Epilepsy Research: Where Are We Now

Raidah Al-Baradie, MD,
ABMS, EMSHA, FAES
Consultant Pediatric Neurology/Epilepsy
Director of Comprehensive Epilepsy Program
Chairwomen Pediatric Neurology
King Fahd specialist Hospital- Dammam
Introduction

- Epilepsy is a common neurological disorder in Saudi Arabia
- The prevalence of epilepsy in Saudi Arabia is estimated at 6.54 per 1000
- The level of public awareness, the public attitudes and knowledge of epilepsy in the Saudi population is limited

Prevalence of Epilepsy in Different Countries of the World

![Graph showing the prevalence of epilepsy in different countries](image)
The prevalence of epilepsy and other seizure disorders in an Arab population: a community-based study

- Door to door survey of a restricted area inhabited by 23,700 Saudi nationals
- All patients with probable seizures were examined by a neurologist and 92% of positive cases were investigated by brain CT and EEG
- Prevalence rate (PR) for active epilepsy was 6.54 /1000 population (95% confidence interval 5.48-7.60).

28% of the patients had focal seizures

21% generalized seizures

51% seizures and epilepsy was unclassified

The epilepsy was symptomatic in 32% of the cases: pre or perinatal encephalopathy 23%, head injury 4%, childhood neurological infection 4% and stroke 1%

Febrile convulsions PR was 3.55 /1000 children under the age of 6 years and isolated seizures were documented in only 0.18 /1000 population
Advances in understanding the causes of epilepsy

# Neurological Disorders in Saudi Arabia:

## The Thugbah study:

<table>
<thead>
<tr>
<th>Neurological Disorder</th>
<th>Prevalence Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache syndromes</td>
<td>20.7</td>
</tr>
<tr>
<td>All seizure disorders</td>
<td>7.6</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>6.54</td>
</tr>
<tr>
<td>Febrile Convulsions</td>
<td>0.84</td>
</tr>
<tr>
<td>Mental retardation</td>
<td>6.27</td>
</tr>
<tr>
<td>Cerebral palsy syndrome</td>
<td>5.3</td>
</tr>
<tr>
<td>Microcephaly</td>
<td>1.99</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.8</td>
</tr>
<tr>
<td>Parkinson's disease</td>
<td>0.27</td>
</tr>
<tr>
<td>Alzheimer's disease</td>
<td>0.22</td>
</tr>
<tr>
<td>CNS Malformations</td>
<td>0.49</td>
</tr>
<tr>
<td>Spinal Atrophy</td>
<td>0.13</td>
</tr>
<tr>
<td>Congenital brachial palsy</td>
<td>0.13</td>
</tr>
<tr>
<td>Narcolepsy</td>
<td>0.04</td>
</tr>
<tr>
<td>Multiple Sclerosis</td>
<td>0.04</td>
</tr>
</tbody>
</table>

## Neurological disorders

<table>
<thead>
<tr>
<th>Neurological disorders</th>
<th>Number of patients (%) (n=1767)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epilepsy and seizure disorders</td>
<td>783 (37.71)</td>
</tr>
<tr>
<td>Headache disorders</td>
<td>322 (15.51)</td>
</tr>
<tr>
<td>Stroke</td>
<td>193 (9.29)</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>154 (7.41)</td>
</tr>
<tr>
<td>Cervical and lumbosacral radiculopathy</td>
<td>75 (3.61)</td>
</tr>
<tr>
<td>Carpal tunnel syndrome</td>
<td>65 (3.13)</td>
</tr>
<tr>
<td>Parkinson’s disease and other movement disorders</td>
<td>48 (2.31)</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>47 (2.26)</td>
</tr>
<tr>
<td>Static encephalopathy</td>
<td>32 (1.54)</td>
</tr>
<tr>
<td>Bell’s palsy</td>
<td>24 (1.15)</td>
</tr>
<tr>
<td>Trigeminal neuralgias</td>
<td>24 (1.15)</td>
</tr>
</tbody>
</table>

A systematic review of the epidemiology of epilepsy in Arab countries

*Hani T. S. Benamer and †Donald G. Grosset

*Neurology Department, New Cross Hospital, Wolverhampton, United Kingdom; and †Department of Neurology, Institute of Neurological Sciences, Southern General Hospital, Glasgow, United Kingdom

SUMMARY

In this report the epidemiologic aspects of epilepsy in Arab countries are systematically reviewed. MEDLINE and Embase were searched, and six papers were identified: one incidence report from Qatar and five prevalence reports (two from Sudan, and one from each of Libya, Tunisia, and Saudi Arabia). An incidence of 174 per 100,000 persons in 2001 was reported in a hospital-based study from Qatar. Prevalence ranged between 0.9/1,000 in Sudan and 6.5/1,000 in Saudi Arabia, with a median of 2.3/1,000. An approximate 724,500 people with epilepsy live in the Arab world. All the studies report higher prevalence in males, which was statistically significant in the Saudi study. The prevalence is approximately 2-fold higher in children and young adults, compared to the rates in middle age. Two studies showed a high prevalence in individuals older than 60 years of age. Primary generalized seizures are reported in 28–97% of cases, partial seizures in 3–43.8%, and unclassified seizures in 18–51%. Idiopathic epilepsy represents 73.5–82.6% of cases. Early childhood brain damage such as in cerebral palsy and mental retardation represented a major cause of symptomatic epilepsy, whereas infection was the main cause in Sudan. The epidemiologic data from Arab states are lacking, especially from populous countries like Egypt, Algeria, and Syria. Well-designed studies are needed to accurately determine the burden of epilepsy in the Arab world.

KEY WORDS: Epilepsy, Incidence, Prevalence, Epidemiology, Arab countries.
A comprehensive review of epilepsy in the Arab world

Devender Bhalla a,b,c, Elham Lotfalinezhad e,d, Utsav Timalsina e, Saloni Kapoor f, Kailash Suresh Kumar g, Abdallah Abdelrahman n, Brenda Giagante i, Manjari Tripathi i, Kavita Srivastava i, Irmonsyah Irmonsyah k

a Nepal Interest Group of Epilepsy and Neurology, Kathmandu, Nepal
b Faculté de Médecine, Université de Limoges, Limoges, France
c University of Social Welfare and Rehabilitation Sciences, Tehran, Iran
d Tribhuvan University, Kathmandu, Nepal
e All India Institute of Medical Sciences, Delhi, India
f Chettinad Health and Research Institute, Chennai, India
g University of Khartoum, Khartoum, Sudan
h Department of Neurosciences, El Cruce Hospital, Buenos Aires, Argentina
i Bharati Vidyapeeth Medical University, Pune, India
k Marozeri Mahdi Hospital, Bogor, Indonesia

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Epidemiology
Prevalence
Incidence

A B S T R A C T

Purpose: We conducted a comprehensive review of the epidemiology of epilepsy in the Arab world.

Methods: Epidemiological literature about epilepsy from 22 countries of the Arab League was searched in French and English using several keywords (specific and wider) and combinations, individually for each country. The search was conducted on Google First and then on PubMed. The results are presented as counts, proportions, and medians along with 95% confidence intervals (CI). Unpaired t-test with unequal variance and regressions were performed, altogether and individually, for lifetime and active epilepsy prevalence as well as incidence.

Results: Google provided 21 prevalence, four camp and nine incidence estimates while PubMed provided ten such estimates; none of them was identified by Google. No epidemiological data about epilepsy was found from 10/22 countries. Excluding pediatric studies, 13 prevalence estimates from six countries were identified. Including pediatric studies, 21 estimates from nine countries were found. Median lifetime and active epilepsy prevalence were 7.5/1000 (95% CI 12.6–12.3, range 1.9–12.9) and 4.4/1000 (95% CI 2.1–9.3, range 0.6–11.3), respectively, excluding pediatric studies. Median lifetime and active incidence was 56/100,000 (n = 9, N = 122,484, 95% CI 13.7–147.9, range 10.4–12.0).

Conclusion: The fact that no epidemiological data about epilepsy is available in the public domain for almost one half of all Arab countries offers opportunities for future research. This thorough review of existing literature demonstrates a prevalence of epilepsy three times higher than previously reported for this region. The median incidence is similar to other regions of the world, e.g. North America. Google yielded additional valuable sources not indexed in PubMed and provided pertinent references more quickly.
Studies of lifetime prevalence of epilepsy in children in the Arab world

<table>
<thead>
<tr>
<th>Country</th>
<th>R/U</th>
<th>Year</th>
<th>N</th>
<th>P/1000</th>
<th>Additional comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egypt [24]</td>
<td>U</td>
<td>2012</td>
<td>12093</td>
<td>9.0</td>
<td>DTD among children; neurologist-diagnosis and EEG + Scan</td>
</tr>
<tr>
<td>Egypt [25]</td>
<td>U</td>
<td>2009</td>
<td>8750</td>
<td>7.2</td>
<td>Random sample of conventional schools, health insurance system, school doctor records, school health visitor records, filling of questionnaire by parents and parent’s interview neurologist-diagnosis and EEG</td>
</tr>
<tr>
<td>Egypt [25]</td>
<td>U</td>
<td>2009</td>
<td>120</td>
<td>133.3</td>
<td>Random sample of schools for mentally retarded, health insurance system, school doctor records, school health visitor records, filling of questionnaire by parents and parent’s interview; neurologist-diagnosis and EEG</td>
</tr>
<tr>
<td>Egypt [20]</td>
<td>U</td>
<td>1992</td>
<td>-</td>
<td>10.0</td>
<td>Random sample of school children &lt; 15 years age</td>
</tr>
<tr>
<td>Egypt [35]</td>
<td>Both</td>
<td>2013</td>
<td>8027</td>
<td>7.3</td>
<td>DTD; neurologist-diagnosis; Psychiatrist, and EEG + Scan; children 0–14 years;</td>
</tr>
<tr>
<td>Iraq [26]*</td>
<td>–</td>
<td>2005</td>
<td>-</td>
<td>1.0</td>
<td>Refer footnote</td>
</tr>
<tr>
<td>Morocco [27]</td>
<td>U</td>
<td>1998</td>
<td>-</td>
<td>11.0</td>
<td>–</td>
</tr>
<tr>
<td>Sudan [19]</td>
<td>U</td>
<td>1979</td>
<td>-</td>
<td>0.9</td>
<td>Entire school population, hospital and private clinics</td>
</tr>
</tbody>
</table>

DTD, door-to-door; EEG, electroencephalogram; P, prevalence; R, rural; U, urban; N, population size; *government estimate.
Prevalence studies of epilepsy in the Arab world

<table>
<thead>
<tr>
<th>Country</th>
<th>R/U</th>
<th>Year</th>
<th>Age</th>
<th>N</th>
<th>P-L</th>
<th>P-A</th>
<th>Additional comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Algeria [28]</td>
<td>Both</td>
<td>2012</td>
<td>All ages</td>
<td>8046</td>
<td>8.3</td>
<td>-</td>
<td>Randomly selected primary care clinics of five regions; neurologist-diagnosis and EEG + Scan</td>
</tr>
<tr>
<td>Algeria [29]</td>
<td>-</td>
<td>2002</td>
<td>-</td>
<td>-</td>
<td>1.9</td>
<td>-</td>
<td>MOH survey</td>
</tr>
<tr>
<td>Algeria [30]</td>
<td>U</td>
<td>2011</td>
<td>&gt;2 months</td>
<td>3002</td>
<td>12</td>
<td>-</td>
<td>Random sample of private and public practitioners and pediatricians of 5 regions; neurologist-diagnosis</td>
</tr>
<tr>
<td>Egypt [31]</td>
<td>Both</td>
<td>2010</td>
<td>All ages</td>
<td>6498</td>
<td>12.6</td>
<td>9.3</td>
<td>DTD; neurologist-diagnosis and EEG + Scan</td>
</tr>
<tr>
<td>Egypt [32]</td>
<td>U</td>
<td>2012</td>
<td>All ages</td>
<td>33283</td>
<td>5.5</td>
<td>-</td>
<td>DTD for multiple neurological disorders; neurologist-diagnosis</td>
</tr>
<tr>
<td>Egypt [33]</td>
<td>-</td>
<td>2008</td>
<td>All ages</td>
<td>62583</td>
<td>6.7</td>
<td>4.9</td>
<td>DTD; neurologist-diagnosis and EEG + Scan</td>
</tr>
<tr>
<td>Egypt [34]</td>
<td>Both</td>
<td>2008</td>
<td>All ages</td>
<td>62583</td>
<td>2.1</td>
<td>-</td>
<td>DTD for uncontrolled epilepsy; neurologist-diagnosis and EEG + Scan</td>
</tr>
<tr>
<td>Egypt [35]</td>
<td>Both</td>
<td>2013</td>
<td>All ages</td>
<td>8027</td>
<td>12.4</td>
<td>2.1</td>
<td>DTD; neurologist-diagnosis; Psychiatrist, and EEG + Scan</td>
</tr>
<tr>
<td>Libya [17]</td>
<td>U</td>
<td>1984</td>
<td>Adults &gt; 15</td>
<td>-</td>
<td>2.3</td>
<td>-</td>
<td>Polyclinics, EEG labs, university hospitals; DTD; neurologist-diagnosis and EEG + Scan</td>
</tr>
<tr>
<td>Saudi [36]</td>
<td>U</td>
<td>1995</td>
<td>All ages</td>
<td>1485</td>
<td>10.2</td>
<td>-</td>
<td>DTD for multiple neurological disorders; DTD; neurologist-diagnosis</td>
</tr>
<tr>
<td>Saudi [37]</td>
<td>U</td>
<td>1989</td>
<td>All ages</td>
<td>23700</td>
<td>6.5</td>
<td>-</td>
<td>DTD of restricted area; DTD; neurologist-diagnosis and EEG + Scan</td>
</tr>
<tr>
<td>Tunisia [38]</td>
<td>-</td>
<td>1985</td>
<td>All ages</td>
<td>34874</td>
<td>-</td>
<td>4.0</td>
<td>DTD for multiple neurological disorders; neurologist-diagnosis</td>
</tr>
<tr>
<td>UAE [39]*</td>
<td>Both</td>
<td>2014</td>
<td>All ages</td>
<td>-</td>
<td>12.9</td>
<td>-</td>
<td>Refer footnote</td>
</tr>
</tbody>
</table>

DTD, door-to-door; EEG, electroencephalogram; *Unofficial estimate; MOH, Ministry of Health; N, population size; P-A, prevalence active/1000; P-L, prevalence lifetime/1000; R, Rural; U, urban.

Bhalla D. et al., A comprehensive review of epilepsy in the Arab world. Seizure 34 (2016) 54–59
Prevalence of epilepsy stigma in Riyadh, Saudi Arabia

- Cross sectional study in King Abdul Aziz Medical City for (NGHA)
- Total of 166 participants including males (n=50) and females (n=66)
- A self-developed questionnaire including personal data (age, profession, gender, education level) and the general perception of epilepsy
- Descriptive statistics was used to assess the stigma expression
- A two-sided probability of <0.05 was considered as statistically significant

Abdulrahman Khalid Al-Yemni, Final year medical student, Dr. Sajida Agha, Associate Professor of Psychology, Salman Aldakhil, Final year medical student, King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Kingdom of Saudi Arabia, SES Annual Meeting 2015
Most participants were aware of the causes of epilepsy & perceived it as a hereditary problem

They thought schooling and marriage for epileptic pts. is possible

The majority (72%) rated seizure as a cause of death and epilepsy is not curable (8%)

Marriage of epilepsy pts. is possible (78%), but they should not have children (86%)

This study confirms the prevalence of stigma among males and females.
Epilepsy; what do Saudi's living in Riyadh know?

- To investigate the level of public awareness, attitudes & knowledge of epilepsy in the Saudi population in Riyadh – KSA

- A survey consisting of 19 questions pertaining to epilepsy awareness was distributed to Saudi citizens living in Riyadh older than 15 years of age in malls, supermarkets, health clubs, mosques, universities and schools

- 6756 / 7078 (95%) respondents who completed the questionnaire had heard about epilepsy

- 3024 (42.7%) had witnessed a seizure

- 5164 (73%) would allow their children to interact with an epilepsy pt.
Epilepsy; what do Saudi's living in Riyadh know?

- 5382 (76%) respondents would not want their children to marry an epileptic pt
- 1004 (14.2%) believed that epilepsy was infectious
- 574 (8.1%) believed that epilepsy was a mental illness
- 1509 (21.3%) respondents were not aware of any cause of epilepsy
- 3493 (50.6%) would not seek medical advice if they had epilepsy
- 2221 (31.4%) did not know how to deal with a seizure
- 6554 (92.6%) did not know that surgery was a treatment option for epilepsy
- 3237 (45.7%) would not abide by a physician's advice not to drive

The effect of age and level of education were statistically significant on most of the study variables.

Publications


The Global Burden of Epilepsy

- Epilepsy affects approximately 70 million people of all ages throughout the world

- Epilepsy affects all ages, races & social classes with no geographic, or national boundaries

- The impact of epilepsy on the pt., the family and the community

- The burden of epilepsy is due to:
  - Physical hazards of epilepsy
  - Psychosocial consequences such as the stigma, unemployment, no schooling, no marriage, increased levels of anxiety, depression & poor self-esteem compared with people without this condition.

De Boer HM. et al, Epilepsy Behav. 2008 May;12(4):540-6
Epilepsy Burden in the WHO Eastern Mediterranean Region

- The “treatment gap”
- The limited availability of AEDs
- Limited number of trained health care providers
- Limited advanced epilepsy centers for advanced epilepsy management & epilepsy surgery
- Economic barriers
- Limited health care planning & lack of epidemiological data

domains of burden

- **uncontrolled seizures**
  - injuries
  - medications
  - “sword of Damocles”
- **epilepsy comorbidities**
  - depression
  - anxiety
  - attention problems
  - learning problems
- **stigma, limitations**
  - family-initiated
  - self-initiated
  - school initiated
  - employer initiated
  - society initiated
- **neurologic deficits**
  - cognitive
  - motor
EASTERN MEDITERRANEAN DECLARATION ON EPILEPSY

Under the aegis of the Global Campaign Against Epilepsy of the World Health Organization (WHO), International League against Epilepsy (ILAE) and International Bureau for Epilepsy (IBE), a meeting "Epilepsy as A Public Health Concern in the Eastern Mediterranean Region" was held in Cairo, Egypt, on 3 and 4 March 2003. Professionals from Health and Social Sciences sectors and representatives from universities coming from the member states of the Eastern Mediterranean Region unanimously agreed to the following Declaration:

CONSIDERING THAT:
- epilepsy is the most common serious chronic brain disorder, estimated to affect at least 50 million people in the world of which at least 4 million live in the Eastern Mediterranean Region,
- contrary to many misconceptions, epilepsy is a brain disorder with natural causes and requiring medical treatment,
- it is often not realised that epilepsy is treatable, and that most people with epilepsy can lead productive lives as a result of relatively inexpensive, cost-effective treatment,
- in parts of the Eastern Mediterranean Region many people, especially in rural areas, have no access to appropriate healthcare provisions and treatment,
- general information about epilepsy, trained expertise, diagnostic facilities, antiepileptic drugs and surgery are not available for or affordable by many people with epilepsy, for geographic, financial, cultural or communication reasons,
- epilepsy has serious physical, psychological and social consequences for the afflicted and their families,
- the impact of epilepsy is most severe in children and adolescents,
- epilepsy does not receive adequate attention in existing national health plans in many countries,
We call on the governments of the member states of the Eastern Mediterranean Region, national and regional, public and private organisations, all health care providers, and the general public to join us in taking strong and decisive action to meet the objectives of the Global Campaign Against Epilepsy of the WHO/ILAE/IBE “Epilepsy: Out of the Shadows”.
Specifically we urge action to:

- address the needs with respect to epilepsy in terms of prevention, access to trained personnel, modern diagnostic equipment, antiepileptic medication, surgical treatment where necessary, and social integration,
- include antiepileptic drugs in the list of essential drugs in all countries, and make them constantly available to avoid the serious consequences of treatment interruptions,
- educate and train health care and other relevant professionals and volunteers on all levels of health care about epilepsy,
- educate those affected by epilepsy, their families and the general public about epilepsy as a universal neurological condition, to eradicate misconceptions, and empower the affected to seek appropriate treatment and improve their quality of life,
- eliminate discrimination in all spheres of life, particularly concerning school and employment,
- encourage the public and private sectors and NGO's to get involved in the local activities of the Global Campaign against Epilepsy,
- encourage basic and applied research on epilepsy as an integral part of epilepsy services on all levels,
- proclaim a National Epilepsy Day,
- encourage regional and international co-operation.

CAIRO, March 04, 2003
General Principles of Epilepsy Management

- Treat the first onset seizure when the risk of recurrence is 60% or more
- Use a single drug whenever possible
- Start low and go slow
- Carbamazepine, phenytoin, & valproic acid are the first-line agents among most specialists for focal epilepsies
- Gabapentin, lamotrigine, oxcarbazepine, tiagabine, topiramate & levetiracetam are new anticonvulsants for treatment of focal epilepsies

Why do we do clinical trials?

- The American Public looks to its government for assurance that therapies developed to treat diseases are both SAFE and EFFECTIVE.

- The Food and Drug Administration (FDA) is charged with ensuring that safety and effectiveness are proven before a drug is put on pharmacy shelves, or before a device is marketed.

- They are also responsible for LABELING drugs so that the public is aware of risks and benefits.

- There are very strict rules that govern the conduct of clinical trials to determine safety and efficacy (effectiveness).

- Without clinical trials, no new therapy would be marketed!
Anti-seizure drugs

- All available therapies only treat symptoms of epilepsy (seizures)

- We now call drugs that only address seizure symptoms “Anti-seizure drugs” (ASD’s)

- Most current clinical trials are for testing of ASD’s

- Almost every person with epilepsy takes at least one ASD
Timeline: ASD approvals by FDA since 1990

- Ezogabine (Potiga™)
- Eslicarbazepine (Zebinix™)
- Perampanel (Fycompa™)
- Clobazam (Onfi™)
- Topiramate (Topamax™)
- Oxcarbazepine (Trileptal™)
- Tiagabine (Gabitril™)
- Lacosamide (Vimpat™)
- Lamine (Zonegran™)
- Levetiracetam (Keppra™)
- Gabapentin (Neurontin™)
- Felbamate
- Vigabatrin (Sabril™)
- Zonisamide (Zonegran™)
- Lamotrigine (Lamictal™)
- Pregabalin (Lyrica™)
- Rufinamide (Banzel™)
- Brivaracetam (Rikelta™)
- Levetiracetam (Keppra™)

http://www.accessdata.fda.gov

Not approved
ASD’s: How do we make progress?

- **Revolutionary Drugs**
  - Drugs that work with new mechanisms never tried before
  - *Expectation:* They will control seizures that existing drugs can’t control e.g. Perampanel

- **Evolutionary Drugs**
  - Improve on existing drugs
  - *Expectation:* We can eliminate some of the problems/side effects of good drugs, without reducing their effect on seizures e.g. Rikelta (brivaracetam) Stedesa (eslicarbazepine acetate)
Is That All

- There is a desperate need for
  - Drugs that prevent epilepsy
  - Drugs that modify or treat underlying disease
    - True antiepileptic drug
  - Drugs that address co-morbidities such as cognitive disturbance, mood disorder, anxiety
Conclusions

- Several countries in the Arab world are yet to have fundamental data on epilepsy that influence strategic planning to overcome the epilepsy burden & treatment gap
- The prevalence of epilepsy is far higher than what has been previously reported for this region
- The regional estimate of the median incidence of epilepsy suggests that the rate is similar to other regions such as North America
- Urgent need to standardize methods, initiate systematic investigations, test interventions, and quantify many of the Arab world-specific epilepsy risk factors
The future

- Need active pipeline with good compounds moving through
- Need better trial designs
  - Shorten placebo period?
  - Weed out effective drugs from non-effective
  - Improve risk-benefit
Thank you