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The India brain infections guidelines project: Global evidence for local application

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ABSTRACT

Background: Brain infections are a major cause of morbidity and mortality globally. India lacks systematically evidence-informed guidelines for brain infections.
Methods: We had set up a group of experts in brain infections, evidence synthesis and guideline development to produce guidelines for hospital clinicians diagnosing and treating patients with suspected and confirmed brain infections in India. Questions are being drafted and prioritised, and a plan for GRADE-informed evidence synthesis and guideline development is in place, using methods to increase efficiency of the process where possible.
Dissemination and outputs: The guidelines will be disseminated through publication as well as on a dedicated website. Training of clinicians in evidence synthesis and guideline development, and setting up a network of institutions and professional societies, will provide lasting impact in terms of national capacity strengthening.

1. Background

Brain infections, particularly encephalitis and meningitis, have a devastating impact worldwide.[1,2] In India, they present an ongoing significant public health challenge, with the epidemiology being particularly complex. For example, one systematic review reported cases of meningococcal meningitis rising by 39% between 2005 and 2012,[3] while a Global Burden of Disease Study detailing the burden of neurological disorders across Indian states (1990–2019) found a substantial reduction in incidence of and disability-adjusted life years lost (DALYs) due to both meningitis and encephalitis across the country, while the contribution to total DALYs from all causes of communicable neurological disorders (encephalitis and meningitis) fell from 4.1% in 1990 to 1.1% in 2019.[4] The burden is still large: there were an estimated 610,000 cases and 51,900 deaths due to encephalitis in 2019; for meningitis, 552,000 cases and 34,700 deaths; so evaluating interventions and diagnostics is key in a country with resource limitations.[4]

Aetiology of brain infections in India is also complex. Recent literature reports increasing cases of meningitis and encephalitis due to *Orientia tsutsugamushi* (scrub typhus), dengue and chikungunya, whereas *Japanese encephalitis virus* and *Haemophilus influenzae* have become less common, probably in response to successful vaccination programmes.[5–8] Up-to-date guidelines incorporating this changing landscape are important to ensure patients receive optimal diagnostic workup and treatment.

While guidelines on diagnosis and management strategies for brain

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infections have been made, there are limitations to their usefulness in India: 1) most are made for higher-income countries, and therefore not applicable to lower resource settings[9,10]; 2) they usually focus on specific diseases, e.g. encephalitis or meningitis, or even further on specific pathogens, while most patients present with a syndrome yet to be confirmed as a specific disease or due to a specific cause; 3) few guidelines have used formal evidence synthesis and GRADE approaches. Therefore, there is a need to make guidelines for all brain infections, using GRADE, which are tailored to an Indian context. These could also benefit other low- and middle-income countries.

The NIHR Global Health Research Group on Acute Brain Infections (Brain Infections Global) has been working to establish best practice and algorithms for diagnosis and management of patients with suspected acute brain infections presenting to hospitals in Brazil, Malawi and India.[11] While informed by some systematic reviews[12,13] and existing guidelines, the process has been largely consensus-based, and has not used GRADE methodology.[14] The algorithms are also very context-specific, and would require translation to other hospitals, with different case & pathogen mix and availability of resources.

This guidelines project will build upon the Brain Infections Global group's attempts to improve diagnosis and management, using a formal guideline development process, including a systematic structure for evidence summaries and consensus, and dissemination to relevant stakeholders across India.

2. Objectives

1. Address unanswered priority questions concerning brain infections, using systematic evidence summaries.
2. Provide guidelines for practice, using a GRADE approach to make recommendations, incorporating certainty in the evidence, or best practice statements, where recommendations are not possible.
3. To ensure relevance of the guidelines to a variety of hospitals nationally, and other low- and middle-income countries.
4. Disseminate guidelines so that they are widely accessible and easy to update.

3. Methods

Development of the guidelines will be led by the Centre for Guideline Development at Christian Medical College (CMC), Vellore, India. Scientific input will be provided by representatives of the Clinical Infectious Diseases Society of India, the Indian Academy of Neurology, the Indian Academy of Pediatrics, the National Institute of Mental Health and Neuro Sciences (NIMHANS), and the BV Moses Centre and Clinical Epidemiology Unit at CMC Vellore.

The guidelines will focus on diagnosis and management of inpatients (adults and post-neonatal children) with suspected or confirmed acute brain infections (meningitis and encephalitis) in India. The target end users will be clinicians and those developing local guidelines in secondary and tertiary settings. They will also take into account what is likely to be relevant for other low- and middle-income countries. Questions will be grouped into the following areas, with expert working groups comprising subject area specialists for each: laboratory diagnosis; radiological investigations; pharmacological therapy; and adjunctive & supportive management. The groups formed long lists of priority questions, after which an in-person meeting was held in July 2023 to refine these and decide on shortlists. As of October 2023, the core committee worked with the methodology and steering groups and decided on a final list of questions. Next steps will be to define which methods would be required for each question, finalising these in the form of a protocol.

Evidence summaries will be prepared by an evidence synthesis team in collaboration with individual working groups, in consultation with the methodology group, and then presented to the wider group. The summaries will then be vetted by an external advisory panel and teams of reviewers and experts. Some will be standalone systematic reviews, which will be conducted using Cochrane rapid review methodology.[15] Where guideline recommendations or high-quality systematic reviews exist, these will be reviewed to see how the process can be streamlined to feed these into the recommendation or good practice statement development process.[16] Following review by the methodology committee, including those not consulted when making the evidence summary, expert working group meetings will be held to review the evidence, and make recommendations, following a GRADE approach. Methodologists will moderate these meetings, as well as a delegate from the external advisory panel. Where the evidence is too indirect to make a recommendation, a good practice statement will be made, using GRADE guidance.[17]

4. Dissemination and outputs

A full guidelines document will be compiled, which will be submitted for open-access publication in a peer-reviewed journal and disseminated on the group's purpose-built website. This will include detailed evidence summaries for all questions, documentation of the evidence to decision process, and further details to support practical use of the guidelines by clinicians. It is hoped that this will provide comprehensive, up-to-date, accessible evidence-based guidelines for diagnosis and management of brain infections, relevant to India and other low- and middle-income country settings. Other outputs will include capacity strengthening of individuals, through training of clinicians in evidence synthesis and guideline development methods, building institutional capacity for making evidence-informed guidelines, and establishing a guidelines network between national professional societies and institutions.

5. Ethical approval statement

Ethical clearance was not sought separately for the Brain Infection Guidelines Project. However, this activity is undertaken by the Center for guideline development at Christian medical college (CMC) Vellore India which is approved by the institutional review board and ethics committee (IRB Min. No. 14563 dated March 23, 2022). Additionally, participating experts provided conflict of interest statements before the commencement of the initiative.

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CRediT authorship contribution statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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