


Prevalence and Incidence of Drug-Resistant Temporal Lobe Epilepsy in Qatar

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ABSTRACT

BACKGROUND: Information on the epidemiology of temporal lobe epilepsy associated with hippocampal sclerosis (TLE-HS) from Qatar and the developing countries is scarce. To acquire knowledge on the incidence and prevalence of drug-resistant TLE-HS in Qatar, we designed this analytical and extrapolative systematic review of the existing literature.

MATERIAL AND METHODS: We searched the electronic database PubMed from 1947 until April, 2018, using the following search terms in the title: “epilepsy” OR “temporal lobe” OR “hippocampal sclerosis” AND “epidemiology” OR “incidence” OR “prevalence.” Relevant original studies, reviews, and their references, were included. We extrapolated from the previous international literature to estimate the epidemiology of drug-resistant TLE-HS in Qatar.

RESULTS: The estimated Qatar incidence of epilepsy varies from 50 to 61 per 100 000 persons per year, and the estimated prevalence of epilepsy is 6.54 per 1000 population; the estimated incidence of TLE varies from 9.5 to 11.6 patients per 100 000 population per year and the estimated prevalence of TLE is 1.76 patients per 1000 people, with 4721 patients having TLE in Qatar. Finally, the reviewed studies also helped in making an estimate of the Qatar prevalence of drug-resistant TLE-HS to be between 0.3 and 0.6 cases per 1000 people (804-1609 current patients) and the Qatar incidence of drug-resistant TLE-HS (2.3-4.3 cases per 100 000 people, per year) with 62 to 116 new patients per year.

CONCLUSION: Our study suggests that 804 to 1609 current patients (with 62-116 additional patients per year) in Qatar are suffering from drug-resistant TLE-HS; emphasis should be placed on the surgical aspect of the current Qatar Comprehensive Epilepsy Program.

KEYWORDS: Epidemiology, epilepsy, seizure, temporal lobe, Qatar

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Introduction

Temporal lobe epilepsy (TLE) due to hippocampal sclerosis (HS), also known as mesial temporal sclerosis (MTS), is a common occurrence; this condition is often resistant to anti-epileptic drugs (AEDs), but responds well to surgery.^{1,2} However, information on the epidemiology of TLE-HS in developing countries is rare, if not nonexistent in Qatar and the Middle East³⁻⁵; in addition, epilepsy surgery (ES) is not available and is not practiced in many developing countries, particularly in the Middle East region where only 2 countries, Kingdom of Saudi Arabia (KSA) and Lebanon, manage an ES program.

Studies from the Middle East region dealing with ES, report the quality of life (QOL) after temporal lobectomy^{6,7} or describe how to develop an ES program according to requirements and local needs⁸; in developing countries, another study compares the cost of ES between developed and developing countries⁹; a review, the special considerations and limitations

of the introduction of ES in developing countries¹⁰; Interestingly, both studies agree that ES is an effective treatment option and a workable project for epilepsy patients in developing countries.

Qatar's population of 2 682 556 people as of June 30, 2019,¹¹ represents a unique mixture of native Qataris (10.5 % of total population, 2019) and a large number of expatriates (89.5% of total population by nationality, 2019),¹² an image very similar to the neighboring population of the KSA; most expatriates are, as in KSA, from other countries: Asia, the Middle East, and North Africa.^{5,11-13} There are no health care databases or other direct methods available to extract data on the epidemiology of TLE-HS in Qatar, and information on this important condition is also lacking in the region.

The objectives of this study are to gain knowledge of the epidemiology (incidence and prevalence) of drug-resistant TLE-HS in Qatar, and with current plans to develop and



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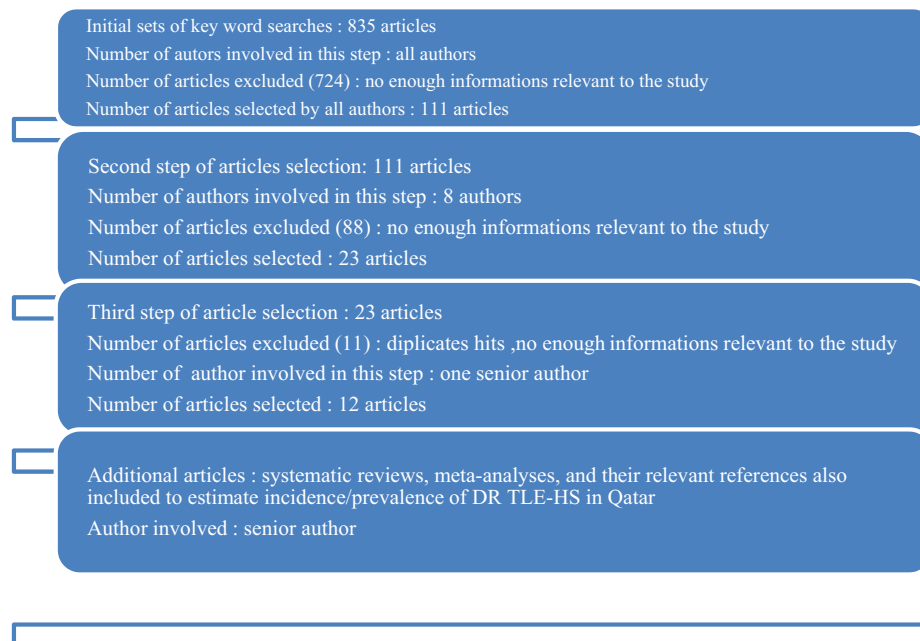


Figure 1. Flow chart to calculate the prevalence and incidence of drug-resistant TLE-HS in Qatar.

HS indicates hippocampal sclerosis; TLE, temporal lobe epilepsy. Diagram showing the successive numbers of articles examined, the number of authors examining these articles, the number of articles excluded and the articles included in the final data. DR TLE-HS indicates drug-resistant temporal lobe epilepsy hippocampal sclerosis.

improve surgical therapies for epilepsy in Qatar in the near future, provide valuable information to authorities and health professionals in Qatar and even other countries in the region. To this end, we have designed this systematic analytical and extrapolative review of the existing literature.

Methods

We investigated the electronic database PubMed from 1947 through April, 2018, for papers that encompassed the following keywords in their title: “epilepsy” OR “temporal lobe” OR “hippocampal sclerosis” AND “epidemiology” OR “incidence” OR “prevalence.”

Inclusion criteria: relevant original articles from all countries in the World Health Organization (WHO) Eastern Mediterranean Region (22 countries extending from Morocco to Pakistan were identified).

We also investigated several previous systematic reviews, meta-analyses, and their relevant references. When regional studies were lacking, original articles from other countries were identified and investigated.

Exclusion criteria: articles that included special patient populations only (eg, elderly, intellectually disabled, and veterans), papers that reported lifetime prevalence of epilepsy, articles that investigated special circumstances (eg, posttraumatic epilepsy), and papers not written in English were not included.

We then extrapolated from the published data to estimate the prevalence and incidence of drug-resistant TLE-HS in Qatar in 2019. Qatar total population of 2 682 556 people as of June 30, 2019, (data confirmed by telephone with the Qatar Planning and Statistics Authority) was used to calculate the prevalence, incidence of epilepsy, and all other measures.

Role of the research team: all authors actively participated in the initial sets of keyword searches; the results of these authors search were carefully examined by 8 authors; after excluding the duplicate hits and reviewing their full texts, a senior author finally selected the articles to be included in the study.

Results

The initial sets of the keyword searches produced 835 references; Figure 1 shows the number of articles initially identified, the number of articles considered during each step, how many were excluded and the reasons why they were excluded, and the number of articles retained for the final analysis. We also included additional relevant manuscripts (systematic reviews, meta-analyses, and their relevant references,) when estimating the incidence and prevalence of drug-resistant TLE-HS in Qatar.

The following text provides a detailed description of how, in a step-wise method, we extrapolated from the published data to estimate the prevalence and incidence of TLE, then TLE-HS, and finally drug-resistant TLE-HS in Qatar (Figure 2).

Incidence of TLE in Qatar

There are few studies from the Middle East on the incidence of epilepsy. One study from Egypt reported an annual incidence rate of 48/100 000.¹⁴ Another study from Egypt reported an annual incidence rate of epilepsy of 43.14/100 000.¹⁵ In a previous study,¹⁶ the median incidence of epilepsy was 50.4/100 000/year; it was 45.0 for high-income countries and 81.7 for low- and middle-income countries.¹⁶ In a more recent systematic review and meta-analysis of international studies,¹⁷ the incidence rate was 61.44 per 100 000 person-years. Since Qatar is a high-income country but still has a mixed population of natives

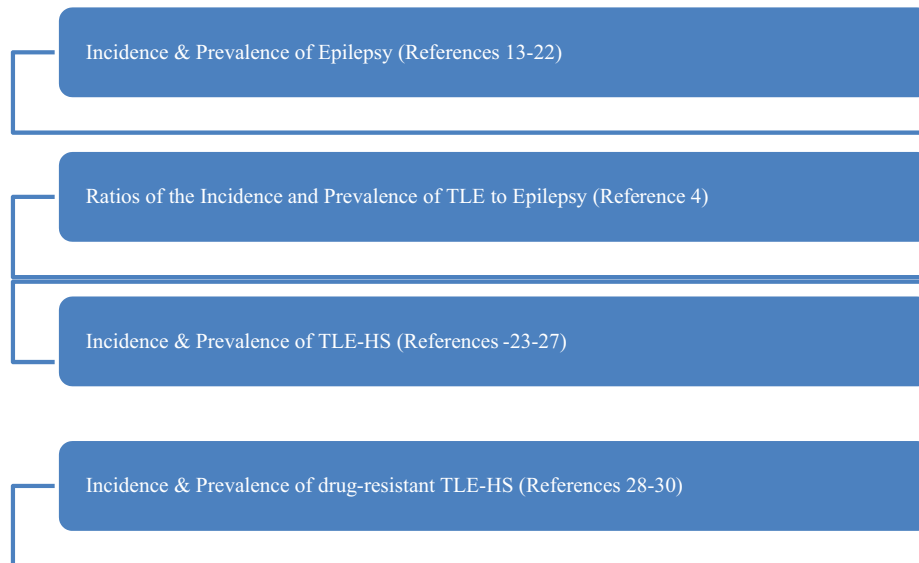


Figure 2. Flow chart to calculate the prevalence and incidence of drug-resistant TLE-HS in Qatar. HS indicates hippocampal sclerosis; TLE, temporal lobe epilepsy.

and expats most of them from the Indian subcontinent, we considered the incidence of epilepsy in Qatar to be from 50 to 61 per 100000 persons per year. This means that there are 1341 to 1636 ($2682556/100000 \times 50 = 1341$ to $2682556/100000 \times 61 = 1636$) new cases of epilepsy per year in Qatar. In one study, the ratio of the incidence of TLE/epilepsy was calculated to be 0.19.⁴ Hence, we calculated an estimated Qatar incidence of TLE of 9.5-11.6 ($50 \times 0.19 = 9.5$ – $61 \times 0.19 = 11.6$) patients per 100000 population, per year; this means that there are an estimated 254 to 310 ($1341 \times 0.19 = 254$ to $1636 \times 0.19 = 310$) new patients of TLE per year in Qatar.

Prevalence of TLE in Qatar

In a recent systematic review and meta-analysis of international studies,¹⁷ the point prevalence of active epilepsy was 6.38 per 1000 persons. In a community-based study from Saudi Arabia,¹⁸ prevalence rate for active epilepsy was 6.54/1000 population. In a study from Iran,¹⁹ point prevalence of active epilepsy was 7.87 per 1000 individuals. In a door-to-door survey from Egypt,²⁰ the prevalence of active epilepsy was 5.1 per 1000 inhabitants, and in another study from Egypt, prevalence of active epilepsy was 4.99 per 1000 population.¹⁵ In one study from Algeria, the prevalence rate was reported to be 8.32 per 1000.²¹ In one study from Turkey,²² the prevalence of active epilepsy was 5 per 1000 inhabitants. In a comparative epidemiology of epilepsy in Pakistan and Turkey,²³ the prevalence rate of epilepsy was 9.98 in 1000 people in Pakistan and 7.0 in 1000 persons in Turkey. Based on the above research, and given the fact that Qatar has a similar population and the same mix of local and expats than KSA,¹¹⁻¹³ we considered the prevalence of epilepsy to be 6.54 per 1000 population in Qatar. In one study, the ratio of the prevalence of TLE/epilepsy was calculated to be 0.27.⁴ Using the following calculation, we concluded that an estimated Qatar prevalence of TLE is $6.54/1000 \times$

$0.27 = 1.76$ patients per 1000 people. Therefore, using $1.76/1000 \times 2682556$ for our calculation, we concluded that about 4721 patients have TLE in Qatar.

Prevalence and Incidence of TLE-HS in Qatar

The prevalence of HS in various ES series has varied significantly from 33.6%²⁴ to 66%.²⁵ In one study of temporal lobe surgeries of the 2812 patients in Germany,²⁶ 1461 (52.0%) patients were classified as having HS. Based on this pathology study, we estimated a Qatar TLE-HS prevalence of $1.76/1000 \times 0.52 = 0.92$ patients per 1000 people, yielding a calculated estimate of $0.92/1000 \times 2682556 = 2468$ patients. One hospital-based observational study of 2200 patients from France,²⁷ classified them according to the ILAE criteria; 238 patients (10.8%) had HS on their brain magnetic resonance imaging (MRI). Based on this hospital-based observational study, we estimated a Qatar prevalence of TLE-HS of $6.54/1000 \times 0.108 = 0.71$ patients per 1000 people, yielding a calculated estimate of $0.71/1000 \times 2682556 = 1905$ patients. In one retrospective study of 468 patients with epilepsy from Qatar,⁵ 7% of patients had HS. Based on this Qatari study, we estimated a Qatar prevalence of TLE-HS of $6.54/1000 \times 0.07 = 0.46$ patients per 1000 people, yielding a calculated estimate of $0.46/1000 \times 2682556 = 1234$ patients. It is important to keep in mind that studies based on MRI may underestimate the prevalence of TLE-HS because as many as 20% of the patients who have a normal brain MRI and suffer from TLE have HS in their pathology studies.²⁸ Likewise, studies that investigated patients who had ES do not represent the whole population of the patients with epilepsy. The pathology study from Germany²⁶ was limited because it included surgery patients only. The MRI studies from France²⁷ and Qatar⁵ were also limited, like other MRI studies (see above). Despite inherent limitations and sources of bias, the above studies give a reasonable estimate of

the Qatar prevalence of TLE-HS (0.46-0.92 patients per 1000 people or 1234 to 2468 current patients).

Depending on the pathology study from Germany,²⁶ we concluded a Qatar incidence of TLE-HS of 9.5 (incidence of TLE) \times 0.52 = 4.9 to 11.6 (incidence of TLE) \times 0.52 = 6 or 4.9 to 6 patients per 100000 people, per year. According to the hospital-based observational study from France,²⁷ we estimated an incidence of 50 (incidence of epilepsy) \times 0.108 = 5.4 to 61 (incidence of epilepsy) \times 0.108 = 6.5, or 5.4 to 6.5 patients per 100000 people, per year. Finally, depending on the Qatari study,⁵ we estimated an incidence of 50 (incidence of epilepsy) \times 0.07 = 3.5 to 61 (incidence of epilepsy) \times 0.07 = 4.2, or 3.5 to 4.2 patients per 100000 people, per year. These investigations and calculations help provide a reasonable estimate of the Qatar incidence of TLE-HS from 3.5 to 6.5 patients per 100000 people, per year; a calculated annual occurrence of $3.5/100000 \times 2682556 = 93$ to $6.5/100000 \times 2682556 = 93 = 174$ new patients with TLE-HS per year in Qatar.

Prevalence and Incidence of Drug-Resistant TLE-HS in Qatar

About two-thirds of the patients with TLE-HS have drug-resistant epilepsy. In a previous study of 47 patients,²⁹ just 34% of the patients remained seizure-free at the end of the study. In another previous study that investigated 73 patients with TLE-HS,³⁰ 68% of the patients had drug-resistant epilepsy. Finally, in one research that investigated 142 patients with TLE-HS,³¹ 67% of the patients had drug-resistant seizures. Hence, we used 67% as the basis of our calculations to estimate the epidemiology of drug-resistant epilepsy in patients with TLE-HS. The reviewed studies provide a reasonable estimate of the prevalence of drug-resistant TLE-HS in Qatar (0.46-0.92 patients per 1000 people \times 0.67 = 0.3 and 0.6 patients per 1000 people; $0.3/1000 \times 2682556 = 804$ to $0.6/1000 \times 2682556 = 1609$ current patients). These studies also help provide a reasonable estimate of the incidence of drug-resistant TLE-HS in Qatar (3.5-6.5 patients per 100000 people, per year \times 0.67 = 2.3-4.3 patients per 100000 people, per year; $93 \times 0.67 = 62$ to $174 \times 0.67 = 116$ patients per year).

Discussion

We came to the conclusion that the estimated current prevalence of drug-resistant TLE-HS in Qatar is 0.3 to 0.6 patients per 1000 people (804-1609 current patients) and the estimated incidence of drug-resistant TLE-HS in Qatar is 2.3 to 4.3 patients per 100000 people, (62-116 new patients per year). Our study has significant limitations; the data presented here are extrapolations, and we did not adjust for the population age pyramids of different countries: however, in making these extrapolations, we considered Qatar population similar to neighboring KSA population and used the same epilepsy prevalence rate, 6.54 for further calculations^{11,12,17}; we calculated the population estimates from the previous epidemiological and observational studies (that may not represent the general

Qatar population of patients with epilepsy) and applied them to the current Qatar population. For example, the numbers used for calculating the ratio of TLE/epilepsy, relies on one investigation from almost 5 decades ago in a relatively homogeneous community (Rochester, Minnesota).³² The methods applied to define epilepsy and TLE in the Rochester research may yield different conclusions if performed today, considering the significant progresses in the diagnostic tools and technologies achieved in the past 50 years; but, other studies that define the ratio of TLE/epilepsy do not exist in the recent literature. Finally, the population in Qatar is mobile and the great majority of the population consists of migrants, like neighboring KSA. Considering the fact that the state of Qatar mandates pre-employment assessment to all employees, the healthy worker effect becomes quite real, and it can influence both morbidity and mortality rates. Qatar's population consists of expatriates (89.5%) and native Qataris (10.5%).¹² If we apply our estimation to native population of Qatar only (10.5%), then the estimated current prevalence of drug-resistant TLE-HS in native population of Qatar is 84 to 169 current patients and the estimated incidence of drug-resistant TLE-HS in Qatar is 6.5 to 12 new patients per year. Therefore, with only few studies of good quality from the Middle East and North Africa region, the current extrapolations may provide valuable information for the authorities, healthcare professionals, and researchers involved in the management of these patients in Qatar and in the region.

In drug-resistant epilepsy, seizures continue to occur and a seizure-free state is very unlikely to be achieved with any further AED therapy. In patients with drug-resistant TLE-HS, resective ES may result in seizure freedom in 70% of the patients,^{33,34} while less than 5% of patients who do not receive surgery and continue taking AEDs enter remission each year.³⁵ There are also helpful palliative surgical procedures (eg, vagus nerve stimulation and deep brain stimulation techniques) that may help some patients with drug-resistant epilepsy.^{36,37} Currently, many patients in Qatar suffer from drug-resistant TLE-HS. Surgery is a valuable option that offers these patients a reasonable chance to reduce or eliminate their seizures. The scenario becomes more complicated by the estimate that each year many more patients are being added to this pool. In spite of the estimated relatively high prevalence and incidence of drug-resistant TLE-HS in Qatar and the significant aftermaths of ongoing epileptic seizures (eg, increased risks of morbidity and mortality),^{38,39} an active ES program does not currently exist in Qatar. The roughly estimated incidence and prevalence of epilepsy and refractory epilepsy in Qatar suggest that there may be a large enough population of patients with refractory epilepsy to potentially benefit from a surgical epilepsy program in Qatar.

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Author Contributions

The material described in the manuscript is the work of all authors; the corresponding author (BM) acknowledge that all co-authors were substantially involved in the study and that no undisclosed group or person played a leading role in this work; the authors contributions is clearly reported in the method section of the manuscript (role of the research team) and is also shown in Figure 1.

Disclosures

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