

Epilepsy in India I: Epidemiology and public health

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Abstract

Of the 70 million persons with epilepsy (PWE) worldwide, nearly 12 million PWE are expected to reside in India; which contributes to nearly one-sixth of the global burden. This paper (first of the two part series) provides an in-depth understanding of the epidemiological aspects of epilepsy in India for developing effective public health prevention and control programs. The overall prevalence (3.0-11.9 per 1,000 population) and incidence (0.2-0.6 per 1,000 population per year) data from recent studies in India on general population are comparable to the rates of high-income countries (HICs) despite marked variations in population characteristics and study methodologies. There is a differential distribution of epilepsy among various sociodemographic and economic groups with higher rates reported for the male gender, rural population, and low socioeconomic status. A changing pattern in the age-specific occurrence of epilepsy with preponderance towards the older age group is noticed due to sociodemographic and epidemiological transition. Neuroinfections, neurocysticercosis (NCC), and neurotrauma along with birth injuries have emerged as major risk factors for secondary epilepsy. Despite its varied etiology (unknown and known), majority of the epilepsy are manageable in nature. This paper emphasizes the need for focused and targeted programs based on a life-course perspective and calls for a stronger public health approach based on equity for prevention, control, and management of epilepsy in India.

Key Words

Aetiology, control, epilepsy, epidemiology, etiology, gender, incidence, prevalence prevention, risk factors, urban-rural differentials

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Introduction

Epilepsy is the second most common and frequently encountered neurological condition that imposes heavy burden on individuals, families, and also on healthcare systems. As per a recent study, 70 million people have epilepsy worldwide and nearly 90% of them are found in developing regions.^[1] The study also estimated a median prevalence of 1.54% (0.48-4.96%) for rural and 1.03% (0.28-3.8%) for urban studies in developing countries. With a conservative estimate of 1% as prevalence of epilepsy, there are more than 12 million persons with epilepsy (PWE) in India, which contributes to nearly one-sixth of the global burden. Though existing for centuries and well-known for more than 2,000 years (as described by Hippocrates), it is

only in recent years that epilepsy has attracted the attention of the medical community. Consequently, efforts are being made for better understanding of the disease and also to organize comprehensive services. In order to organize preventive, promotive, curative, and rehabilitative services for PWE (the public health approach); understanding the burden, distribution, risk factors, and determinants of epilepsy through epidemiological approaches becomes crucial.

The purpose of the present review is to bring together available information on the distribution and determinants of epilepsy through comprehensive review of published research from India. The review undertaken in two parts provides a complete understanding of epilepsy with part 1 focusing on disease, risk factors, and causes; while part 2 focuses on impact, burden, and program-related aspects.

Data sources and searches

A systematic literature search was performed for English language literature with a combination of electronic and manual methods. Databases searched included PubMed, Medline, Ebscohost, and Google Scholar. The keywords and Medical Subject Headings (MeSH) used for electronic search were "epilepsy" combined with each of the

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following: "epidemiology", "prevalence", "incidence", "mortality", "morbidity", "aetiology", "risk factors", "infections", "neurocysticercosis", "traumatic brain injuries", and "febrile seizures". The above search words were combined with other search words "India", "South Asia", "developing countries", "tropical countries", "West Asia" using Boolean operator "AND" for retrieving studies related to India. Manual search was done from National Institute of Mental Health and Neurosciences (NIMHANS) library for those articles whose full text was not available electronically. Publications not available in the public domain were obtained by contacting the authors directly. Reference lists of the identified articles were snowballed and the relevant articles, abstracts, and book chapters were reviewed further.

In this review, all epidemiological studies on epilepsy (from 1950 to July, 2014) from India have been included. Studies included are predominantly population based, published in peer-reviewed journals, that used valid study instruments, standard definitions, and methodology with adequate information on sample size, age and gender distribution, classification if any, along with diagnostic information were preferred for inclusion. Some studies from outside India, school based, and those from medical care settings that are relevant to the current scenario were also included. Case reports, clinical trial studies, animal studies, articles that focused exclusively on specific forms of epilepsy (e.g., electroclinical syndrome), specific etiologic categories of epilepsy (genetic/structural/provoked), and seizures were excluded. The initial search retrieved 1,059 records. After exclusion, 147 full text records and references from six reviews were reviewed for relevance [Figure 1]. Studies were classified and stored in the respective databases based on the subthemes, which were then abstracted into respective tables that included information on author, year of publication, place of study, study setting, study sample, diagnostic tool, prevalence, incidence, and other remarks. Recent estimates on disability-adjusted life years (DALYS) were arrived by analyzing the data of Global Burden of Disease (GBD) 2010 from the Institute of Health Metrics and Evaluation.^[2]

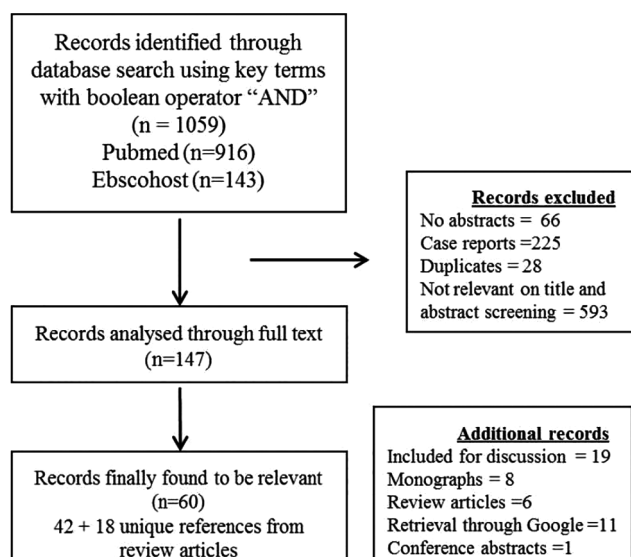


Figure 1: Flowchart of study selection

Methodological Issues

Most recently, the International League against Epilepsy (ILAE) has revised its conceptual definition of epilepsy to an operational definition to bring the term in concordance with common usage. Accordingly, epilepsy is defined as a disease of the brain with any of the following conditions: i. At least two unprovoked (or reflex) seizures occurring >24 h apart; ii. one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years; and iii. diagnosis of an epilepsy syndrome.^[3]

From a classification perspective, ILAE has moved from validation of history; neurological or clinical evaluation; to the proposed multiaxial classification using five level or axes namely ictal semiology, seizure type, epilepsy syndrome, epilepsy etiology, and impairment.^[4] Even though the proponents and opponents of this classification method debate fiercely on its broad applications, the problems of definition exist in this classification and many strongly believe that it is still not best suited for population-based epidemiological studies; thus reemphasizing the need for case definition, which is the central pillar of epidemiological research.^[5] Despite these merits and demerits, epilepsy epidemiology has been making significant strides to refine methodological issues in India over the year.

From a methodological perspective, differences exist across the studies due to varying sample sizes, data collection personnel, nature of the population (urban or rural), duration of study, data collection tools (questionnaires and interviews), and other factors.^[6] From a diagnostic perspective, a good history by an observant witness remains the hallmark in the diagnosis of epilepsy. Earlier, the diagnosis of epilepsy was established by non-neurologists (medical or trained non-medical staff) or through a two-step process of screening and diagnostic evaluation, which at times has given rise to fallacious results due to false positives and false negatives. Even though some investigative procedures have been used in a few studies, significant limitations exist in India as such facilities are not available in rural areas and are also not reliable in the absence of specific history.

It is important to differentiate acute symptomatic seizures from unprovoked seizures (epilepsy) in order to systematically classify cases and determine prognosis. Acute symptomatic seizures are events, occurring in close temporal relationship with an acute nervous system insult, which may be metabolic, toxic, structural, infectious, or due to inflammation. Acute symptomatic seizures differ from epilepsy in several important aspects. Unlike epilepsy, the proximate cause, temporal sequence, biological plausibility, and dose effect of acute symptomatic seizures are clearly identifiable to ascertain the cause. Acute symptomatic seizures are not necessarily characterized by a tendency for recurrence and have better prognosis, thus exempting them from the criteria of enduring predisposition to seize for epilepsy.^[7] As sophisticated skills and techniques are required to distinguish acute symptomatic seizures from unprovoked seizures, most of the epidemiologic studies relying on field surveys have included such seizures

as “epilepsy”, or failed to distinguish these from unprovoked seizures.^[8,9] If all people with acute symptomatic seizures are categorized as having epilepsy, it would add to the burden and stigma, and hence this distinction is important. Thus, the results of such epidemiological studies on epilepsy need to be appraised and interpreted with caution.

Despite all these limitations, epidemiological research on epilepsy in India has progressed significantly in terms of methodology, data analysis, and management along with interpretations of data.

Epilepsy: Global Scenario

At the global level, it is estimated that nearly 70 million people suffer from epilepsy and the prevalence of epilepsy across the globe is estimated to be 5-9 per 1,000 population.^[1,10] As per the GBD analysis for 2010, epilepsy accounted for 0.7% of the global burden or more than 17 million DALYs and nearly 90% of these were reported from low and middle-income countries (LMICs). DALYs across the globe has varied from 6.2 million in Africa to as low as 1.6 million in the European region with southeast Asia contributing for 3.2 million DALYs; an increase from 0.3 to 0.5% during 1990-2010 [Figure 2]. Within the southeast Asia region, the prevalence of epilepsy varied from 2 to 10 per 1,000 population and more than half of the total DALYs due to epilepsy (as estimated from GBD 2010) were accounted from India [Figure 3].^[2] This huge burden from India can probably be attributed to large population, lower income and education, sociocultural prejudices, inadequate resources, competing infectious and noncommunicable diseases, and the low importance given for public health aspects of epilepsy.

Epilepsy in High-Income Countries (HICs)

The existence of well-established health information and medical record systems along with countrywide census allow for accurate estimates of epilepsy burden in the HICs. The prevalence of epilepsy in HICs has varied from 4 to 7 per 1,000 population.^[11] Many countries have reduced the burden due to earlier and prompt response with significant emphasis on prevention of conditions that lead to epilepsy, besides the socioeconomic progress.

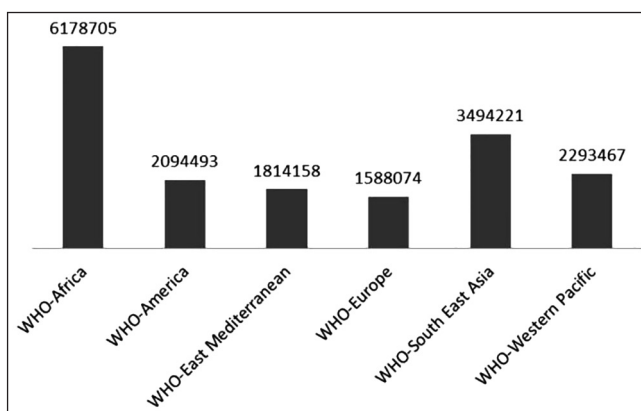


Figure 2: Disability-adjusted life years (DALYs) due to epilepsy among six WHO regions (GBD 2010). WHO = World Health Organization, GBD = Global Burden of Disease

Epilepsy in India

Prevalence

The prevalence of epilepsy is a strong indicator reflecting the presence of epilepsy (in the past or at a given point of time) indicating the number of people requiring services. Earlier, epilepsy was considered a mental and behavioral problem, and hence the initial studies on epilepsy were carried out by psychiatrists as a part of psychiatric morbidity survey using locally developed study instruments.^[12-21] Methodological issues mentioned earlier prevailed in all these studies. With advances in diagnosis and management in the neurological sciences, there was a transitional shift with studies on epilepsy carried out as a part of neuroepidemiological surveys on large population by a two-stage process. This involved an initial screening by trained non-professionals followed by diagnostic confirmation by professionals using the standardized protocol and study instruments. Over time, there has been a notable shift in the areas of study instruments, case ascertainment, and case definition. Case definitions of International Classification of Diseases (ICD), World Health Organization (WHO),^[18,22] and others (Hauser and Kurland^[23]) that were used initially are being replaced with the adoption of ILAE definition.^[24] In recent times, there have been studies focusing exclusively on epilepsy and even epilepsy registries have been established in India.^[25] These developments have helped in better understanding of the epidemiology of epilepsy in the development of programs and services. Recently, a three-stage survey methodology was used for detecting active convulsive epilepsy in population-based studies in health and demographic surveillance systems. Even though, this was found to be cheaper than a two-stage survey, it has low sensitivity and cannot be replicated in many places.^[26]

In countries with better access to healthcare and good recording system, various newer methods, data sources, and techniques have been used to understand the epidemiology of epilepsy. Besides two-stage methods and surveillance, three-stage method (field screening by neurologist, neurological evaluation at hospital, and EEG confirmation at hospital) and audit of epilepsy services were used.^[27-29] Various sources of data like coded medical records,^[30] national or regional registers,^[31] general practice record,^[32] indexed record filing system (medical records linkage system),^[33] hospital records (inpatients, outpatients, and electroencephalography),^[34] and prescription database^[35,36] were used to identify the study population. In some studies,

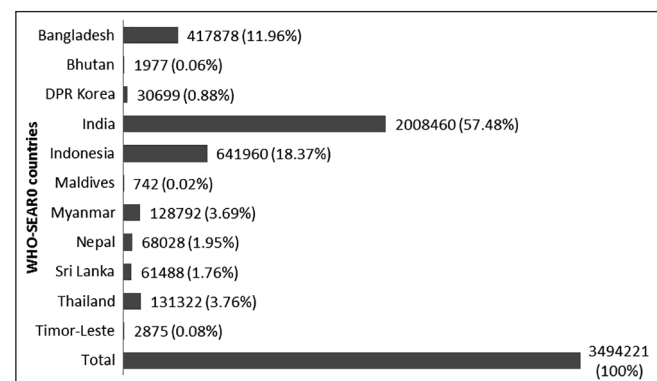


Figure 3: DALYs due to epilepsy in Southeast Asia (GBD 2010). SEARO = South-East Asia Regional Office

community sources like insurance and sickness funds have been used to measure disease prevalence (more often in the occupational groups).^[37,38] In some countries with universal healthcare systems, administrative data of an individual healthcare from hospitals, clinics, and physician offices can be linked to study the epidemiology of epilepsy.^[39] Some studies have used multiple sources of information like key informant (teachers, health workers, religious leaders, and traditional healers) to improve the sensitivity of case ascertainment.^[40] Data collection using diagnostic epilepsy interviews from computer-assisted telephonic interview (CATI)/computer-assisted personal interview (CAPI) and data analysis using imputation techniques were also used in some studies.^[41,42] In most recent times, capture-recapture methods have been used to estimate the prevalence of epilepsy by cross-referencing information from multiple sources.^[43,44] Presently, the limited availability and content of different data sources restrict the application of some of the newer methods in Indian setting.

Several studies in India that have shown varying prevalence rate at different times and places are shown in Tables 1a-c. Temporal trends and higher mortality rates have to be considered besides the methodological issues while interpreting the results from earlier studies which invariably reported lower prevalence rates. Excluding the study, which reported a 5-year period prevalence of 22.2 per 1,000 population among children aged 8-12 years^[71], the prevalence rate of epilepsy among adults and elderly varied from 1.2 to 11.9 per 1,000 population. Some studies have reported prevalence of active epilepsy defined as the number of individuals with epilepsy per thousand population at the time of study,^[40,58,60,63] while some reported on lifetime prevalence which includes anyone who developed epilepsy prior to the study.^[24]

Few studies reported the prevalence rate adjusted for standard population, while Mani *et al.*, and Pal *et al.*, provided the prevalence rate adjusted for survey sensitivity.^[24,40,60,63] During 1980s, Gourie-Devi *et al.*, reported a prevalence of 5.6 per 1,000 for rural and 2.5 per 1,000 for urban area (overall - 4.6 per 1,000) from a mixed population of Gowribidanur in Karnataka, while Koul *et al.*, reported a prevalence of 2.5 from the rural population of Kuthar valley in Kashmir.^[72,53] In 1990s, Mani *et al.*, reported a lifetime prevalence of 5.4 per 1,000 among the rural population of Yelandur in Karnataka, while Radhakrishnan *et al.*, reported a prevalence of 4.9 per 1,000 from the urban population in Kerala.^[24,60] During 2000s, the largest Bangalore Urban Rural Neuro-Epidemiological Survey (BURNs) in Karnataka by Gourie-Devi *et al.*, provided a prevalence rate of 5.8 per 1,000 for urban and 11.9 per 1,000 for rural (overall - 8.82 per 1,000), while Das *et al.*, reported a prevalence of 5.7 per 1,000 for the urban population of Kolkata.^[70,59] Interestingly, the prevalence rate within a defined region (Karnataka) as shown by two studies at an interval of 20 years has shown a rising trend from 5.6 to 11.9 per 1,000 for rural population and 2.5 to 5.7 per 1,000 for urban population (an overall prevalence varying from 4.6 to 8.8 per 1,000).

To develop a better understanding of prevalence issues, meta-analysis approaches are helpful; however, there are very few studies. Reddy and Chandrasekhar analyzed data from 13 psychiatric epidemiological studies (1967-1995) that yielded a prevalence estimate of 4.4 per 1,000 population (3.7-5.1 per

1,000 population).^[75] The estimated rural rate was 4.8 per 1,000 and the urban rate was 2.5 per 1,000, while the prevalence rate estimated for male and female was 4.9 per 1,000 and 3.9 per 1,000, respectively. Sridharan and Murthy included 20 studies (majority being psychiatric epidemiological studies) and using a pooled sample of 598,910, arrived at a prevalence of 5.34 per 1,000 (4.25-6.41 per 1,000), after correcting for interstudy variation.^[76] The estimated rural rate was 5.5 per 1,000 and the urban rate was 5.1 per 1,000; while the prevalence rate estimated for male and female was 5.9 per 1,000 and 5.5 per 1,000, respectively. Though the prevalence estimates from both the meta-analysis have not included larger population-based neuroepidemiological studies, the estimates of prevalence are comparable with the estimates of Mani *et al.*, BURNs, Radhakrishnan *et al.*, and Das *et al.*^[24,59,60,70]

Amidst these different rates, the interpretation and extrapolation of the data to the vast country like India needs to be made with caution in the presence of few well-designed, multicentric, population-based studies conducted using standardized protocols. Among recent studies in the past 20 years, the prevalence estimates were found to range from 3.0 to 11.9 per 1,000 population, when either standard study instrument or ILAE case definition was used among the general population.^[23,24,40,45,46,48,54,56,60,61,68,70] It is important to recognize that these prevalence estimates of India were comparable with rates of developed countries (2.7-12.4 per 1,000) and the problem is as similar as in HICs of the world.^[1]

Incidence

The rate at which the new cases are developing in the community during a defined time point (incidence rate) is helpful for organizing preventive services and estimating the true burden. But there is an inherent complexity and resource intensity involved in conducting such incidence studies. Data from HICs reported the incidence rates varying from 0.4 to 0.7 per 1,000.^[10] In 1993, Hauser *et al.*, reported an incidence rate of 0.44 per 1,000 per year from Rochester through a 50-year follow-up period.^[77] Among the developing countries, an annual incidence rate of 0.73 per 1,000 population per year was reported from a rural Tanzanian district in Africa, while it varied from 1.2 to 1.9 per 1,000 population per year in the Andean region of Ecuador.^[8,78] These differences in incidence rate were largely explained by the inherent regional and socioeconomic differences and the variations in the inclusion of epilepsy subtypes and methodological issues.

Studies from India have reported incidence rates varying from 0.2 to 0.6 per 1,000 population [Table 2]. The incidence rates reported from India are comparable with developed countries and lower than most of the developing countries which ranged from 1.0 to 1.9 per 1,000 per year.^[10,81] Saha *et al.*, reported an incidence rate of 0.42 per 1,000 per year from a 5-year longitudinal study in rural West Bengal, which was quite similar to the incidence rate of 0.49 per 1,000 per year reported by Mani *et al.*, from the 1-year Yelandur study in rural area.^[24,79] However, the incidence rates reported from urban regions were quite variable with higher rate of 0.60 per 100 per year from an urban resettlement colony compared to 0.27 per 1,000 per year from urban area.^[56,80] The heavily concentrated migrant rural population in the urban resettlement colonies and slums in recent years might be one of the possible reasons for high incidence rate reported in urban

Table 1a: Prevalence of epilepsy in rural population of India

Author	Year of publication	Place of study	Study sample	Study instrument	Prevalence per 1,000	Remarks
Goel <i>et al.</i> ^[45]	2009	Dehradun, Uttrakhand	14,086 subjects through H-H survey of randomly selected villages	Modified WHO protocol	7.5	Screening followed by neurologic examination with the use of CT and EEG. Prevalence rate was 6.5/1,000 when neurocysticercosis was excluded
Sureka and Sureka ^[46]	2007	Churu tehsil, Rajasthan	172,442 subjects sampled through H-H survey	Standard validated Placencia's nine questions screening questionnaires	3.0	Case finding through H-H survey along with IEC activities, followed by neurologist confirmation using ILAE case definition
Murthy <i>et al.</i> ^[47]	2004	West Godhavari, Andhra Pradesh	74,086 subjects sample through H-H survey	Clinical assessment	6.2	All cases ascertained clinically had a plain and contrast CT
Saha <i>et al.</i> ^[48]	2003	West Bengal	20,842 subjects through H-H survey	Modified WHO protocol	3.6	Trained professionals screened the population followed by neurologist examination
Pal <i>et al.</i> ^[40]	1998	Bishnupur block, West Bengal	40,574 children aged 2-18 years through H-H survey and key informant interview	Screening questionnaire used in Ecuador	3.2	Prevalence of active epilepsy was 3.2/1,000 as per ILAE case definition and the prevalence was 5.5 (after adjusting for survey sensitivity)
Kokkat and Verma ^[49]	1998	Haryana	8,595 subjects in four adjoining villages through random survey	Elaborate screening instrument on seizure and paralysis	8.0	A cross-sectional survey of four adjoining villages was carried out. Epilepsy, active and inactive were defined
Mani <i>et al.</i> ^[24]	1998	Yelandur, Karnataka	64,963 subjects through H-H survey	Modified ICEBERG (International Community Based Epilepsy Research Group) screening instrument	3.9	Initial screening by paramedical workers followed by neurologist validation using ILAE case definition. The prevalence of active epilepsy, inactive epilepsy, and lifetime prevalence were 4.63, 0.77, and 5.41/1,000, respectively, after correcting for survey sensitivity
Das and Sanyal ^[23]	1996	Malda, West Bengal	37,286 residents through H-H survey	Modified WHO protocol	3.1	Prevalence reported based on screening by non-health professionals
Bharucha <i>et al.</i> [Unpublished]	1996	Vasai, Maharashtra	16,325 students through H-H survey	WHO protocol	4.8	Single, febrile, and symptomatic seizures were excluded
Shaji <i>et al.</i> ^[50]	1995	Ernakulum, Kerala	5,284 subjects through H-H survey	Indian Psychiatric Survey Schedule (Kapur <i>et al.</i> , 1974)	5.1	Initial screening followed by psychiatric examination using ICD-10 criteria
Premarajan <i>et al.</i> ^[51]	1993	Pondicherry	1,115 subjects selected by simple random sampling through H-H survey	Indian Psychiatric Survey Schedule (Kapur <i>et al.</i> , 1974)	1.3	Children less than 13 years were excluded. Initial screening followed by psychiatric examination using ICD-10 criteria
Kapoor and Banerjee ^[52]	1989	Ballabgarh, Haryana	48,798 subjects through H-H survey	Symptom enquiry for convulsions by field workers	4.0	Prevalence of convulsions was 3.2/1,000 in males and 8.5/1,000 in females
Koul <i>et al.</i> ^[53]	1988	Kuthar valley, Kashmir	63,645 residents through H-H survey	WHO protocol	2.47	Initial screening by Anganwadi workers followed by neurologist diagnosis using diagnostic criteria of Hauser and Kurland (1975)
Isaac ^[12]	1987	Multicenter study	H-H survey Bangalore - 35,548 Baroda -39,655 Calcutta - 34,582 Patiala -36,595	Indian Psychiatric Survey Schedule (Kapur <i>et al.</i> , 1974)	Bangalore-7.8 Baroda -1.3 Calcutta-1.7 Patiala- 3.2	A research team of psychiatrist initial screened the population using "symptoms in others" questionnaire followed by detailed evaluation using IPSS
Sachdeva <i>et al.</i> ^[13]	1986	Faridkot, Punjab	1,989 residents through H-H survey	Indian Psychiatric Survey Schedule (Kapur <i>et al.</i> , 1974)	2.5	Initial screening followed by psychiatric examination using ICD-9 criteria

(Continued)

Table 1a: (Continued)

Author	Year of publication	Place of study	Study sample	Study instrument	Prevalence per 1,000	Remarks
Mehta <i>et al.</i> ^[14]	1985	North Arcot, Tamil Nadu	5,941 subjects through H-H survey of randomly selected villages	Indian Psychiatric Survey Schedule (Kapur <i>et al.</i> , 1974)	7.4	Initial screening was followed by psychiatric examination
Bhide ^[15]	1982	Ootacamund, Tamil Nadu	1,658 subjects	Information on study instrument could not be retrieved	9.1	Data could not be retrieved
Kapur and Isaac ^[16]	1978	Bangalore, Karnataka	4,209 subjects through H-H survey	Indian Psychiatric Survey Schedule (Kapur <i>et al.</i> , 1974)	10.4	The study cross-validated the simple inexpensive method of case identification against H-H survey
Murthy <i>et al.</i> ^[17]	1978	Raipur Rani, Haryana	3,500 subjects selected by health staff referral in one village and H-H visit by psychiatrist in other village	Use of vignettes and interviewing of key informants	3.7	Not a true epidemiological study as more than half of the case finding did not come from H-H survey
Nandi <i>et al.</i> ^[18]	1975	Barasat, West Bengal	1,060 subjects through H-H survey	Questionnaire schedule, case record schedule as per ICD (1965 R)	10.4	Case definition as per WHO tech report series (1960)no.185 with minor modification
Sethi <i>et al.</i> ^[19]	1972	Lucknow, Uttar Pradesh	2,691 subjects through H-H survey	Questionnaire for assessment of psychiatric state of the family	2.2	Screening was conducted by team of clinical psychologist, physician with psychiatric training, and social worker followed by psychiatrist examination; sex specific rates: Male (4.1) and female (0)
Elnagar <i>et al.</i> ^[20]	1971	Hooghly, West Bengal	1,383 subjects through H-H survey	Case finding questionnaire	4.3	Case finding was followed by detailed work-up and psychiatrist examination
Gopinath ^[21]	1968	Bangalore, Karnataka	423 subjects through H-H survey	A survey questionnaire giving various symptoms of mental illness	2.4	A team of doctors, psychologists, and social workers interviewed the head of the household and elicited information about presence of these symptoms

WHO = World Health Organization, ICD = International Classification of Diseases, ILAE = International League Against Epilepsy, CT = computed tomography, H-H = house-to-house

resettlement colony. Thus, it is evident that there exists a wide rural-urban gap for incidence of epilepsy with likely hot spots in urban regions due to migrant rural population.

Mortality

Even though mortality from epilepsy is low, various studies from across the world have revealed a higher risk of premature mortality among people with epilepsy.^[82] Given the higher prevalence and incidence along with poor socioeconomic status and higher treatment gap, higher epilepsy related mortality is likely to be more frequent in India. Data is extremely limited on this issue in India due to absence of defined cohort for follow-up studies, poor medical record system, and the weak vital registration system failing to capture precise cause or conditions at the time of death. The commonest causes of death among PWE that are related directly to seizures are injuries, status epilepticus (SE), and sudden unexpected death in epilepsy (SUDEP). The other causes of death among PWE are certain infections like pneumonia, chronic intoxication with drugs, suicides, cerebral vascular lesions, and other medical conditions.

Mortality data is usually represented by four indices namely specific mortality rate (number of deaths from epilepsy per 1,000

population), proportionate mortality rate (number of deaths from epilepsy per 1,000 total deaths), case fatality rate (deaths from epilepsy per 100 cases), and standardized mortality ratio (SMR; ratio of number of deaths in those with epilepsy to the expected deaths in the people with epilepsy, if they experience the death rates of standard population). The mortality rate of epilepsy reported from western literatures has varied from 1 to 2 per 100,000 population and are often influenced by the nature and characteristics of death certificates.^[83] Among the hospital-based studies in India, a case fatality rate of 29% was reported among 117 hospitalized patients with SE, while another study reported a mortality rate of 29.7% among SE patients with central nervous system infection.^[84,85] Abnormality on neurological examination, older age group, refractoriness, and male sex were associated with higher mortality besides other factors like socioeconomic status, time since diagnosis, higher seizure frequency, prolonged seizure duration, delay in initiating treatment, poor Glasgow Coma Scale (GCS) score at admission, and poor drug compliance.^[86,87] Earlier, only two community-based studies on Parsi population in India reported the epilepsy-related mortality.^[88] The study from Mumbai urban Parsi population reported a SMR of 0.76, while the study from Vasai Parsi rural population reported a SMR of 7.8 for 5-year follow-up and 3.9 for 10-year follow-up. Recently, an annual mortality rate of 7.6 per 100,000 per year and a SMR of 2.58 was reported for epilepsy

Table 1b: Prevalence of epilepsy in urban and semiurban populations in India

Author	Year of publication	Place of study	Study sample	Study instrument	Prevalence per 1,000	Remarks
Singh <i>et al.</i> ^[54]	2012	Jamalpur, Punjab	15,750 subjects through H-H survey	Modified WHO protocol	7.2	Initial screening, followed by epileptologist confirmation using ILAE case definition. Inactive epilepsy, nonepileptic seizure, and single seizure were excluded
Raina <i>et al.</i> ^[55]	2011	RS Pura, Jammu	3,966 children <10 years identified through H-H survey	Modified WHO protocol	2.0	Initial screening by Anganwadi workers followed by neurologist examination using ILAE case definition
Banerjee <i>et al.</i> ^[56]	2010	Kolkata, West Bengal	52,377 subjects through two-stage H-H survey of stratified random sample	NIMHANS screening questionnaire	5.7	Initial screening followed by neurologist examination using ILAE case definition
Banerjee <i>et al.</i> ^[57]	2009	Kolkata, West Bengal	16,979 subjects ≤19 years selected through two-stage H-H survey of stratified random sample	NIMHANS screening questionnaire	7.0	Initial screening by trained field workers followed by neurologist examination using ILAE case definition
Das <i>et al.</i> ^[58]	2008	Kolkata, West Bengal	5,430 elderly aged>60years selected through two-stage H-H survey of stratified random sample	NIMHANS screening questionnaire	2.6	Initial screening followed by neurologist examination using ILAE case definition. Prevalence of active epilepsy was reported
Das <i>et al.</i> ^[59]	2006	Kolkata, West Bengal	52,377 subjects selected through two-stage H-H survey of stratified random sample	NIMHANS screening questionnaire	5.6	Initial screening by field workers and neuropsychologist followed by neurologist examination using ILAE case definition. The prevalence was 7.6 (after correction for survey sensitivity) and 5.2 (after age standardization)
Radhakrishnan <i>et al.</i> ^[60]	2000	Central districts, Kerala	238,102 population belonging to 10 panchayats of Thrissur, Palakkad and Malappuram districts through H-H survey	Modified WHO screening questionnaire	4.9	Survey was carried out in three phase; namely, screening, diagnostic, and confirmation phase using ILAE case definition. Prevalence of active epilepsy was reported. Age-adjusted rate was 4.7/1,000
Gourie-Devi <i>et al.</i> ^[61]	1996	Bangalore, Karnataka	3,040 subjects through two-stage study design	Modified WHO screening questionnaire	7.8	Screening by lay interviewers followed by clinical examination
Sohi <i>et al.</i> ^[62]	1993	Chandigarh	13,968 subjects of urban resettled colony through H-H survey	Information on study instrument could not be retrieved	8.7	Data could not be retrieved
Bharucha <i>et al.</i> ^[63]	1988	Bombay, Maharashtra	14,010 subjects through H-H survey	Modified WHO protocol	4.7	Screening followed by clinical examination in a closed well-educated and affluent Parsi community. The prevalence rate of active epilepsy was 3.6
Sen <i>et al.</i> ^[22]	1984	Kolkata, West Bengal	2,168 subjects in an urban slum through H-H survey	Case detection schedule, case record schedule as per ICD (1965 R)	3.4	Case detection followed by psychiatrist examination with case definition as per WHO technical report series (1960) no.185 with minor modifications
Sethi <i>et al.</i> ^[64]	1967	Lucknow, Uttar Pradesh	1,733 subjects through H-H survey	Questionnaire for assessment of psychiatric state of the family	1.2	Initial screening by physician, clinical psychologist, social worker, and field worker was followed by on spot examination
Surya <i>et al.</i> ^[65]	1964	Pondicherry	2,731 subjects through H-H survey	Mental health screening questionnaire	2.2	H-H survey by social worker in urban slum

WHO = World Health Organization, ICD = International Classification of Diseases, ILAE = International League Against Epilepsy, H-H = House-to-house

Table 1c: Prevalence of epilepsy from mixed (both urban and rural) population in India

Author	Year of publication	Place of study	Sample	Study instrument	Prevalence per 1,000	Remarks
Pandey <i>et al.</i> ^[66]	2014	Chandigarh	3,684 children aged 1-18 years	Modified Placencia's screening questionnaires	6.2	6.99 for rural area, 5.48 for urban area, and 4.07 for active epilepsy. ILAE case definition was used
Shah <i>et al.</i> ^[67]	2009	Kashmir	15,218 children aged 6-18 years	A pre-structured questionnaire	3.2	Rural rate was 3.9 and urban rate was 2.96. ILAE case definition was used
Rajshekhara <i>et al.</i> ^[68]	2006	Vellore, Tamil Nadu	50,617 subjects through cluster sampling	Modified WHO protocol	3.8	Prevalence in the urban clusters more than twice that in the rural clusters (6.23 vs 3.04/1,000). NCC is the cause of nearly one-third of all cases in both the urban and rural regions
Srinath <i>et al.</i> ^[69]	2005	Bangalore, Karnataka	2,064 children aged 0-16 years through stratified random sampling	Multiple screening tools	10 (children aged 0-3 years) 7.0 (children aged 4-16 years)	The screening stage was followed by a detailed evaluation stage with use of ICD-10 DCR criteria. The rates were higher for rural followed by slum and urban
Gourie-Devi <i>et al.</i> ^[70]	2004	Bangalore, Karnataka	102,572 through two-stage stratified random sampling	Modified WHO protocol	8.8	The overall age-adjusted rate was 8.3/1,000. The prevalence was 11.9/1,000 for rural areas and 5.7/1,000 for urban areas
Hackett <i>et al.</i> ^[71]	1997	Calicut, Kerala	1,172 children aged 8-12 years through two-stage H-H survey	Modified Rose's screening questionnaires	22.2	Five-year period prevalence was reported
Gourie-Devi <i>et al.</i> ^[72]	1987	Gowribidanur, Karnataka	576,60 subjects through H-H survey	NEPSIG: Modified WHO screening questionnaire	4.6	Screening was followed by clinical examination. The semiurban rate was 2.5/1,000 and rural rate was 5.6/1,000
Mathai ^[74]	1971	Vellore, Tamil Nadu	258,576 subjects through a door-to-door survey	Elaborate checklist on seizure symptoms	8.97	The prevalence was 9.8/1,000 for rural areas and 7.5/1,000 for urban areas
Dube ^[73]	1970	Agra, Uttar Pradesh	29,468 subjects through H-H survey	No objective screening questionnaire	2.3 (active epilepsy) 3.2 (lifetime prevalence)	A team of psychologist, social worker, field investigator, and statistician did the initial screening which was not objective. Suspected cases were confirmed by psychiatrist

WHO = World Health Organization, ICD-10 DCR = International Classification of Diseases, 10th revision, Diagnostic Criteria for Research, ILAE = International League Against Epilepsy, NCC = Neurocysticercosis, H-H = House-to-house

in a 5-year follow-up among the general population in Kolkata.^[56] Overall, the mortality among the rural population with epilepsy was found to be higher than the urban population which probably is linked to access and availability of services.

Epidemiological Correlates

Age

Similar to Hauser *et al.*, who reported a bimodal distribution of epilepsy incidence with peaks during the 1st year of life and in persons aged more than 74 years, Mani *et al.*, and Banerjee

et al., have reported a bimodal incidence with peaks during early childhood and during 70s and 80s of life.^[24,56,77] This bimodal distribution with the second peaking of epilepsy in later years, warrants further investigation to explore the possible association with increasing incidence of stroke and injuries (and its complications) in India.^[56]

With respect to prevalence, Nandi *et al.*, reported a higher prevalence of epilepsy in the 1st decade of life as early as 1970s.^[18] The prevalence rate for children varied from 2.02 per 1,000 to as high as 22.2 per 1,000.^[55,71] Perinatal injury,

newborn distress, head trauma, neonatal hypoglycemia, malnutrition, and neurocysticercosis were reported as important risk factors of epilepsy in Indian children.^[89,90] Later, majority of studies from India reported a higher prevalence during the 2nd decade, while a recent estimate from Raina *et al.*, have reported a higher prevalence in the 4th decade.^[24,55,56,59,60] This changing pattern in the age-specific occurrence of epilepsy might be linked to demographic transition, changing living conditions, improved healthcare services, changing dietary habits (related to neurocysticercosis (NCC)), increasing awareness, and better help-seeking behaviors.

Gender

Except for the recent study by Pandey *et al.*, earlier studies from India reported higher prevalence among males as compared to females [Table 3]. Poor reporting due to cultural factors and differentially higher mortality among female children due to poor care might have contributed to this difference. With the progress of time, this difference appears to have been narrowed. Radhakrishnan *et al.*, reported a prevalence rate of 5.2 per 1,000 for males and 4.7 per 1,000 for females,^[60] while Gourie-Devi *et al.*, reported the rates of 6.1 per 1,000 and 5.2 per 1,000 for males and females, respectively (unpublished data). Similarly, Das *et al.*, reported a prevalence rate of 5.9

Table 2: Incidence of epilepsy in Indian epidemiological studies

Author	Year of publication	Place of study	Study sample	Study instrument	Incidence per 1,000 per year	Remarks
Banerjee <i>et al.</i> ^[56]	2010	Kolkata, West Bengal	52,377 subjects through two-stage H-H survey of stratified random sample	NIMHANS screening questionnaire	0.27	Annual incidence calculated from 5-year follow-up among urban population
Saha <i>et al.</i> ^[79]	2008	Baruipur, West Bengal	20,966 through purposive cluster sampling	Modified WHO protocol	0.42	Annual incidence calculated from 5-year follow-up among rural population
Sawhney <i>et al.</i> ^[80]	1999	Chandigarh	140,000 subjects through H-H survey	Information on study instrument could not be retrieved	0.6	Annual incidence was estimated from 4-year follow-up among urban resettlement colony
Mani <i>et al.</i> ^[24]	1998	Yelandur, Karnataka	64,963 subjects through H-H survey	Modified ICEBERG (International Community Based Epilepsy Research Group) screening instrument	0.493 excluding hot water epilepsy	Annual incidence calculated from 1-year follow-up among rural population

NIMHANS = National Institute of Mental Health and Neurosciences, WHO = World Health Organization, H-H = House-to-house

Table 3: Gender-specific prevalence rates for epilepsy in India

Author	Year of publication	Place of study	Sample	Setting	Prevalence rate for male (per 1,000)	Prevalence rate for female (per 1,000)
Pandey <i>et al.</i> ^[66]	2014	Chandigarh	3,684 children aged 1-18 years	Mixed	4.9	8.0
Raina <i>et al.</i> ^[55]	2011	Jammu	2,209 subjects through H-H survey	Rural	15.4	6.8
Banerjee <i>et al.</i> ^[56]	2010	Kolkata, West Bengal	52,377 subjects through H-H survey of stratified random sample	Urban	6.6	5.2
Banerjee <i>et al.</i> ^[57]	2009	Kolkata, West Bengal	16,979 children <20 years through two-stage stratified random sample	Urban	8.1	5.8
Shah <i>et al.</i> ^[67]	2009	Kashmir	15,218 children aged 6-18 years	Mixed	3.7	3.1
Das <i>et al.</i> ^[59]	2006	Kolkata, West Bengal	52,377 subjects through H-H survey of stratified random sample	Urban	5.9	5.2
Radhakrishnan <i>et al.</i> ^[60]	2000	Kerala	238,102 subjects through H-H survey	Semiurban	5.2	4.7
Mani <i>et al.</i> , ^[24]	1998	Yelandur, Karnataka	64,963 subjects through H-H survey	Rural	4.4	3.4
Shaji <i>et al.</i> ^[50]	1995	Ernakulam, Kerala	5,284 subjects through H-H survey	Rural	4.1	6.1
Nandi <i>et al.</i> ^[91]	1992	Bankura and North 24 Pargana, West Bengal	653 subjects of rural Santal community through H-H survey	Rural	9	3.1
Banerjee <i>et al.</i> ^[92]	1986	Nadia, West Bengal	771 subjects of urban Santal community through H-H survey	Urban	5.1	0
Mehta <i>et al.</i> ^[14]	1985	Vellore, Tamil Nadu	5,941 subjects through two-stage stratified random sampling	Rural	9	5.8
Sen <i>et al.</i> ^[22]	1984	Kolkata, West Bengal	2,168 subjects through H-H survey	Urban slum	3.6	2.9

H-H = House-to-house

per 1,000 for males and 5.2 per 1,000 for females.^[59] This study also reported higher prevalence for men in the younger age group and women in the older age group. Thus, despite the narrowing of gender differentials, the prevalence and incidence of epilepsy in males are still higher than females requiring further exploration. Among females, it is estimated that there are about 2.73 million women with epilepsy (WWE) in India with 52% of them belonging to the reproductive (15-49 years) age group.^[93]

Urban-rural differences

Clearly the rural rates outnumbered the urban rates in almost all of the studies at any point of time in India. This clearly highlights the need to focus and strengthen services in rural areas and to examine the reasons for the differences. The BURNs study from Bangalore and surrounding region reported a nearly two times higher prevalence of epilepsy in rural areas as compared to the urban areas.^[70] Similarly, a striking urban-rural difference with higher rural rates has been reported for incidence of epilepsy also. An annual incidence rate of 0.42 per 1,000 per year was reported for rural population by Mani *et al.*, as compared to 0.27 per 100,000 per year for urban population by Banerjee *et al.*^[24,56] Besides social issues, the possible reasons for this observed difference could be attributed to lack of facilities for good antenatal/postnatal care, birth injury, malnutrition, systemic and central nervous system (CNS) infections, high rates of neurotrauma, and also limited services in rural areas. Infections other than NCC and exposure to toxins such as lead and other pollutants could also be contributory in nature.^[68]

Socioeconomic Correlates (Education, Occupation, and Income)

Detailed data on occurrence of epilepsy as per education, occupation, and income are limited due to difficulties in measuring these variables in field studies. However, socioeconomic factors by its strong association with birth trauma, infections, poor nutrition, poor hygiene, and poor health-seeking behavior influence the risk of epilepsy and its outcome. Even among the few incidence studies, the socioeconomic parameters were rarely assessed for valid association. In an earlier hospital-based study, 71.6% of PWE had education up to middle school; probably linked to differentially higher representation from urban areas.^[94] With regard to education, people who have completed up to high school education in slum area had higher rates for epilepsy.^[56] A recent hospital-based study on 196 cases in Karnataka has showed that more than 80% patients belonged to low socioeconomic status and were unskilled workers.^[95] Findings from these hospital-based studies should be interpreted with caution due to differential health-seeking pattern of poor people in the public sector hospitals. In a recent community based study by Banerjee *et al.*, higher proportion of epilepsy was reported among manual workers and those who had a monthly income between 2,000 and 5,000 INR both in the slum and non-slum area.^[56] However; across the globe, low socioeconomic status, low income, and less education are regarded as risk factors for epilepsy. These factors have a direct impact on hospitalization, uncontrolled seizures, and drug-related side effects among the PWE.^[96,97]

Etiology

A complex interaction between genes and environment was found to be involved in the early pathogenesis of epilepsy. The etiology of primary and secondary epilepsy varies significantly with the causes being unclear for primary epilepsy and, many conditions being causative for secondary epilepsy. Among the secondary seizures, conditions like brain injury and hypoxia due to poor medical care at the time of delivery, malnutrition and infection in the mother during pregnancy, traumatic/acquired brain injuries, and certain metabolic conditions play a major role as risk factors. A population-based, case-control study in India reported family history of the epilepsy, antecedent history of febrile seizures, birth by complicated labor, and neonatal seizures as strong independent predictors of epilepsy.^[98] These seizures are of special relevance and importance in India as majority of them are potentially preventable in nature.

The population-based, case-control studies in India found febrile seizures to be a significant risk factor for developing epilepsy.^[80,99] A study on febrile seizures in a south Indian district found that 2.7% of children with febrile seizures had developed epilepsy.^[100] The risk of developing epilepsy in a child with febrile seizures was further associated with family history of epilepsy, cerebral palsy, or low Apgar scores. It should be noted that these risk factors are different from the risk factors associated with recurrence of febrile seizures (age <18 months, family history of febrile seizures, and multiple febrile seizures during the first episode). Also, there exists a complexity in the cause-effect relationship between febrile seizures and epilepsy.^[101]

The etiology of epilepsy is directly linked to seizure types and the majority of hospital-based studies have recorded a higher frequency for partial epilepsies: 57 and 80%.^[102,103] While the community-based studies recorded a higher frequency for generalized seizures ranging from 79 to 54.5%.^[24,63,53] Within generalized epilepsy, tonic-clonic was the commonest type. The overlooking of most striking symptom by the respondents and interviewer for the generalized seizures and misclassification of partial seizures with secondary generalization as generalized seizures in community studies could be the possible reason for observed differences between hospital- and community-based studies.

Neuroinfections

Despite significant advances in prevention and control of communicable and infectious diseases in India, infections are still a major cause and remain a challenge to policy makers in the country. The most common mechanism causing epilepsy in these conditions is attributed to increased neuronal excitability due to proinflammatory signals induced by nervous system infections. Acute symptomatic seizures are commonly seen as a manifestation of bacterial meningitis (*Meningococcus*, *Pneumococcus*, and *Haemophilus influenzae*), CNS tuberculosis, viral encephalitis (Japanese encephalitis, herpes simplex type I, dengue, and human immunodeficiency virus (HIV)), malaria, NCC, and other emerging and reemerging infectious diseases. Some parts of India are known epidemic regions of Japanese encephalitis where epilepsy occurs as a result of long-term sequelae. A study on 100 autopsied cases of SE from a tertiary care center in India, identified neuroinfections and stroke as

important etiological factors.^[87] However, there is a scarcity of data on epilepsy associated with CNS infections due to lack of advanced investigative facilities in India. A hospital-based study from south India, among 1,117 established cases identified cerebrovascular disease as a major cause in 26% of the cases followed by neuroinfections, birth trauma, and cerebral tumors.^[104]

Even though, acute symptomatic seizures (provoked) are the most common manifestation of neuroinfections, NCC, and neurotrauma, the epilepsy (unprovoked seizures) related to these conditions is equally important, especially in a resource-poor setting like India with huge treatment gap. Neuroinfections, NCC, and neurotrauma along with birth injuries are the most frequent causes of secondary epilepsy, especially in developing countries and are potentially preventable with appropriate community interventions.^[105]

Neurocysticercosis (NCC)

The rising prevalence of epilepsy in recent years in developing countries has been attributed to NCC, an infection caused by *Taenia solium* larvae. NCC, once thought of confined to the defined and focal population has now widespread distribution in the general population due to changing dietary habits and lifestyles. Solitary cystic granuloma (SCG) was the most common presentation accounting for more than 60% of NCC in India with more than 90% of patients with SCG presenting with acute symptomatic seizures.^[106] In a series of 500 children with NCC, 94.8% had seizures at presentation.^[107] The relationship between NCC and epilepsy has been explored for long time and debates are still going on about their relationship. Because of the high prevalence of epilepsy and NCC, there exists a cause and incidental relationship between the two.^[108] The prevalence of active epilepsy related to NCC varied from 1.3 to 4.5 per 1,000 population in Indian studies.^[109-112] In a farming community, prevalence of 6.6% was reported for epilepsy and 18.6% for *Taenia solium* infection.^[113] Even though, NCC was reported in nearly one-third of all cases of acute epilepsy in both the urban and rural areas of Vellore, low seroprevalence of systemic cysticercosis was reported among PWE in Kerala.^[68,114] Koul *et al.*, have attributed relative lack of cysticercal infection in the local community as possible reason for their observed low prevalence of epilepsy.^[53] Altogether, nearly one-third of epilepsy were associated with NCC and the cost estimated for treating all the prevalent cases of SCG was to the tune of INR 1.184 billion in 2007.^[115] Even though more advanced investigative facilities are available to facilitate the proper detection of the cases, the studies on NCC are limited in resource-poor settings due to limited availability of neuroimaging and immunological techniques.

Prevalent cases from large community-based studies might have overestimated the NCC-related epilepsy due to contamination by acute symptomatic seizures associated with the transitional phase of NCC.^[47] Prospective cohort studies are needed to clearly examine the association of different evolutive phases of the parasite and the development of seizures in establishing the causal link between epilepsy and NCC.

Neurotrauma

With increasing modernization and motorization, there is a rising trend for secondary seizures or post-traumatic seizures

(PTSS) resulting from road traffic injuries, falls, violence, and industrial accidents. In a study of acquired brain injuries in Bangalore, it was observed that 9% of individuals with traumatic brain injuries (TBIs) continued to have PTSS at 1 year after discharge.^[116] In another prospective hospital-based study from New Delhi, PTSS was observed in 11.4% of the patients with TBIs during the 2-year follow-up.^[117] Majority of PTSS were reported in age groups of 5-44 years, because of the vulnerability of these age groups to injuries. Early PTSS (seen in 4-25% of patients) are observed more common in children, while late seizures (reported in 9-42% of patients) are observed more common in patients of TBI with early PTSS, brain contusion, and subdural hematoma.^[118]

Metabolic conditions

Epilepsy also occurs as a common accompanying condition of certain disorders like brain tumors and other metabolic conditions associated with low calcium, sodium, or blood sugar levels. However, studies on these risk factors of epilepsy in India are very few. Electrolyte and fluid imbalance due to diarrhea and other inborn errors of metabolism such as phenylketonuria or aminoacidurias are the other risk factors for infancy and childhood seizures besides birth injury and brain infections; while in the elderly, stroke is observed as the most common causes of seizures followed by metabolic derangements.^[119] Hypo/hyperglycemia, uremia, hyponatremia, or hypocalcemia, are the common metabolic derangements which provoke seizures among the elderly. It was observed that several risk factors of stroke, such as hypertension were found to be associated with epilepsy independently, without the occurrence of stroke. Dementia particularly Alzheimer, major depression and alcohol abuse were the other risk factors for seizures in elderly.^[120-123]

Natural course and management of epilepsy

The causes and risk factors of epilepsy vary widely, and so the treatment protocol and outcome also. Generally it is known that epilepsy tends to worsen in untreated patients or in whom treatment is initiated late or among those who discontinue. In a series of longitudinal surveys by Nandi *et al.*, among the rural population of West Bengal, no appreciable change was observed in epilepsy status at the end of 1 year, while 45.6% got cured and 9% died at the end of 10 years.^[124,125]

Many studies have demonstrated that patients with fewer seizures before optimal treatment are more likely to achieve complete seizure control.^[126] With regard to outcome, four prognostic groups can be defined; associated with excellent, good, certain, and bad prognosis.^[127] Special therapeutic modalities are required for management of epilepsy among pregnant mothers, and elderly with associated comorbid conditions, SE and refractory epilepsy.^[93,128-130] In a study on "difficult-to-control" epilepsy, onset below 2 years of age, male sex, perinatal insults, and certain seizure types emerged as risk factors for refractoriness.^[131] Despite its varied etiology, and majority of them resulting from unknown causes, it has been shown that epilepsy can be managed effectively by single or simple inexpensive medication with 70-80% of persons able to lead a normal life.^[132] Thus, proper understanding of the causes and risk factors of epilepsy are essential for effective management of epilepsy in India

where majority of patients are still untreated or inadequately treated.

Refractory epilepsy in India

If the seizures are difficult to control with medication; they are referred to as refractory or intractable. The exact magnitude of medically intractable epilepsy in India is unknown.^[133]

A study done in the pediatric population found neuroinfections as a leading cause of intractable epilepsy.^[134] A study done in the North Indian population identified structural cerebral abnormality, non-response to first AED, delayed milestones, high initial seizure frequency, partial seizure type, febrile seizures, and age of onset before 14 years as significant predictors of refractory epilepsy.^[98] It is essential to identify those patients at risk of developing refractory epilepsy early in their clinical course to evaluate for a possible surgical treatable cause and this would also minimize the toxicity from overdose of antiepileptic drugs and polytherapy.

Summary

The present review on the distribution and determinants of epilepsy from an epidemiological and population perspective emphasizes the need for life-course approach in prevention and management and also the need for focused and targeted programs. The increasing burden of epilepsy in India in coming years due to sociodemographic and epidemiological transition warrants public health community to give priority for this eminently preventable and manageable condition in healthcare delivery. However, a proper understanding of the epidemiology of epilepsy is required to discern and delineate factors that are of relevance (that can be modified) in prevention, management, and rehabilitation. Future studies need to move to nationally representative populations using well-defined methodologies for developing a strong public health response for prevention and control of epilepsy in India.

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