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Post-traumatic Epilepsy, 33 Years Following Traumatic Brain Injury: Iraq vs. Iran War

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ABSTRACT

Aims Post-traumatic epilepsy is one of the most common and disabling sequels of traumatic brain injury and is defined as repeated unprovoked seizures seven days after traumatic brain injury. The present study aimed to determine the late consequences of epilepsy in veterans with traumatic brain injury during the imposed Iran-Iraq war.

Instruments & Methods This study was observational cohort research in 2022. The sample of the study included all living veterans with a history of Post-traumatic epilepsy who were covered by the services of the "Veterans Affairs Foundation" of Isfahan, Iran. 218 veterans with epilepsy, who were available, were identified, 100 of them had a traumatic brain injury, and 118 did not have any traumatic brain injury. Data were collected using the Mini Mental State Examination (MMSE) and Instrumental Activities of Daily Living and Physical Self-Maintenance Scale (IADL-PSMS).

Findings There was a significant difference between veterans with and without traumatic brain injuries in the age at post-traumatic epilepsy debut ($p<0.05$). Epilepsy characteristics were not significantly different between the two groups ($p>0.05$). The mean score of MMSE in veterans with and without traumatic brain injuries was significantly different ($p<0.05$). The Recall and Registration subscales were significantly different in veterans with/without traumatic brain injuries ($p<0.05$).

Conclusion The ability to perform daily activities and cognitive function are lower in veterans with epilepsy with traumatic brain injuries compared to veterans with epilepsy without traumatic brain injuries.

Keywords Post-Traumatic Epilepsy; Traumatic Brain Injury; War; Veteran; Mini Mental State Examination; Activities of Daily Living

CITATION LINKS

[1] Recent developments in ... [2] Efficacy of levetiracetam ... [3] Epilepsy after ... [4] Quality and value ... [5] A public health perspective ... [6] Veteran and military ... [7] PTSD in U.S. veterans ... [8] Psychiatric disorders ... [9] Comparing the army's ... [10] Returning home from ... [11] Multiplex PCR ... [12] Neuroimaging of traumatic ... [13] Prevention of traumatic ... [14] Traumatic ... [15] Community-level ... [16] Modelling traumatic ... [17] A review of seizures ... [18] Post-traumatic ... [19] Prevalence and incidence ... [20] Prevalence of epilepsy ... [21] Characteristics of veterans ... [22] Sepsis and ... [23] Epilepsy related to ... [24] Health-related quality ... [25] The impact of ... [26] The military injuries ... [27] Post-traumatic epilepsy ... [28] Patterns of reduced ...

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Introduction

Epilepsy is a clinical phenomenon diagnosed by the occurrence of two or more unprovoked seizures [1]. It was reported that there were 45.9 million patients with active epilepsy (idiopathic and secondary epilepsy with an age-standardized prevalence of 621.5 per 100,000 people in the world) in 2016 [2].

Post-Traumatic Epilepsy (PTE) is a type of epilepsy that develops after Traumatic Brain Injury (TBI), which includes 5% of all epilepsies [3]. Most researchers agree that PTE should be differentiated from recurrent seizures in the early stages after TBI, when the brain is severely damaged, inflamed, and metabolically disturbed [4].

The names of more than 87,000 veterans were written in the American healthcare system (2015), and 41% were diagnosed with epilepsy, among whom 16% had traumatic brain injuries, and approximately 25% had Post-Traumatic Stress Disorder (PTSD) [5]. According to studies, PTSD and depression are the most common mental health challenges for veterans, as almost 14 to 16 percent of American troops in Afghanistan and Iraq were diagnosed with PTSD or depression [6]. In this regard, unexplained physical symptoms (8-32%) and pain (43.1%) were other complications [7].

Despite mental health concerns, other issues, such as suicide, substance abuse, and interpersonal violence, are observed among these individuals [8]. Before 2000, the suicide rate was lower in the military and soldier population than in civilians; however, it increased during the last 20 years and now exceeds the civilian rate [9].

Cameron reported that 12% to 35% of soldiers in the Iraq and Afghanistan wars suffered from mild brain damage or concussion due to blast injuries [10]. The main causes of military traumatic brain injury are head injuries caused by bullet penetration and severe collision or shock waves due to explosive weapons, which have long been discussed as a neurological disease or a functional disease [11].

Despite rapid advances in weapons, innovations in combat methods, and movement toward wars without human participation in today's world, there will be complications caused by the war in soldiers for years [12].

The prevalence of TBI in modern military operations is still significant. According to the US Center for Disease Control and Prevention, the number of TBI cases increased dramatically in the United States from 2000 to 2006 [13]. This center reported that approximately 75% out of 244,217 cases of TBI were classified as mild brain injury [14]. The prevalence of epilepsy was estimated to be 0.5% to 2% in the US general population, and the cumulative incidence of PTE varied widely from 2% to more than 50%, depending on the severity of the lesion [15].

TBI patients were reported to have a cumulative incidence of 5% to 7%, and the risk of PTE reached 53% in a military series with penetrating head injuries [16]. The cumulative incidence of late seizures more than 30 years after TBI was 2%, 4%, and more than 15% for mild injuries, moderate injuries, and severe injuries, respectively [17].

Post-traumatic epilepsy occurs with unprovoked seizures more than 7 days after traumatic brain injury. The incidence of PTE varies with injury severity and ranges from 4% to 15% after moderate to severe TBI [18]. Given the importance of this topic, the present study aimed to determine the late consequences of epilepsy in veterans with traumatic brain injury during the imposed Iran-Iraq war.

Instruments and Methods

The present study was an observational cohort study conducted in 2022 on veterans participating in the 8-year Iran-Iraq war and having medical records with different levels of veterans in Isfahan Province Veterans Foundation. The inclusion criteria were as follows: veterans who suffered from traumatic brain injuries during the war and were diagnosed with epilepsy after the war, their epilepsy was confirmed by a neurologist, and consented to participate in the study. A total of 33 years had passed from the end of the war to the completion of the present study. The exclusion criteria included veterans who had mental and physical problems and therefore could not participate in the examination in person and veterans who had epilepsy before traumatic brain injury or did not have any traumatic brain injury during the war.

Finally, 218 veterans with epilepsy, who were available and could answer the questions, were identified, 100 of them had a traumatic brain injury, and 118 did not have any traumatic brain injury. Figure 1 shows the process of selecting veterans.

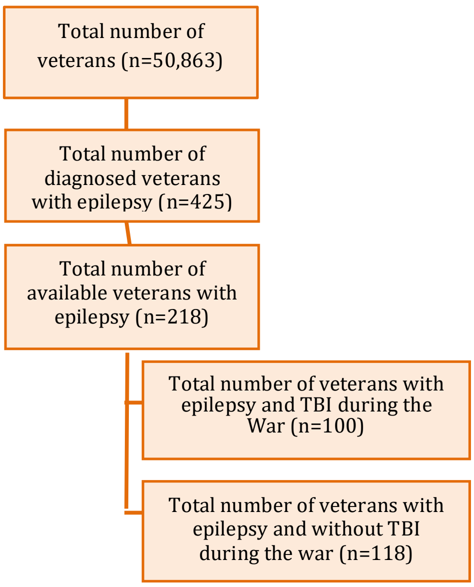

Figure 1) Diagram of veteran selection

The researcher visited the Foundation of Veterans after receiving an ethical code from Isfahan

University of Medical Sciences (IR.MUI.MED.REC.1400.167) and the required permissions. The veterans were selected according to the inclusion criteria, and they were contacted by phone. The researcher asked about the veterans' medical history and explained the research objectives. If the veterans could attend the foundation, they were asked to visit the Foundation of Veterans on a certain day and to be examined for epilepsy. In this session, the researchers and a neurologist visited the veterans.

The data collection tool included a checklist and standard questionnaire, which were completed after the clinical examination of the veterans and the question-answer phase. It is worth mentioning that the examination did not impose any cost on the patients.

Mini Mental State Examination (MMSE) and Instrumental Activities of Daily Living and Physical Self-Maintenance Scale (IADL-PSMS) were two standard questionnaires.

Mini Mental State Examination (MMSE)

The MMSE is a simple cognitive function test developed by Folstein *et al*. MMSE scores decrease with age, and patients with less education tend to have lower MMSE scores. The MMSE comprises 11 sub-items that measure varied brain functions. Each item is scored according to the number of subordinate examination items as follows: "orientation to time" (5 points), "orientation to place" (5 points), "registration" (3 points), "calculation" (5 points), "repetition" (1 point), "3-step command" (3 points), "reading and obeying" (1 point), "recall" (3 points), "naming" (2 points), "writing" (1 point), and "copying" (1 point). "Orientation to time", "orientation to place", "calculation", "recall", "copying", and "3-step command" are related to attention and working memory. In addition, "copying" requires complex cognitive functions such as visuospatial cognition and praxis functions. "Writing" involves writing sentences and thinking voluntarily; therefore, it requires complex cognitive functions such as language-specific processes, executive functions, and visuospatial cognition. "Registration" and "repetition" evaluate verbal abilities and immediate memory.

Activities of Daily Living Scale (ADL)

The IADL–PSMS is an informant-based measure of IADLs (Instrumental Activities of Daily Living, including shopping, housekeeping/maintenance, cooking, driving, finances, medication management, telephone use, laundry) and BADLs (Basic Activities of Daily Living, including bathing, grooming, dressing, feeding, toileting, physical ambulation). Scoring is based on performance needs (i.e., dependence, requires assistance, independence).

SPSS 23 software (IBM Corp., Armonk, NY, USA) was used for data analysis, and the significance level was considered less than 0.05. The correlation between IADL-PSMS total score and MMSE total score was investigated using Spearman's correlation coefficient. T-test and chi-square tests were also used in this study.

Findings

All the veterans were male, and one had Afghan nationality. There was no significant difference between the veterans with and without TBI in demographic characteristics ($p>0.05$), but a significant difference was observed between the two groups in the mean age at PTE debut ($p<0.05$; Table 1).

Table 1) Comparison of demographic characteristics of veterans with epilepsy with/without TBI

Demographic characteristics	With TBI (n=100)	Without TBI (n=118)	P-value
Age, years (mean±SD)	57.38±5.34	56.17±2.33	0.347
Age at TBI, years (mean±SD)	22.15±4.22	-	-
Age at PTE debut, years (mean±SD)	23.64±3.44	41.12±3.87	0.016
Body mass index, Kg/m2 (mean±SD)	22.65±4.75	22.12±3.94	0.369
Time from injury to PTE debut, years (mean±SD)	3.07±6.98	-	-
Smoking & drug abuse, No. (%)	36 (36.0)	42 (35.6)	0.148

In veterans with TBI, the latency period or the time interval between TBI and the occurrence of PTE varied from a few days to several years and ranged from 0 to 34 years. In 62% of cases, the latency period was less than one year.

The characteristics of epilepsy did not show any significant difference between the veterans with/without TBI ($P>0.05$; Table 2).

Table 2) Comparison of epilepsy characteristics of veterans with epilepsy with/without TBI

Epilepsy characteristics	With TBI (n=100)	Without TBI (n=118)	P-value
Dominant hand, No. (%)			
Right	78 (78.0)	92 (78.0)	0.298
Left	22 (22.0)	26 (22.0)	
Family history of epilepsy, No. (%)			
Yes	5 (5.0)	1 (0.85)	0.921
No	95 (950)	117 (99.15)	
Type of epilepsy, No. (%)			
Generalized	93 (93.0)	96 (81.4)	0.247
Focal	7 (7.0)	22 (18.6)	

The incidence rate of meningitis was significantly different between the two groups ($p<0.05$). However, other underlying diseases of the veterans were not significantly different between the two groups ($p>0.05$; Table 3).

The mean score of MMSE was 22.33±2.06 in the veterans with TBI and 20.15±1.33 in veterans without TBI, which was significantly different ($p<0.05$). On the research subscales, the veterans with/without TBI were significantly different in

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terms of the "Recall" and "Registration" subscales (p<0.05; Table 4).

Table 3) Frequency (percentage) of underlying diseases of veterans with epilepsy with/without TBI

Underlying diseases	With TBI (n=100)	Without TBI (n=118)	P-value
Diabetes	27 (27.0)	37 (31.3)	0.104
Hyperlipidemia	27 (27.0)	43 (36.5)	0.362
Cancer	7 (7.0)	12 (10.1)	0.109
Asthma	57 (57.0)	49 (41.5)	0.582
Heart disease	47 (47.0)	43 (36.4)	0.137
Brain disease	4 (4.0)	6 (5.0)	0.763
Dementia	7 (7.0)	16 (13.5)	0.247
Headache	87 (87.0)	94 (79.6)	0.312
Neurological pain	81 (81.0)	77 (65.3)	0.061
Meningitis	4 (4.0)	0 (0)	0.014

Table 4) The mean scores of MMSE and ADL and their subscale in veterans with epilepsy with/without TBI

MMSE	With TBI (n=100)	Without TBI (n=118)	P-value
MMSE			
Orientation to time	4.04±1.15	3.98±2.58	0.069
Orientation to place	4.80±0.20	4.41±0.35	0.321
Registration	2.99±1.06	1.64±0.90	0.012
Calculation	2.48±0.91	2.38±0.82	0.102
Repetition	0.86±0.20	0.74±0.50	0.145
3-Step command	2.69±0.32	2.44±0.61	0.462
Reading and obeying	0.68±0.14	0.74±0.27	0.521
Recall	0.41±0.70	0.19±0.30	0.003
Naming	1.76±0.36	1.98±0.69	0.452
Writing	0.91±0.40	0.82±0.20	0.369
Copying	0.71±0.25	0.83±0.43	0.369
Total	22.33±2.06	20.15±1.33	0.014
Activities of Daily Living (ADL)			
IADL (Range: 0–16)	11.69±0.36	10.98±1.02	0.421
BADL (Range: 0–12)	9.74±0.83	9.85±0.71	0.098
Total	7.10±0.80	6.90±0.70	0.321

Discussion

Approximately 5% to 20% of epilepsy cases in a community can be caused by previous TBI. Since PTE following TBI has a significant negative impact on the physical safety and quality of life of patients, this study was conducted on Iranian veterans of the 8-year Iran-Iraq war with epilepsy.

In this study, 0.83% of veterans had epilepsy. In fact, for every 1000 veterans, 8.36 people were diagnosed with epilepsy. In the latest published systematic review in 2017, the prevalence of active epilepsy was reported as 6.38 per 1000 people in the world, which indicates that the prevalence of epilepsy in veterans is higher than in the general population [19]. In Iran in 2014, a review study estimated the combined prevalence of epilepsy to be about 5% for all regions, and the prevalence was higher in veterans. Among the examined veterans, 23.5% had epilepsy with TBI during the war, and 76.5% had no history of brain concussion during the war [20].

In a study conducted in Durham on veterans, Rehman *et al*. observed that the prevalence of TBI with epilepsy and PTSD was 52.6% and 70.4%, respectively, so TBI was recognized as a risk factor for epilepsy and psychogenic non-epileptic seizures in veterans, which included a lower percentage than the present study [21].

In a study on Colorado veterans, Frey showed that 24.5% developed epilepsy after TBI, which was similar to the results of our study [22].

In a study conducted in Finland, Pitkänen and Immonen stated that during the last decade, an increasing number of laboratories have investigated the molecular and cellular mechanisms of post-traumatic epileptogenesis in experimental models. In this study, veterans were also examined based on whether or not they had TBI before epilepsy [23]. Salinsky *et al*. in America showed that health-related quality of life measured by Quality of Life in Epilepsy-31 Inventory (QOLIE-31) was worse in veterans with psychogenic nonepileptic seizures compared to people with epileptic seizures [24].

Pugh's study in Texas found that older veterans (>65 years) with epilepsy had lower scores on measures of physical and mental health than their non-epileptic counterparts. Therefore, while previous studies stated that chronic neurological disorders such as epilepsy have a more destructive impact on measures of mental health, these data showed that older patients experience worse problems in physical and mental health than young patients with neurological disorders [25]. Pugh stated in another study that Physical functioning and health-related quality of life were lower for people with epilepsy after TBI compared to people with epilepsy without TBI [26]. In the present study, MMSE was higher in veterans with epilepsy with TBI than those without a history of TBI. There was no female veteran in the study, and all participants were male because women did not participate in the war. Although, Karlander *et al*. indicated that being male was an independent risk factor for PTE after TBI [27].

Mackin *et al*., in a study on San Francisco veterans, observed that there are significant clinical cognitive disorders in learning and memory disorders in veterans with epilepsy after a head injury, which had no significant relationship with their demographic variables, but it was related to blood pressure and severity of the head injury [28]. In the present study, cognitive disorders in veterans with epilepsy after head injury showed a significant difference with veterans with epilepsy without TBI and were more.

Most of the participants in the study were from Isfahan and surrounding areas. Therefore, the results might not be representative of the general situation around Iran. The results of long-term EEG monitoring and neuroimaging during the acute phase of TBI were lacking in most of the subjects. Thus, further population-based prospective studies are needed to fully clarify the clinical characteristics of PTE and factors affecting the latency of PTE. Interviewing and data collecting from the veterans were extremely difficult for numerous reasons, including their deteriorating status.

Finally, it is suggested that these patients receive regular rehabilitation programs and mental and physical support.

Conclusions

The characteristics of epilepsy in veterans with and without TBI do not show a significant difference. The cognitive disorders of the veterans with epilepsy and TBI are more than the veterans without TBI, and they should be provided with practical rehabilitation treatments and find solutions to improve the two subscales of Recall and Registration. On the other hand, performing daily life activities in both groups of veterans shows the inability to perform these activities, which increases their need for caregivers. Also, the inability to perform daily life activities has a significant relationship with veterans' cognitive disorders.

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Ethical Permission: Written consent was obtained from the families of patients to enter this study. The current study was approved by the Isfahan University of Medical Sciences Ethics Committee with the code of IR.MUI.MED.REC.1400.2.167.

Conflict of Interests: There is no conflict of interests.

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