Review Article

Psychosocial Factors in Brain Infections Research in the Last Decade: A Scoping Review

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Abstract

Background: Brain infections are serious neurological events that require immediate care, with around 171 districts of 19 states in India reporting cases every year. Along with the biomedical factors, psychosocial factors of health (BPS) are influential in the outcomes of brain infections as well. **Materials and Methods:** A scoping review was conducted to understand the psychosocial factors explored in brain infections in the last decade. Articles focusing on social, psychological, public health factors, sequelae, and rehabilitation of inflammatory conditions, both pathogenic and autoimmune were covered. The search was conducted using keywords related to brain infections in electronic databases: PubMed, EBSCO, ProQuest, Scopus, and Google Scholar. Prisma-ScR guidelines were used to screen articles and the identified factors were categorized under eight psychosocial factors using Arksey and O'Malley's framework of analysis. **Results:** From a total of 6012 documents retrieved, 11 articles met the criteria. Global burden associated with brain infections, disability and death, the vulnerable population at risk of developing brain infections, gaps in existing literature, pathways to care, mental health, cognitive difficulty associated with infections and their sequelae were the major psychosocial factors identified. **Conclusions:** The review focussed to understand the multitude of psychosocial factors causing delay and damage in brain infections in LMIC context. Along with biomedical factors, there exist several psychosocial factors that could potentially influence the outcome of treatment in brain infections. However, only few have been explored, suggesting the need for more studies to inform the care and sustainable interventions at the macro level to improve the outcomes and reduce the burden in brain infections.

Keywords: Biopsychosocial factors, brain infections, neuro infections, psychological factors, scoping review, social factors

Introduction

Brain infections are potentially reversible neurological events that affect the brain and spinal cord resulting in death and disability globally, especially in the lower-middle income countries (LMIC).[1] In the Indian context, the first case of Japanese Encephalitis (JE) was reported in Vellore, Tamil Nadu, in 1955 while the first outbreak was reported in 1973 in the Burdwan district of West Bengal. Ever since, cases of brain infections have been reported from 171 districts of 19 states.[2] Globally infections are said to contribute to 30% of the total global burden,[3] and is the fifth major contributor to Disability Associated Life Years (DALY) lost among the neurological disorders.[1] However, the real number of cases could not be identified completely due to the under-reporting or misdiagnosis of cases. Therefore, in the absence of a complete cure, or effective control strategies, brain infections remain a public health challenge in India and worldwide.

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The clinical spectrum of the disease ranges from fever, headache, vomiting, neck stiffness, altered sensorium, behavioral disturbances, seizures, movement disorders, and focal neurological deficits. These conditions could be pathogenic or auto-immune which then based on the clinical scenario determines the prognosis and sequelae.[4]

In the list of communicable diseases, it is estimated that bacterial meningitis causes a global burden of 1.2 million cases[5] and is reported to be higher in children and infants making the neurological sequelae increase by 30% in the survivors.[6] It is estimated that out of 5.6 million DALY,

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95% is caused by meningitis and is predominantly prevalent in lower- and middle-income countries.[7] In the meantime, in developing countries research shows though the burden is high, most infectious diseases are preventable with awareness of risk behaviors (magico-religious practices, substance usage, unhygienic food patterns, etc.,).[8] Thereby establishing the fact that if social determinants are understood and addressed, the level of burden in the developing countries could be reduced.[9] Limited efforts have been made globally to recognize and explore the psychosocial factors that could influence the outcome in the management of neuroinfections. We conducted a scoping review of the available literature on psychosocial factors and brain infections to learn what has been described in this topic, to answer the research question 'What are the psychosocial factors explored in brain infections in the last decade?'

Methods

A scoping review was conducted following the framework proposed by Arksey and O'Malley (2005).[10] Based on the research question, the current review aimed to understand the psychological factors in brain infections in acute and chronic phases, to understand the social determinants that influence brain infections, and to understand the factors influencing recovery of brain Infections in the last decade.

Research studies in English that were published from 2011 to 2021 were included in the study. All articles focusing on social, psychological, public health factors, and rehabilitation in brain Infections and on the psychosocial factors related to its sequelae were included. All forms of infections namely pathogenic and autoimmune were covered.

Articles that report brain infections as part of other forms of systemic infections and/or opportunistic infections were excluded. Thus, the articles focusing on human immunodeficiency virus (HIV) and coronavirus disease 2019 (COVID-19) were excluded as it was felt that the psychosocial factors for these are potentially different from those for brain infections. The review was conducted using the keywords of brain infections, neuro infections, psychological factors, social factors, biopsychosocial, and the databases searched were PubMed, EBSCO, ProQuest, Scopus, Google Scholar, and Web of Science.

Screening of articles

After the initial filtering from the electronic database, with the title and then a review of the abstracts, the references were stored in the Zotero library and screened further for potentially relevant articles. The initial search and screening were conducted by the researcher and reviewed by the co-authors. The identified papers were then evaluated for meeting the criteria by the researcher. Cross-checking of references to previously identified articles provided additional sources of information after screening.

Data extraction

The documents selected based on the inclusion criteria were then assessed and then captured the information using the data extraction form following the PRISMA-ScR checklist items.[11] The information captured was entered into data extraction records and synthesized in a summary format, using the form developed in Microsoft Excel. Specific information such as brain infections diagnosis, burden, pathways to care, and other psychosocial components were also included. Although the documents were subjected to a quality assessment, all eligible documents were included in the review, regardless of the results of that assessment [Figure 1].

Data synthesis and analysis

The collected information was summarized under different themes to chart the findings of the available literature [Figure 2, Table 1]. Articles were grouped under eight psychosocial dimensions:

For this synthesis, a content analysis was conducted wherein each article was considered as a separate case and was categorized under the eight themes: Burden, Disability and Death, Vulnerable Population, Gaps in the Study, Pathways to Care, Infections and Mental Health, Infections and Cognitive Difficulty and Post-Encephalitic Syndrome.

Results

A total of 6012 documents were retrieved, of which 362 were screened and 11 were included in the review. Figure 1 describes the process followed in the review.

Burden

Of the 11 articles, 4 of them focus on the burden associated with brain infections. Brain infections are one of the emerging debilitating diseases in this century with severe morbidity and mortality as well as difficulty in treating the patients involved. It is considered the leading cause of sensorineural hearing loss (SNHL) in children and an important cause of neurodevelopmental delay.[12] The largest burden of tuberculosis (TB), and childhood tuberculous meningitis (TBM), is borne by low- and middle-income countries.[13]

More than one million cases of acute bacterial meningitis among adults and children occur annually in sub-Saharan Africa associated with a high burden of death and disability.[14] Worldwide, rabies and Japanese encephalitis virus (JEV) are responsible for estimated annual mortality of 60,000 and 17,000 people, respectively. In LMICs in which neurocysticercosis is endemic, it is the leading identified cause of seizures.[15]

Vulnerable population

Seventeen percent of the documents focused on the vulnerable population who are at risk of developing brain infections as compared to the regular population. Commonly affected groups in brain infections are identified to be infants and immunocompromised individuals with CNS involvement. The sex distribution shows a male preponderance. The poor

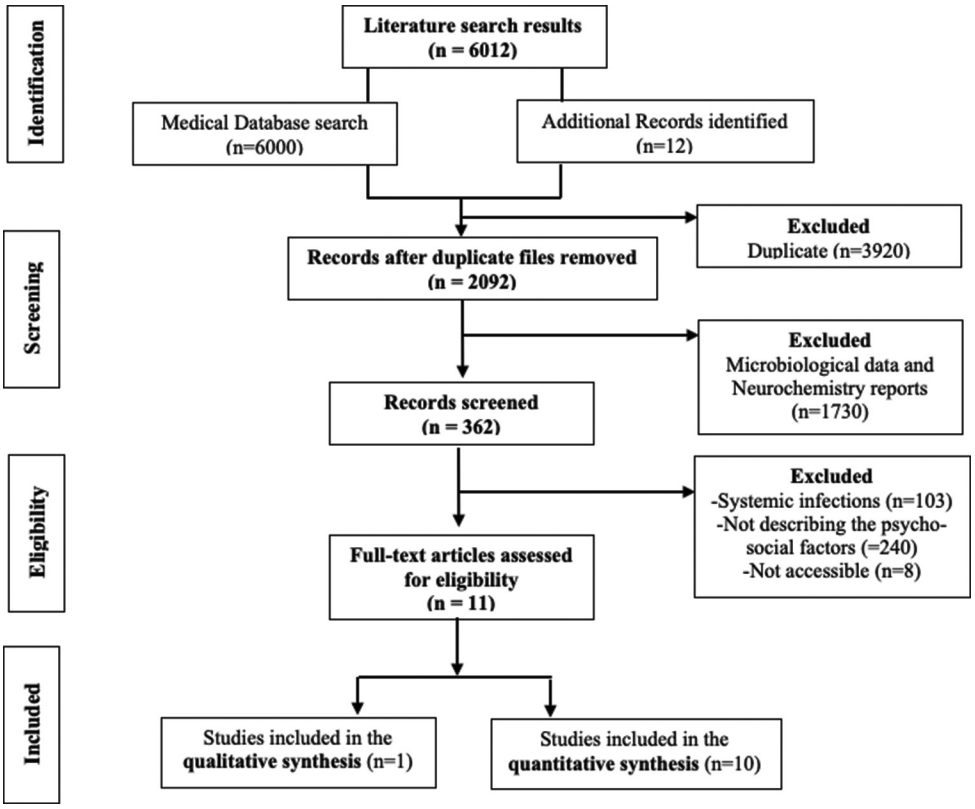

Figure 1: Prisma flow diagram of selected studies

Table 1: Synthesis of the articles

Article	Burden	Vulnerable population	Gaps in the study	Pathways of care	Infections and mental health	Infections and cognitive difficulty	Disability and death	Post-encephalitic syndrome
Abdullahi *et al*., 2020	X							
Adinolfi *et al*., 2015	X					X		
Davis *et al*.,2019	X		X				X	
John *et al*., 2015	X	X			X	X		
Kakooza *et al*., 2018		X						
Letsa *et al*., 2018			X				X	
Nath, A, 2015			X					
Desmond *et al*., 2013				X			X	
Olea *et al*., 2017					X		X	
Wiedlocha *et al*., 2015					X	X		X
Morano & Holt, 2017								X

neurodevelopmental outcome is associated with younger age, delayed presentation, treatment initiation, clinical severity, and hydrocephalus.[15]

The risk of sequelae in bacterial meningitis has been shown to increase with younger age and HIV infection. Additional deaths are likely to occur at home without medical intervention, particularly among young children. Sepsis and meningitis are observed predominantly in neonates; bacterial and tuberculous meningitis in children and adults.[16]

Gaps in the study of infections

Three articles the identified, focusing on different gaps in the existing literature. A paucity of information regarding the management of these infections especially in infants and the clinical burden of these infections is poorly defined. Data are lacking on the effectiveness of medicines for the neuro-psychiatric conditions developed secondary to brain infections.[14]

The lack of establishment of a multidisciplinary approach for the evaluation and management of the neurodevelopmental sequelae of TBM, in the background of low socioeconomic status and limited access to educational support is identified. Risks of long-term complications of infections during the postnatal period and their effect on the quality of life are also significant.[17]

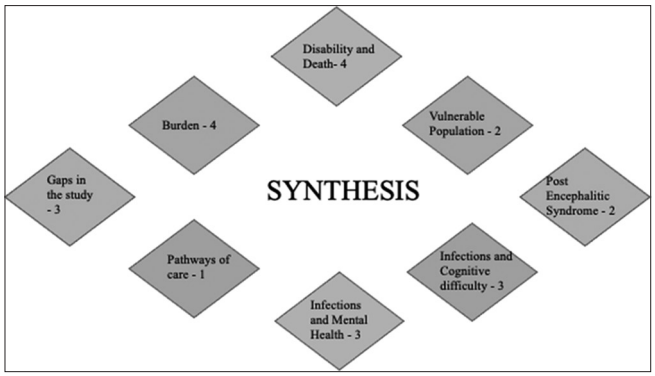

Figure 2: Synthesis of the collected articles

There were no established neuropsychological tests for the functional difficulties of TBM and the interventions focusing on the physical and cognitive disabilities observed in meningitis and the associated socioeconomic burden. Non-availability of robust and standardized assessment measures, which can be adapted across multiple settings. Lack of availability on the mortality rates and associated burden in relation to Neurocysticercosis.[18]

Pathways to care

It is estimated that 37% of illnesses were managed at home without external advice and an additional 16% seek help from traditional healers. Although 72% of children receive medication at home; only 12% receive appropriate treatment. Identification of the illness remains poor and only when the condition is extremely severe does one rush to a tertiary care center. The milder ones are treated with traditional medicine or remain untreated. The ability of a person to receive care depends on a combination of the gender and social position of the carer and patient. Decisions to seek conventional medical treatment during the early stages of illness were dependent on the type of interaction with the primary health system. Major barriers were found as lack of quality care, long waiting period, unclear diagnosis, verbal mistreatment, erratic drug availability, and stigma, especially in the mothers of children with infections.[19]

Infections and mental health

Three articles focused on the different mental health conditions associated with brain infections. Psychiatric disorders like schizophrenia and attention-deficit hyperactivity disorder (ADHD) were reported in children with enterovirus encephalitis. The survivors were found to have conditions of microcephaly, mental retardation, hydrocephalus, visual impairment, and seizure disorder. Herpes simplex encephalitis has a relation with cerebral dysfunction with cognitive, memory difficulty, motor dysfunction, seizure disorders, and altered sensorium reported as common sequelae. Old individuals, female gender, and single status have been to correlate with fatigue. An association between TBM and impairment of a range of executive functions, including reasoning, abstraction, mental flexibility, and verbal response inhibition has also been reported.[15]

In a more recent follow-up study of childhood TBM survivors, the most common impairments were in cognition, learning, emotion, and behavior, all potentially affecting scholastic ability and future employment.[20] The relationship between conditions like Alzheimer's disease (AD), multiple sclerosis (MS), and acute/chronic/reactivated HSV (Herpes Simplex Virus) infection constitutes an interesting field for research.[21]

Infections and cognitive difficulty

Inadequate concentration and working memory speed, the impaired ability of sustained attention, decreased psychomotor speed have been reported with one-third of the cases diagnosed with cognitive impairment. The most frequent psychiatric symptom reported in chronic infection is fatigue, mainly manifesting as physical and mental exhaustion, often in association with attention deficit and word-finding difficulty, depression, headache, pain, and sleep disturbances.[15]

Insomnia though reported in up to 60% of cases, has been stated to be in relation to psychiatric comorbidities, such as depression, or medical conditions like anemia and hypothyroidism. Finally, anxiety and reactive depression may result in receipt of a diagnosis of infections or from infections-associated fatigue and cognitive impairment. Children tend to have developmental retardation, whereas adults exhibit signs of early dementia.[13]

A characteristic triad of symptoms was present in the patients, including social functioning disorders, verbal and non-verbal communication disorders, and stereotyped patterns of behavior.[21]

Disability and death

Four articles focus on the dimension of disability and associated death due to brain infections. Worldwide, encephalitic arboviruses cause life-long neurologic illness at the rate of 50 to 100,000 cases/year with neurocognitive sequelae in survivors such as deafness, mental retardation, emotional liability, and hemiparesis. Death in mumps encephalitis occurs in up to 10-20% of cases, while 33% of survivors show evidence of prolonged neurological sequelae. 43.6% of Japanese Encephalitis causes at least one neuropsychiatric sequelae in the form of reduced IQ, adaptive behavior impairment, paralysis, hemiplegia, limb weakness/incoordination, dysphagia, sensory impairments, and epilepsy.[14]

Subacute sclerosing panencephalitis is a fatal, progressive degenerative central nervous system disease that has a poor prognosis and a high mortality rate of about 35%. About 70% of untreated encephalitis leads to death while the survivors live with a permanent neurologic deficit. Neurocognitive and functional impairment is a long-term complication of TBM is also reported with respect to physical, cognitive, and psychiatric sequelae of TBM, which have lasting socioeconomic implications for patients and their families, are limited.[17]

TBM causes long-term cognitive, motor, language, and behavioral sequelae with childhood TBM having a risk of neurological sequelae among survivors. The TBM survivors were described as ostracized, compulsive, and more aggressive than their unaffected siblings. Parents of childhood TBM survivors reported significant social maladjustment and aggression.[20] In a systematic review of childhood infective encephalitis, 42% had at least one long-term sequela (with a higher proportion (64%) in herpes simplex virus encephalitis). More than one-third suffered from developmental delay, and 10-18% had a behavioral impairment, motor-deficit, intellectual disability, and/or convulsions.

Majorly difficulty remains that the availability of these vaccines in LMICs is variable, and bacterial meningitis still affects 1.2 million individuals annually, causing neurocognitive sequelae in 23% of affected children.[19]

Post-encephalitic syndrome

Nearly 35-58% of patients have been reported to suffer from post-encephalitic Tick-Borne Encephalitis syndrome, which causes a long-term condition that contributes to a lower quality of life. The prevalence of mental disorders increased to 72.5% and organic depressive disorders became more common than cognitive impairment.[22]

Among the stated psychopathological symptoms, are attention deficits (72.1% of the patients), slowness of thought (69.8%), learning impairment (60.5%), depressed mood (60.5%), emotional liability (46.5%), and mutism (41.9%) were the most frequent. Residual difficulties were reported in as many as two-thirds of the cases. In more than one-third of subjects, executive functioning was impaired, especially in initiating and organizing activities and working memory.[21] Persistent cognitive impairment and depressive disorders are sequelae of TBE that lead to a significant decrease in the patients' quality of life.

Discussion

This scoping review is an attempt to summarize the existing understanding of the psychosocial factors in brain infections identification and management. From the extensive literature search, this review focused on the articles across a decade providing important information to understand the different factors in association with brain infections which have been the cause of delayed care and management for brain infections worldwide and especially in the LMIC context.

Public health implications for brain infections resonate with the amount of increased burden of the condition, the long-term sequelae which could be cognitive, social, motor, and other forms of difficulty and disability. The pathways to seeking care have a huge impact as it determines the barriers and facilitators in seeking care for brain infections which has an effect on the residual damage and disability caused by the condition thereby affecting the quality of life of the persons with brain infections, their families, and the community at large.

Different types of documents were reviewed having different study designs with outcomes in the form of numbers or narratives which were classified into eight major themes with social causation as the major relevant factor. However, it is to be noted that there is a serious lack of social science literature focusing on the varied psychosocial factors that are available. The literature available is not pure in nature either as they were predominantly covered along with other bio-medical and psycho-pharmacological studies. Hence, while our review showed that there is a need to recognize the reciprocal influence of psychological and social factors in brain infections management and subsequent care, there is an assumption that this relationship is to be expected, limited studies have attempted to explore the same.

This review's inclusiveness and the comprehensiveness of the analysis are major strengths. It includes a variety of documents which has been covered in the last decade. Based on the inclusion criteria, selection bias was reduced thereby increasing the scope of getting psychosocial literature. The study thereby defines the need for having the convergence of literature and practice and the need of the practice to inform the policy. While the limitations were that unpublished, grey literature and other forms of articles have been excluded from the review.

Conclusion

Brain Infections management is multidimensional with the information currently available predominantly on the presence, symptoms, and medical management of the condition. The findings of the study reveal that there is limited understanding of the psychosocial factors associated with the condition. There is sparse literature available on the psychosocial factors as well thereby making it imperative to focus on the psychosocial factors for better quality care through a multi-disciplinary approach. In the growing context of brain infections, the studies need to focus on the Barriers and Facilitators in seeking care ranging from awareness, availability, accessibility, and affordability of treatment across different levels that either increase or decrease the delay, disability, and residual damage of various brain infections.

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Conflicts of interest

There are no conflicts of interest.

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