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Burden, spectrum and predictors of neurological sequelae in children surviving acute bacterial meningitis in sub-Saharan Africa: a protocol for a systematic review and meta-analysis

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Study protocol

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Abstract

Background.

Acute bacterial meningitis (ABM) is a leading cause of childhood death and acquired lifelong disability in sub-Saharan Africa (SSA). The convergence of the African meningitis belt, a high force of infection from Streptococcus pneumoniae, Haemophilus influenzae type b and Neisseria meningitidis, frequent late presentation, and constrained diagnostic and audiology capacity means that survivors carry a substantial and often unmeasured neurological burden. Region-specific pooled estimates that could inform structured survivor follow-up and the World Health Organization “Defeating meningitis by 2030” roadmap are lacking. This protocol describes a systematic review and meta-analysis to synthesise the prevalence, clinical spectrum and predictors of neurological sequelae among children who survive ABM in SSA.

Methods.

We will search PubMed/MEDLINE, Embase, Scopus, Web of Science, African Journals Online and the Cochrane Library from January 2000 to the date of the search, with no language restriction. Observational studies (cohort, cross-sectional, case-control) and trial cohorts reporting neurological outcomes in children younger than 18 years surviving ABM in SSA, with at least 10 survivors, will be eligible. Two reviewers will independently screen records, extract data and appraise methodological quality using the Joanna Briggs Institute (JBI) checklist for prevalence studies. The primary outcome is the pooled prevalence of any major neurological sequela at hospital discharge and at latest follow-up. Proportions will be pooled with a random-effects model after Freeman-Tukey double-arcsine transformation using the meta package in R. Heterogeneity will be quantified with the I^2 statistic and explored through prespecified subgroup analyses (causative pathogen, HIV status, age band, timing of assessment, and SSA sub-region) and random-effects meta-regression. The certainty of pooled estimates will be rated using a GRADE-informed approach for prevalence data.

Discussion.

This review will generate the first SSA-specific pooled estimates of the neurological sequelae burden after childhood ABM, disaggregated by sequela type, pathogen and time since illness. The findings are intended to inform survivor follow-up pathways, audiology and neuro-rehabilitation service planning, and the monitoring of conjugate-vaccine impact on disabling disease. Anticipated limitations include clinical heterogeneity in how sequelae are ascertained, variable follow-up duration, and probable under-ascertainment of subtle cognitive and behavioural outcomes.

Systematic review registration.

PROSPERO CRD420261446042.

Background

Acute bacterial meningitis (ABM) is an infection of the meninges and subarachnoid space that, despite effective antibiotics and expanding conjugate-vaccine programmes, continues to cause a disproportionate share of childhood mortality and acquired neurodisability in sub-Saharan Africa (SSA) [1, 2]. The region carries the highest global incidence of endemic and epidemic meningitis, driven by the semi-arid “meningitis belt” stretching from Senegal to Ethiopia and by year-round endemic disease elsewhere [1]. The dominant childhood pathogens (Streptococcus pneumoniae, Haemophilus influenzae type b [Hib] and Neisseria meningitidis) are compounded in neonates by group B Streptococcus, Escherichia coli and other Gram-negative organisms, and in many settings by a high background prevalence of HIV and malnutrition that worsen outcomes [2].

Even when a child survives the acute illness, the disease frequently does not end at discharge. Inflammation of the meninges, cortical and cranial-nerve involvement, cerebral oedema, vasculitic infarction and hydrocephalus can leave permanent damage. The resulting sequelae span sensorineural hearing loss, epilepsy and recurrent seizures, motor deficits including hemiparesis and spastic cerebral palsy, cognitive impairment and developmental delay, visual impairment, hydrocephalus, and speech and language disorders [3, 4]. These impairments carry lifelong educational, economic and psychosocial consequences for the child and family, and place a recurring demand on already stretched rehabilitation, audiology and special-education services.

A widely cited global synthesis estimated that roughly one in five survivors of childhood bacterial meningitis is left with a major or minor sequela, with the risk substantially higher in low-income regions and after pneumococcal disease [3]. However, the primary data underlying African estimates are sparse, heterogeneous and often derived from single hospitals [4, 5, 6, 7]. Ascertainment of sequelae varies widely: some studies rely on clinical examination at discharge alone, others on formal audiometry, standardised neurodevelopmental testing or long-term follow-up, so that headline prevalence figures are not directly comparable. Subtle cognitive, behavioural and learning outcomes, which may only become apparent as a child grows, are frequently missed in short hospital-based studies.

This measurement gap has direct policy relevance. The World Health Organization “Defeating meningitis by 2030” roadmap sets explicit targets not only for reducing cases and deaths but also for reducing meningitis-associated disability and improving support for survivors [8]. Meeting the disability target requires reliable, region-specific estimates of how many survivors are affected, by which impairments, and which children are at greatest risk: precisely the evidence that is currently fragmented across the SSA literature. Robust pooled estimates would also strengthen the case for structured survivor follow-up, early hearing screening, and continued investment in pneumococcal and Hib conjugate vaccination by quantifying the disability averted.

To our knowledge, no systematic review has pooled the prevalence and clinical spectrum of neurological sequelae specifically among children surviving ABM across sub-Saharan Africa using contemporary proportion meta-analysis methods, nor formally examined predictors such as causative pathogen, HIV status, age and timing of assessment. We therefore propose a systematic review and meta-analysis to address this gap.

Objectives

The primary objective is to estimate the pooled prevalence of any major neurological sequela among children surviving ABM in sub-Saharan Africa. The specific objectives are:

1. To estimate the pooled prevalence of individual neurological sequelae (hearing loss, epilepsy or seizure disorder, motor deficit, cognitive impairment or developmental delay, visual impairment, hydrocephalus, and speech or language disorder) at hospital discharge and at latest follow-up.
2. To describe the clinical spectrum and severity of sequelae reported.
3. To examine predictors of sequelae, including causative pathogen, HIV co-infection, age band, and time to presentation, through subgroup analysis and meta-regression.
4. To describe in-hospital case fatality among the same populations as a contextual outcome.

Methods and design

This protocol is reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) statement [9, 10], and the review will be reported following the PRISMA 2020 statement [11] and the Meta-analysis of Observational Studies in Epidemiology (MOOSE) recommendations [12]. The completed PRISMA-P checklist is provided as Additional file 1.

Protocol and registration

This review was registered prospectively with the International Prospective Register of Systematic Reviews (PROSPERO) on 9 July 2026, before formal screening began, under registration number CRD420261446042 (available from https://www.crd.york.ac.uk/PROSPERO/view/CRD420261446042). Any amendments to this protocol will be documented in the registration record and reported in the final review, together with the date, rationale and description of each change.

Eligibility criteria

Population. Children and adolescents younger than 18 years, resident in a sub-Saharan African country, who have survived an episode of acute bacterial meningitis. ABM will be defined as a clinical diagnosis of meningitis supported by cerebrospinal fluid (CSF) findings consistent with bacterial infection (e.g.

raised CSF white-cell count with neutrophil predominance, low CSF glucose, raised CSF protein) and/or microbiological confirmation by culture, Gram stain, antigen detection or nucleic-acid amplification. Both confirmed and probable ABM, as defined by study authors, will be eligible; the definition used will be extracted for each study. Neonatal meningitis (first 28 days of life) will be included and analysed as a prespecified subgroup.

Exposure. Acute bacterial meningitis of any bacterial aetiology. Studies restricted to a single pathogen (e.g. pneumococcal or meningococcal meningitis) will be eligible and used in pathogen-specific subgroups.

Comparator. No comparator is required for the primary prevalence outcome. Where studies report outcomes by pathogen, HIV status or other factors, these strata will be used for subgroup and predictor analyses.

Outcomes. The primary outcome is the prevalence of any major neurological sequela among survivors. Secondary outcomes are the prevalence of each individual sequela and in-hospital case fatality (see Outcomes and prioritisation).

Study designs. Cohort studies (prospective and retrospective), cross-sectional studies, case-control studies, and the observational cohorts of randomised or non-randomised trials will be eligible, provided they report neurological outcomes in at least 10 child survivors of ABM. Case reports, case series with fewer than 10 survivors, narrative and systematic reviews, editorials, commentaries, conference abstracts without extractable data, modelling studies and animal studies will be excluded.

Setting and timeframe. Studies conducted in one or more of the countries of sub-Saharan Africa and published from January 2000 onwards, to reflect the period of expanding Hib and pneumococcal conjugate-vaccine introduction and contemporary care. No language restriction will be applied; non-English records will be translated as required.

Information sources

We will systematically search PubMed/MEDLINE, Embase, Scopus, Web of Science Core Collection, African Journals Online (AJOL) and the Cochrane Library from January 2000 to the date of the search. To capture grey literature and reduce publication bias, we will search Google Scholar (first 200 records), screen the reference lists of all included studies and relevant reviews, and search preprint servers (medRxiv). The search will be re-run before final analysis to capture recent records. The date of each search will be recorded.

Search strategy

The search strategy combines controlled vocabulary (MeSH/Emtree) and free-text terms across three concept blocks (bacterial meningitis, neurological sequelae/outcomes, and children), restricted to sub-Saharan Africa, using Boolean operators. The strategy was developed iteratively and will be finalised with an information specialist. A draft PubMed strategy is shown below and provided in full for all databases as Additional file 2.

#1 "Meningitis, Bacterial"[Mesh] OR meningitis[tiab] OR "pneumococcal meningitis"[tiab] OR "meningococcal meningitis"[tiab] OR "Haemophilus meningitis"[tiab] OR "neonatal meningitis"[tiab] OR "purulent meningitis"[tiab] OR "pyogenic meningitis"[tiab] #2 sequela*[tiab] OR "neurological outcome*"[tiab] OR "neurologic sequela*"[tiab] OR disability[tiab] OR "hearing loss"[tiab] OR deafness[tiab] OR "hearing impairment"[tiab] OR epilepsy[tiab] OR seizure*[tiab] OR "cerebral palsy"[tiab] OR "motor deficit*"[tiab] OR hemiplegia[tiab] OR hemiparesis[tiab] OR hydrocephalus[tiab] OR "cognitive impairment"[tiab] OR "developmental delay"[tiab] OR "intellectual disability"[tiab] OR "visual impairment"[tiab] OR blindness[tiab] OR neurodevelopment*[tiab] OR outcome*[tiab] #3 Infant[Mesh] OR Child[Mesh] OR Adolescent[Mesh] OR child*[tiab] OR children[tiab] OR infant*[tiab] OR neonat*[tiab] OR newborn*[tiab] OR paediatric[tiab] OR pediatric[tiab] OR adolescen*[tiab] #4 "Africa South of the Sahara"[Mesh] OR "sub-Saharan Africa"[tiab] OR Africa[tiab] OR [each of the individual sub-Saharan African countries, e.g. Uganda[tiab] OR Kenya[tiab] OR Nigeria[tiab] OR Malawi[tiab] OR …] #5 #1 AND #2 AND #3 AND #4 Filters: publication date 2000/01/01 to present

Study records

Data management. Records from all databases will be exported to Zotero for de-duplication and then uploaded to the Rayyan web application for screening. A screening log will record the number of records at each stage to populate the PRISMA 2020 flow diagram.

Selection process. Two reviewers (AN, MN) will independently screen titles and abstracts against the eligibility criteria. Potentially eligible records will undergo independent full-text assessment by the same two reviewers. Disagreements at either stage will be resolved by discussion, with a third reviewer (KCN) arbitrating where consensus is not reached. Inter-reviewer agreement at full-text stage will be reported using Cohen’s kappa. Reasons for full-text exclusion will be recorded.

Data collection process. Two reviewers will independently extract data into a piloted, standardised electronic form; discrepancies will be reconciled by consensus or third-reviewer arbitration. Where data are missing or ambiguous, corresponding authors will be contacted at least twice over four weeks before the study is analysed on available data. Studies reporting the same cohort will be linked and the most complete report used to avoid double-counting.

Data items

Extracted variables will include: first author, year of publication, country and sub-region, study design, setting (hospital/community; single/multi-site), study period, sampling and recruitment, sample size and number of survivors, participant age distribution and sex, case definition of ABM and method of confirmation, causative pathogen(s), vaccination status where reported, HIV prevalence/status, malnutrition, time from symptom onset to presentation, treatment received, method and timing of sequelae ascertainment (clinical examination, audiometry, standardised neurodevelopmental assessment), definitions used for each sequela, numerators and denominators for each outcome at discharge and at latest follow-up, duration of follow-up, and in-hospital case fatality.

Outcomes and prioritisation

Primary outcome. The prevalence of any major neurological sequela, defined as the presence of one or more of the following among survivors: sensorineural hearing loss, epilepsy or recurrent seizure disorder, motor deficit (hemiparesis, quadriparesis, spasticity or cerebral palsy), cognitive impairment / developmental delay / intellectual disability, visual impairment or blindness, hydrocephalus, and speech or language disorder. Prevalence will be assessed at two prespecified time points: at hospital discharge (early) and at latest reported follow-up (late).

Secondary outcomes. The prevalence of each individual sequela listed above, and in-hospital case fatality among children presenting with ABM (reported as a contextual denominator for the survivor-based prevalence estimates).

Risk of bias in individual studies

Methodological quality and risk of bias will be assessed independently by two reviewers using the Joanna Briggs Institute (JBI) critical appraisal checklist for studies reporting prevalence data [13], which evaluates sampling frame and method, sample size, setting description, coverage of analysis, valid and standardised outcome measurement, and appropriate statistical analysis. For comparative (case-control and cohort) analyses of predictors, the Newcastle-Ottawa Scale [14] will be applied additionally. Disagreements will be resolved by consensus or third-reviewer arbitration. No study will be excluded solely on the basis of quality; instead, risk of bias will be incorporated through sensitivity analysis restricted to studies at low risk of bias and, where feasible, into the certainty assessment.

Data synthesis

Study characteristics and definitions will be tabulated and synthesised narratively. Where two or more studies report a given outcome using comparable definitions, prevalence will be pooled quantitatively. Meta-analysis will be performed in R using the meta package (metaprop function) [15, 16]. Study-level proportions will be stabilised using the Freeman-Tukey double-arcsine transformation [17] before

pooling, and a random-effects model (DerSimonian-Laird or restricted maximum likelihood estimator for the between-study variance) will be used given anticipated clinical and methodological heterogeneity. Pooled prevalence will be reported with 95% confidence intervals, and exact (Clopper-Pearson) confidence intervals will be used for individual study proportions. Results will be displayed as forest plots.

Statistical heterogeneity will be quantified using the I^2 statistic and the between-study variance τ^2, with the Cochran Q test [18]; I^2 values of approximately 25%, 50% and 75% will be interpreted as low, moderate and high heterogeneity, respectively. Given the expected heterogeneity, prespecified subgroup analyses will be conducted by causative pathogen (pneumococcal, Hib, meningococcal, neonatal/Gram-negative, mixed/unspecified), HIV status, age band (neonatal, infant, older child), timing of sequelae assessment (discharge versus follow-up), and SSA sub-region (East, West, Central, Southern Africa). Random-effects meta-regression will explore the association between pooled prevalence and study-level covariates including publication year, follow-up duration, and proportion HIV-positive. A p value below 0.05 will be considered statistically significant. All analyses will be conducted in R (version 4.x).

Meta-bias(es)

Publication and small-study effects will be examined visually with funnel plots and formally with Egger's regression test [19] when at least 10 studies contribute to a pooled estimate. Selective outcome reporting will be assessed by comparing outcomes described in methods with those reported in results. Sensitivity analyses will include leave-one-out analysis to identify influential studies and re-analysis restricted to studies at low risk of bias and to microbiologically confirmed cases.

Confidence in cumulative evidence

The certainty of each pooled prevalence estimate will be rated using a GRADE-informed approach adapted for prevalence data [20], considering risk of bias, inconsistency, indirectness, imprecision and publication bias. Findings will be summarised in a table reporting, for each outcome, the number of studies and participants, the pooled prevalence with 95% confidence interval, the I^2 statistic and the overall certainty rating.

Discussion

This systematic review and meta-analysis will provide the first pooled estimates, specific to sub-Saharan Africa, of the neurological sequelae burden among children who survive acute bacterial meningitis, disaggregated by individual impairment, causative pathogen, age and time since illness. By quantifying how many survivors are left with hearing loss, epilepsy, motor and cognitive impairment and other disabilities, the review will supply evidence directly relevant to the disability-reduction and survivor-

support targets of the WHO “Defeating meningitis by 2030” roadmap, and will help make the case for structured survivor follow-up, early hearing screening and sustained conjugate-vaccine coverage.

The main anticipated limitation is clinical heterogeneity: studies differ in how and when sequelae are ascertained, from clinical examination at discharge to formal audiometry and standardised neurodevelopmental testing at long-term follow-up, which may limit comparability and inflate heterogeneity. We mitigate this through prespecified subgroups by timing and method of assessment, transformation-based pooling and meta-regression. Under-ascertainment of subtle cognitive and behavioural outcomes, loss to follow-up, and variable diagnostic confirmation of ABM may bias estimates; these will be examined in sensitivity analyses and reflected in the certainty ratings. Despite these constraints, consolidating the fragmented regional evidence into transparent, reproducible pooled estimates should be of substantial value to clinicians, rehabilitation and audiology services, policymakers and researchers working to reduce the lifelong impact of childhood meningitis in the region.

Declarations

Ethics approval and consent to participate. Not applicable; this study uses published aggregate data and does not require ethical approval.

Consent for publication. Not applicable.

Availability of data and materials. All data generated or analysed during this study will be included in the published review and its additional files. Extracted datasets will be made available in an open repository on publication.

Competing interests. The authors declare that they have no competing interests.

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Authors’ contributions. KCN conceived and designed the study and drafted the protocol. AN and MN contributed to the design of the eligibility criteria, search strategy and data-extraction form. KCN, AN and MN will conduct screening, data extraction and quality appraisal. KCN will perform the statistical analysis. All authors read, revised and approved the final protocol. KCN is the guarantor.

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Supplementary Files

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