh MY, Chou ML. Electroencephalogram pattern predicting neurological outcomes of children with seizures secondary to abusive head trauma. Pediatrics & Neonatology, 2024 May 1; 65(3): 249-54.

29. Davassi C, Pulitano P, Mecarelli O. Cerebral Infectious Diseases. Clinical Electroencephalography, 2019; 647-60.

30. Palaniappan R., Raveerndran P., Omatu S.: 'VEP optimal channel selection using genetic algorithm for neural network classification of alcoholics', IEEE Trans. Neural Netw., 2002; 13(2): 486 –491. (doi: https://doi.org/10.1109/72.991435).

31. Aiyekomogbon JO. Value of computed tomography scan in evaluation of adult onset seizures in north-central Nigeria. Sub-Saharan African Journal of Medicine, 2018 Oct 1; 5(4): 111-6.