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Cerebral Infarction in Tuberculous Meningitis in Adults: A Systematic Review

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Abstract

Cerebral infarction is a major neurological complication of tuberculous meningitis (TBM) in adults, potentially contributing to neurological deterioration and long-term disability. This systematic review aimed to examine cerebral infarction frequency and anatomical patterns, associated clinical and inflammatory factors, neuroimaging findings, and therapeutic interventions reporting vascular outcomes. A structured PubMed search covered publications from 2016 to 2026, with searches conducted between October 3 and November 4, 2026. Primary studies involving adults were selected through predefined eligibility criteria, critically appraised using relevant National Heart, Lung, and Blood Institute methodological domains, and synthesized qualitatively without meta-analysis. Among 234 identified records, 66 reports were sought for retrieval, 35 full texts were assessed, and 11 primary studies were included; 31 reports could not be retrieved. Reported cerebral infarction frequencies ranged from 20.0% to 81.0% across selected populations, with substantial clinical and methodological heterogeneity. Infarction frequently involved the basal ganglia, while older age, focal neurological deficits, cerebrospinal fluid inflammatory characteristics, and meningeal enhancement showed associations of uncertain predictive validity. Magnetic resonance imaging, angiography, venography, and perfusion techniques provided complementary vascular information. Two randomized trials failed to establish definitive benefits of adjunctive antiplatelet therapy. These findings support integrated neurological and imaging assessment while highlighting insufficient evidence for routine antiplatelet prevention and the need for standardized prospective investigations.

Keywords: *Adult patients, Cerebral infarction, Neuroimaging, Systematic review, Tuberculous meningitis.*

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INTRODUCTION

Tuberculous meningitis (TBM) remains one of the most severe manifestations of extrapulmonary tuberculosis, presenting substantial challenges to neurological care because of its association with mortality, long-term disability, and complex intracranial complications despite the availability of antituberculosis treatment. Cerebral infarction constitutes a particularly consequential complication because inflammatory involvement of the cerebral vasculature may produce ischemic injury, neurological deterioration, and persistent functional impairment during the course of infection. Contemporary clinical management increasingly recognizes that neurological outcomes depend not only on microbiological control but also on the identification and management of secondary vascular, inflammatory, and cerebrospinal fluid abnormalities (Donovan et al., 2026; Garg, 2026). The relationship between cerebral ischemia and TBM is biologically complex, involving meningeal inflammation, vascular narrowing, altered cerebral perfusion, and potentially overlapping pathological processes that cannot always be distinguished through clinical examination alone (Lamb et al., 2026). Observational evidence indicates that cerebral infarction occurs across heterogeneous clinical populations, including patients without conventional vascular risk factors, while its reported frequency varies according to disease severity, demographic characteristics, and neuroimaging assessment (Deng et al., 2025; Sahu et al., 2026). Recent advances in magnetic resonance imaging, vascular imaging, and perfusion assessment have expanded the possibilities for characterizing intracranial abnormalities beyond conventional structural evaluation, although the clinical interpretation of these findings remains dependent on the underlying disease process and examination protocols (Mertiri et al., 2024; Wang et al., 2026). The continuing clinical burden of TBM, combined

with uncertainty surrounding the mechanisms, recognition, and prevention of cerebral infarction, establishes a substantial need for a focused evaluation of contemporary evidence concerning vascular complications in adult patients.

Current scientific knowledge concerning cerebral infarction in TBM has developed through several interconnected research directions, particularly vascular pathophysiology, clinical risk identification, neuroimaging characterization, and therapeutic intervention. Research examining clinical and laboratory characteristics has investigated associations between cerebral infarction and inflammatory abnormalities, including cerebrospinal fluid composition, hematological parameters, and neurological manifestations, suggesting that ischemic complications may reflect interactions between infection-related inflammation and vascular susceptibility rather than conventional cerebrovascular risk factors alone (Tang et al., 2022; Harahap et al., 2023; Aggrohia et al., 2024). Investigations of cerebrospinal fluid biomarkers have further emphasized the biological heterogeneity of TBM, although associations with inflammatory activity, mortality, or paradoxical reactions cannot automatically be interpreted as evidence of infarction-specific predictive performance (Dian et al., 2025; Deswal et al., 2026; Tugume et al., 2025). Neuroimaging research has developed a complementary evidence base by identifying abnormalities involving cerebral arteries, venous structures, brain parenchyma, and regional perfusion, thereby supporting a multidimensional interpretation of neurological complications (Naik et al., 2022; Kumar & Gutch, 2020). Clinical studies examining disease severity and age-related characteristics have also demonstrated the importance of population differences when evaluating vascular outcomes, particularly among critically ill and older patients (Cantier et al., 2018; Zhu et al., 2023). Therapeutic research has progressed from investigating adjunctive aspirin toward comparative assessments of antiplatelet strategies, while corticosteroid trials and investigations of antimicrobial regimens have addressed broader treatment outcomes rather than establishing uniform evidence for infarction prevention (Mai et al., 2018; Donovan et al., 2023; Bhatia et al., 2025). These research directions collectively demonstrate considerable progress in understanding TBM-associated neurological complications, but their differing objectives and outcome definitions limit direct integration into a consistent interpretation of cerebral infarction in adults.

The principal research gap concerns the absence of sufficiently integrated, adult-focused interpretation of cerebral infarction that simultaneously accounts for vascular characteristics, associated clinical factors, imaging findings, and intervention-related outcomes while critically examining differences in study design and outcome measurement. Existing investigations frequently address particular dimensions of the disease, such as ischemic stroke in selected younger populations, clinical predictors of neurological complications, or the diagnostic value of cerebrospinal fluid and inflammatory biomarkers, without necessarily establishing comparable definitions or observation periods for cerebral infarction (Zhang et al., 2019; Pandey et al., 2024). Research assessing cerebrospinal fluid characteristics has contributed to understanding the inflammatory environment of TBM, yet findings related to general disease activity, treatment response, or mortality cannot be directly transferred to predictions of radiologically confirmed ischemic injury (Imron et al., 2025; Dian et al., 2025). Reviews examining cerebrovascular complications and ischemic mechanisms have provided valuable conceptual and quantitative perspectives, but their broader synthesis objectives do not eliminate the need to distinguish adult-specific evidence, imaging-confirmed infarction, clinically apparent stroke, and composite neurological outcomes (Tomidy et al., 2023; Lamb et al., 2026). Therapeutic studies present additional interpretative difficulties because differences in antiplatelet exposure, treatment protocols, follow-up imaging, and outcome ascertainment restrict conclusions about vascular protection. Investigations of linezolid pharmacokinetics and clinical treatment have advanced understanding of antimicrobial management, although their principal endpoints do not independently establish effects on cerebral infarction (Abdelgawad et al., 2024; Fei et al., 2025). The methodological gap is therefore not merely a shortage of published investigations, but the limited comparability of existing evidence concerning the temporal relationship between clinical factors and ischemic events, the distinction between vascular abnormalities and confirmed infarction, and the interpretation of therapeutic outcomes across heterogeneous adult populations.

The unresolved relationship between clinical risk characteristics, neurovascular imaging abnormalities, and intervention-related outcomes carries substantial consequences for both scientific interpretation and clinical decision-making. Failure to distinguish cerebral infarction from other

manifestations of neurological deterioration may obscure the mechanisms responsible for functional impairment and complicate the assessment of treatment effectiveness in patients with TBM. Clinical investigations have demonstrated that ischemic lesions may occur without clearly recognizable stroke manifestations, reinforcing the limitations of neurological examination as the sole method of identifying vascular involvement (Deng et al., 2025). Imaging-based investigations have similarly illustrated the complementary roles of magnetic resonance imaging, angiographic assessment, and advanced perfusion techniques, although their diagnostic contributions require interpretation according to the vascular territory, lesion characteristics, and clinical circumstances of individual patients (Naik et al., 2022; Wang et al., 2026). The practical implications extend to the interpretation of inflammatory and hematological indicators, since associations observed in selected samples may not retain their predictive performance when applied to patients with different ages, comorbidities, or disease severity (Aggrohia et al., 2024; Harahap et al., 2023). Therapeutic uncertainty introduces a further concern because the neurological benefits of adjunctive corticosteroid strategies cannot be presumed to represent equivalent reductions in cerebral infarction, while randomized evaluations of antiplatelet treatment have not established a definitive overall protective effect against vascular outcomes (Donovan et al., 2023; Bhatia et al., 2025). Clinical investigations comparing dexamethasone regimens also emphasize the importance of distinguishing general treatment responses from specific cerebrovascular endpoints when interpreting intervention effectiveness (Saluja et al., 2023). A rigorous appraisal of these distinctions is necessary to prevent premature clinical extrapolation, improve the interpretation of heterogeneous findings, and identify research priorities capable of strengthening the evidence base for neurological monitoring and vascular complication management in adult TBM.

The present study is positioned as a focused systematic review of primary research investigating cerebral infarction and related vascular outcomes in adults with TBM, with particular emphasis on the analytical separation of infarction patterns, associated factors, neuroimaging findings, and therapeutic evidence. Its proposed contribution differs from investigations restricted to individual clinical predictors, particular imaging techniques, or specific pharmacological interventions because it examines these domains through a common framework that distinguishes radiologically confirmed infarction, clinical ischemic stroke, vascular abnormalities, and broader neurological outcomes. The review also differs in scope from neuroimaging-oriented publications addressing multiple forms of central nervous system tuberculosis and broader clinical management reviews, as its central unit of analysis is evidence specifically relevant to cerebral infarction in adult TBM populations (Mertiri et al., 2024; Garg, 2026). Previous investigations involving critically ill patients, selected age groups, or individuals without conventional vascular risk factors demonstrate the need to evaluate population eligibility and clinical characteristics before comparing reported frequencies or associations (Cantier et al., 2018; Zhu et al., 2023; Tang et al., 2022). The distinction between predictive associations and concurrent neurological manifestations is particularly relevant because a variable measured after ischemic injury cannot automatically be interpreted as a prospective determinant of infarction. Similarly, randomized antiplatelet investigations require separate consideration of intervention allocation, imaging follow-up, missing outcome data, and composite endpoints before conclusions concerning vascular protection can be justified (Mai et al., 2018; Bhatia et al., 2025). The specific methodological contribution of this review lies in organizing the available adult evidence through descriptive critical appraisal and qualitative synthesis without treating clinically heterogeneous populations or outcome measures as directly interchangeable. Its novelty is therefore analytical and integrative rather than the discovery of a previously unreported biological mechanism, offering a structured interpretation of existing evidence while explicitly identifying the limitations that prevent stronger causal, prognostic, or therapeutic conclusions.

This systematic review aims to critically synthesize primary research concerning cerebral infarction in adults with tuberculous meningitis, focusing on four interrelated objectives: characterizing the reported frequency and anatomical patterns of cerebral infarction; examining clinical, demographic, inflammatory, and cerebrospinal fluid factors associated with ischemic complications; evaluating the contribution of structural, vascular, and perfusion neuroimaging to identifying cerebral infarction and associated abnormalities; and assessing evidence from therapeutic investigations reporting ischemic or other vascular outcomes. The review employs a structured literature search covering publications from 2016 to 2026, applies predefined eligibility criteria

emphasizing adult populations and extractable adult-specific findings, and uses descriptive methodological appraisal to examine potential sources of bias and limitations in the included investigations. Qualitative synthesis is undertaken without statistical pooling because differences in population selection, imaging protocols, study designs, outcome definitions, and follow-up procedures may compromise the validity of combined estimates. The scientific contribution is expected to consist of an integrated account of the available evidence that differentiates observed associations from causal interpretations, imaging findings from clinically manifested stroke, and numerical treatment differences from established therapeutic effectiveness. The methodological contribution involves transparent consideration of heterogeneity, selection bias, temporal ambiguity, and incomplete outcome ascertainment when interpreting vascular findings across studies. The anticipated practical contribution is a more defensible evidence base for understanding cerebral infarction in adult tuberculous meningitis, informing the interpretation of neurological and imaging assessments, and identifying priorities for future investigations requiring standardized vascular outcomes, prospective observation, and more consistent evaluation of therapeutic interventions.

RESEARCH METHODS

This study employed a systematic review design using a structured literature search, descriptive methodological appraisal, and qualitative synthesis of primary research investigating cerebral infarction and associated vascular complications in adults with tuberculous meningitis (TBM). The review covered publications from January 1, 2016, to November 4, 2026, with literature searches conducted through PubMed between October 3 and November 4, 2026. The search strategy combined Medical Subject Headings (MeSH) and title/abstract terms related to tuberculous meningitis with terms describing cerebral infarction, ischemic stroke, vasculopathy, vasculitis, vessel wall abnormalities, and transcranial Doppler assessment. The complete search strategy was documented in Supplementary Appendix 1. No restrictions based on participant age or study design were applied during the initial database search. PubMed served as the sole database for systematic identification, while PubMed Central, Europe PMC, and publisher websites were consulted exclusively to retrieve full-text publications. Eligible studies comprised original investigations involving patients aged 18 years or older, including studies explicitly describing adult cohorts without evidence of pediatric participation and mixed-age investigations providing separately extractable adult data. Tuberculous meningitis diagnoses were accepted according to the diagnostic criteria specified in the individual studies. Eligible outcomes included neuroimaging-confirmed cerebral infarction or ischemic stroke, associated vascular abnormalities, clinical or laboratory factors analyzed in relation to infarction, and therapeutic interventions reporting relevant vascular outcomes. Case reports, small descriptive case series without an analytical cohort, review articles, editorials, book chapters, laboratory or animal investigations, retracted publications, studies without identifiable adult-specific data, and investigations lacking relevant outcomes were excluded. Publications without obtainable full texts were recorded separately rather than classified as ineligible solely on the basis of abstracts. No language restrictions were applied during searching, although the publications ultimately included in the synthesis were written in English. The study selection process was documented using the PRISMA 2020 reporting framework, without claiming prospective protocol registration or independent duplicate screening.

Retrieved records were examined for duplication using PubMed identifiers, followed by sequential title and abstract screening, full-text retrieval, and eligibility assessment. The initial search identified 234 records without duplicate PubMed identifiers, of which 168 were excluded during preliminary screening and 66 reports were sought for full-text retrieval. Thirty-one full texts could not be obtained, leaving 35 reports for eligibility assessment. Twenty reports were excluded because adult-specific data were unavailable or the adult population could not be established, three because their study designs did not meet the inclusion criteria, and one because the reported outcomes were ineligible; consequently, 11 primary studies were retained for qualitative synthesis. Data extraction covered author and publication year, geographical setting, study design, participant age eligibility, sample size, neuroimaging modalities, investigated clinical or laboratory factors, therapeutic interventions, outcome definitions, reported effect estimates, and methodological limitations. Potentially overlapping cohorts and companion reports were identified where applicable, and sample sizes were not aggregated into a single participant population because the independence of all

included cohorts could not be established. Methodological appraisal was conducted descriptively using relevant domains of the National Heart, Lung, and Blood Institute Study Quality Assessment Tools for observational, case-control, and intervention studies. The appraisal examined population definition, participant selection, outcome ascertainment, temporal relationships, confounding control, randomization, blinding, and missing data, without calculating numerical quality scores or assigning unsupported overall quality classifications. Evidence synthesis followed the reporting principles of synthesis without meta-analysis (SWiM) and organized findings into four analytical domains: infarction frequency and anatomical distribution, associated clinical and inflammatory factors, neuroimaging characteristics, and therapeutic interventions reporting vascular outcomes. Radiologically confirmed infarction, clinically apparent ischemic stroke, mortality, and functional disability were treated as distinct outcomes. Frequencies from observational cohorts were not combined with proportions derived from case-control designs, and no pooled effect estimates were calculated because of differences in participant selection, outcome definitions, imaging protocols, intervention regimens, and follow-up procedures. Formal publication-bias assessment and GRADE certainty evaluation were not undertaken. The review also did not incorporate independently verified duplicate study selection, data extraction, or methodological appraisal; these limitations were retained explicitly when interpreting the evidence.

RESULTS AND DISCUSSION

Study Characteristics, Cerebral Infarction Frequency, and Population-Related Heterogeneity in Adult Tuberculous Meningitis

The systematic review identified 234 records through PubMed, of which 168 were excluded during title and abstract screening, leaving 66 reports for full-text retrieval. Thirty-one reports could not be retrieved, while 35 underwent eligibility assessment, resulting in 11 primary studies that satisfied the predefined criteria for adult populations and cerebrovascular outcomes. The included evidence comprised two randomized controlled trials and nine observational investigations conducted across India, China, Indonesia, Vietnam, and France, with individual study populations ranging from 30 to 237 participants. This distribution reflects considerable geographical and methodological diversity, although the concentration of investigations within selected tertiary-care institutions limits the representativeness of the available evidence for broader adult TBM populations (Cantier et al., 2018; Bhatia et al., 2025; Sahu et al., 2026).

The included investigations demonstrated substantial differences in participant selection, clinical severity, demographic characteristics, and cerebrovascular assessment procedures, producing variations that complicate direct comparisons of cerebral infarction frequency. Studies involving adults without conventional vascular risk factors evaluated a comparatively restricted population, whereas investigations involving critically ill patients or older individuals examined groups with potentially different underlying susceptibility to ischemic injury (Zhang et al., 2019; Zhu et al., 2023). These differences are clinically relevant because the occurrence of cerebral infarction may reflect interactions between infection-associated inflammation, vascular vulnerability, and the severity of neurological disease rather than a uniform pathological mechanism. Contemporary evaluations of TBM-associated ischemia similarly emphasize the importance of interpreting cerebrovascular complications according to patient characteristics and disease-specific vascular processes rather than applying conventional stroke models without qualification (Lamb et al., 2026).

Variation in cerebral infarction frequency was particularly apparent when comparing observational investigations with different imaging protocols and clinical settings. Prospective research involving adult patients reported vascular complications under defined clinical observation, while retrospective investigations frequently depended on the availability of previously obtained neuroimaging and documentation of neurological abnormalities (Naik et al., 2022; Deng et al., 2025; Sahu et al., 2026). Such methodological differences influence the likelihood of identifying clinically silent infarction, determining lesion distribution, and establishing the temporal relationship between meningitis symptoms and ischemic events. The interpretation of reported frequencies consequently requires attention to whether cerebral infarction was identified systematically through imaging or selectively investigated after neurological deterioration, particularly when comparing observational cohorts with different levels of disease severity (Aggrohia et al., 2024).

The available primary studies demonstrated marked differences in the proportions of patients with cerebral infarction, with some cohorts reporting comparatively moderate frequencies and others identifying substantially higher proportions among selected clinical populations. Deng et al. (2025) documented ischemic stroke in 49 of 176 adults without conventional vascular risk factors, whereas Naik et al. (2022) identified cerebral infarction in 10 of 30 participants undergoing vascular neuroimaging assessment. Investigations involving critically ill patients and older adults reported different distributions, suggesting that clinical selection and age-related characteristics may influence the observed burden of cerebrovascular complications (Cantier et al., 2018; Zhu et al., 2023). Table 1 presents the principal descriptive findings from the included observational investigations, preserving the original study denominators and distinguishing clinically heterogeneous populations without calculating an unsupported pooled prevalence.

Table 1. Reported Frequency of Cerebral Infarction in Selected Adult Tuberculous Meningitis Studies

Study	Population or clinical setting	Sample size	Patients with cerebral infarction	Reported frequency
Sahu et al. (2026)	Prospective tertiary neurological care cohort, India	110	22	20.0%
Deng et al. (2025)	Adults without conventional vascular risk factors, China	176	49	27.8%
Zhu et al. (2023)	Adults aged ≥60 years, China	21	17	81.0%
Zhu et al. (2023)	Adults aged 18–59 years, China	176	47	26.7%
Harahap et al. (2023)	Adult patients undergoing CSF and MRI assessment, Indonesia	37	20	54.1%
Naik et al. (2022)	Adult patients undergoing MRI/MRA/MRV, India	30	10	33.3%
Zhang et al. (2019)	Young adults without conventional vascular risk factors, China	52	12	23.1%
Cantier et al. (2018)	Critically ill adults with available MRI, France	75*	38	50.7%

The comparative distribution presented in Table 1 demonstrates that reported cerebral infarction frequencies ranged from 20.0% in the prospective cohort of Sahu et al. (2026) to 81.0% among the 21 older participants examined by Zhu et al. (2023). The exceptionally high proportion in the older subgroup should not be interpreted as a population-level estimate because its small denominator produces substantial uncertainty and does not adequately separate age-related vulnerability from clinical severity or comorbidity. Similarly, the 50.7% frequency reported in the neuroimaged intensive-care population of Cantier et al. (2018) reflects a selected group of critically ill patients rather than the expected frequency among adults with TBM receiving routine hospital care. These findings indicate that differences in population composition, clinical referral pathways, and diagnostic ascertainment are central to interpreting the apparent variability of cerebral infarction across studies (Zhang et al., 2019; Deng et al., 2025).

Age-related heterogeneity represents a clinically relevant dimension of the observed distribution because cerebrovascular vulnerability may differ between younger adults and older patients affected by severe meningeal infection. Zhu et al. (2023) reported cerebral infarction in 17 of 21 patients aged at least 60 years compared with 47 of 176 younger and middle-aged adults, although the unadjusted comparison does not establish age as an independent causal determinant. The interpretation of this association is further complicated by potential differences in cardiovascular comorbidity, baseline neurological condition, inflammatory responses, and the probability of undergoing diagnostic neuroimaging. Investigations addressing clinical prognosis and cerebrovascular risk emphasize that demographic indicators should be evaluated alongside disease severity and

objectively measured vascular abnormalities before being incorporated into prediction frameworks (Aggrohia et al., 2024; Pandey et al., 2024).

The clinical setting also contributes to the observed heterogeneity because hospitalized patients with severe neurological manifestations are more likely to receive intensive diagnostic evaluation and may have a greater underlying burden of intracranial complications. Cantier et al. (2018) evaluated critically ill adults admitted to intensive care, whereas the study by Harahap et al. (2023) examined relationships between cerebrospinal fluid neutrophil percentages and cerebral infarction among patients undergoing MRI assessment. Differences between these settings prevent direct attribution of the reported infarction frequencies to biological disease activity without considering selection mechanisms and the clinical indications for imaging. Contemporary neuroimaging literature further demonstrates that the identification of ischemic lesions depends on the diagnostic capabilities of the imaging modality, particularly when vascular narrowing, tissue injury, and altered cerebral perfusion are investigated through different magnetic resonance techniques (Mertiri et al., 2024; Wang et al., 2026).

An additional methodological consideration concerns the distinction between the proportion of patients with existing infarction and the incidence of newly developed ischemic events during observation. Cross-sectional investigations and retrospective analyses may identify established cerebral lesions without establishing when they occurred relative to the onset of meningeal inflammation, while prospective investigations can provide more informative temporal observations when imaging assessments are consistently scheduled. The retrospective case-control investigation by Tang et al. (2022), which deliberately selected 70 patients with ischemic stroke and 70 controls, illustrates why the proportion of stroke cases within a case-control sample cannot be interpreted as disease prevalence. This distinction is particularly important when comparing predictive models and observational associations, as artificially determined case-control proportions and incomplete follow-up data may distort interpretations of cerebrovascular risk (Tomidy et al., 2023).

The observed variation in cerebral infarction frequency also raises questions concerning the biological interpretation of vascular involvement in TBM, particularly whether radiological infarction represents a distinct manifestation of inflammatory injury or a consequence of several interacting intracranial processes. Investigations of inflammatory biomarkers and cerebrospinal fluid characteristics have identified associations with disease severity, neurological outcomes, and inflammatory activity, although these findings do not establish that individual biomarkers consistently predict cerebral infarction across patient populations (Dian et al., 2025; Tugume et al., 2025). Evidence concerning paradoxical inflammatory reactions further indicates that neurological deterioration may occur through processes that require differentiation from established ischemic lesions, especially when evaluating changes during treatment (Deswal et al., 2026). The heterogeneity identified across the included studies supports a cautious interpretation of cerebral infarction frequency and indicates that future prospective investigations should employ consistent imaging criteria, clearly defined patient populations, standardized observation periods, and explicit separation of prevalent infarction from newly occurring ischemic events.

Clinical and Inflammatory Factors Associated with Cerebral Infarction in Adult Tuberculous Meningitis

Cerebral infarction in adult tuberculous meningitis (TBM) is associated with a complex interaction between meningeal inflammation, cerebrovascular abnormalities, neurological manifestations, and host-related characteristics that cannot be adequately explained by conventional stroke risk factors alone. The available observational evidence indicates that ischemic complications may develop in patients without established vascular comorbidities, suggesting that infection-associated pathological processes contribute substantially to cerebral vascular injury (Zhang et al., 2019; Tang et al., 2022). Inflammatory involvement of the basal meninges may affect penetrating cerebral arteries through vascular wall injury, luminal narrowing, and disturbances in regional cerebral blood flow, although the relative contribution of each mechanism remains difficult to establish without longitudinal vascular assessment. Contemporary interpretations of TBM-associated ischemia emphasize that inflammatory activity, vascular susceptibility, and neurological disease severity should be considered interconnected but analytically distinct dimensions of cerebrovascular injury (Lamb et al., 2026).

The anatomical distribution of cerebral infarction provides relevant evidence for understanding the relationship between meningeal inflammation and intracranial vascular injury. Deng et al. (2025) reported frequent involvement of the basal ganglia among adults experiencing TBM-associated ischemic stroke, with some patients demonstrating multiple lesions or infarction affecting more than one vascular territory. This distribution is anatomically compatible with involvement of perforating arteries located near the basal meningeal inflammatory process, although lesion location alone cannot establish histopathologically confirmed vasculitis. Neuroimaging investigations have also identified arterial abnormalities and venous complications in patients with TBM, indicating that vascular involvement is not restricted to a single pathological compartment (Naik et al., 2022; Mertiri et al., 2024).

Clinical manifestations constitute another important dimension of cerebral infarction assessment, particularly because neurological deterioration may reflect established ischemic injury rather than a factor preceding its development. In the retrospective cohort of Deng et al. (2025), focal neurological deficits were strongly associated with ischemic stroke, with a reported odds ratio of 23.72 and a 95% confidence interval of 9.10–61.83. The magnitude of this association indicates substantial discrimination between patients with and without identified stroke within the studied population, but it does not establish that focal deficits predict future infarction because these manifestations may arise after vascular injury has occurred. This distinction is fundamental to the interpretation of proposed clinical prediction models, which require temporal separation between predictor measurement and outcome occurrence before their prospective utility can be established (Aggrohia et al., 2024).

Cerebrospinal fluid (CSF) inflammatory characteristics have attracted particular attention because they may provide indirect information about the inflammatory environment associated with cerebral vascular injury. Harahap et al. (2023) observed higher CSF neutrophil percentages among patients with cerebral infarction than among those without infarction, while Zhang et al. (2019) identified associations between CSF inflammatory characteristics, basal meningeal enhancement, and ischemic stroke in a selected adult cohort. These findings suggest that inflammatory measurements may have clinical relevance when interpreted alongside neuroimaging, although CSF abnormalities are not specific to cerebral infarction and may reflect broader intracranial inflammatory activity. Research examining CSF inflammatory profiles and neurological outcomes reinforces the importance of distinguishing markers associated with disease severity or mortality from biomarkers independently validated for identifying vascular complications (Dian et al., 2025; Imron et al., 2025).

The principal quantitative associations reported in the included primary studies are summarized in Table 2, which distinguishes neurological manifestations, CSF characteristics, meningeal enhancement, and multivariable identification models. These findings were derived from studies with different populations, designs, and analytical procedures, preventing direct comparison of their effect estimates as measurements of a common predictive construct. Particular caution is required when interpreting variables measured contemporaneously with cerebral infarction, because an observed association may represent a consequence of ischemic injury rather than an antecedent risk factor. The reported estimates are therefore presented according to their original analytical purposes rather than combined into a pooled prognostic measure (Tang et al., 2022; Deng et al., 2025).

Table 2. Clinical, Inflammatory, and Neuroimaging Factors Associated with Cerebral Infarction in Adult Tuberculous Meningitis

Study	Investigated factor	Reported statistical finding	Analytical interpretation
Deng et al. (2025)	Focal neurological deficits	OR = 23.72; 95% CI: 9.10–61.83	Strong association with existing ischemic stroke; temporal predictive value remains uncertain
Deng et al. (2025)	Leptomeningeal enhancement	OR = 2.442; 95% CI: 0.992–6.010; reported p = 0.049	Borderline association requiring cautious interpretation because the reported confidence interval crosses unity
Zhang et	Basal meningeal	OR = 23.91; 95% CI:	Potential association with ischemic

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al. (2019)	enhancement	1.40–408.98	stroke; markedly imprecise effect estimate
Zhang et al. (2019)	Age	OR = 1.30; 95% CI: 1.07–1.58	Association within a selected young-adult cohort; generalizability remains limited
Harahap et al. (2023)	CSF neutrophil percentage	Median 43.5% versus 25%; p = 0.025	Higher neutrophil percentage among patients with infarction; observational association
Harahap et al. (2023)	CSF neutrophil threshold >41%	Kappa = 0.529	Exploratory agreement measure; threshold requires external validation
Tang et al. (2022)	Combined clinical and laboratory identification model	AUC = 0.808; 95% CI: 0.736–0.881; sensitivity = 68.6%; specificity = 84.3%	Apparent discrimination in the development sample; external validation not established
Zhu et al. (2023)	Age ≥60 years versus 18–59 years	Infarction: 81% versus 27%; reported p = 0.001	Unadjusted age-group comparison; potential confounding and limited older-patient sample

The statistical findings summarized in Table 2 indicate that clinical manifestations and inflammatory characteristics differ considerably in their potential relevance to cerebral infarction, particularly when temporal relationships and measurement properties are considered. The association between focal neurological deficits and ischemic stroke reported by Deng et al. (2025) is substantially stronger than the reported association involving leptomeningeal enhancement, but the former may principally reflect clinical recognition of an existing vascular event. The leptomeningeal enhancement estimate also presents an interpretative inconsistency because its reported confidence interval marginally includes unity despite a p value below 0.05, preventing an unequivocal conclusion regarding statistical significance from the published values alone. The exceptionally wide confidence interval reported for basal meningeal enhancement by Zhang et al. (2019) further illustrates how small event numbers and model instability can generate apparently large associations with considerable uncertainty.

The evaluation of inflammatory biomarkers requires an additional distinction between biological plausibility and clinically actionable prediction because markers of meningeal inflammation may be associated with multiple neurological and systemic outcomes. Harahap et al. (2023) identified a relationship between CSF neutrophil percentage and radiologically detected cerebral infarction, but the proposed threshold was derived from a small study population and was not established through independent external validation. Investigations examining inflammatory markers, including CSF profiles and circulating C-reactive protein, have expanded understanding of TBM severity and prognosis without demonstrating that the same markers consistently provide infarction-specific predictive accuracy (Dian et al., 2025; Tugume et al., 2025). Research on inflammatory biomarkers associated with paradoxical reactions further indicates that post-treatment inflammatory changes may influence neurological manifestations, creating potential diagnostic overlap between inflammatory deterioration and ischemic complications (Deswal et al., 2026).

Multivariable identification models offer a potentially more informative approach than isolated biomarkers because cerebral infarction may reflect the combined influence of clinical, hematological, and inflammatory characteristics. Tang et al. (2022) reported an area under the receiver operating characteristic curve of 0.808, with sensitivity of 68.6% and specificity of 84.3%, indicating moderate-to-good apparent discrimination within the investigated case-control sample. The model was developed using an artificially balanced distribution of 70 ischemic stroke cases and 70 controls, which prevents direct estimation of stroke prevalence and limits the interpretation of predictive performance under routine clinical conditions. Subsequent research examining factors associated with cerebral infarction has reinforced interest in risk identification, although clinical implementation requires prospective validation, assessment of calibration, and evaluation of whether proposed models provide information beyond conventional neurological and imaging examinations (Aggrohia et al., 2024).

The temporal dynamics of inflammatory and ischemic manifestations constitute a further source of uncertainty because neurological abnormalities may emerge at different stages of TBM and during therapeutic intervention. Deng et al. (2025) reported that 41 of 49 patients with ischemic stroke experienced the event within three months of meningitis symptom onset, while 10 of the 49 patients lacked clearly recognizable clinical stroke manifestations. These findings indicate that relying exclusively on overt focal neurological deterioration may underestimate radiologically detectable ischemic complications, although they do not establish an optimal universal imaging interval. Investigations of symptom resolution and neuroimaging changes during treatment further demonstrate the importance of longitudinal assessment when distinguishing persistent inflammatory abnormalities from evolving neurological complications (Pandey et al., 2024).

The evidence supports an interpretation of cerebral infarction in adult TBM as a multifactorial complication associated with inflammatory activity, cerebral vascular involvement, and clinically heterogeneous host characteristics rather than a condition reliably identified through any single laboratory or neurological indicator. Associations involving CSF abnormalities, meningeal enhancement, age, and focal deficits remain constrained by retrospective study designs, limited sample sizes, differences in outcome ascertainment, and insufficient independent validation of predictive models. Contemporary clinical management research and therapeutic investigations provide additional evidence concerning infection control and inflammatory responses, but improvements in general TBM outcomes cannot automatically be interpreted as reductions in cerebral infarction unless vascular endpoints are explicitly assessed (Abdelgawad et al., 2024; Fei et al., 2025; Saluja et al., 2023; Garg, 2026). Future investigations should prioritize prospective measurement of candidate predictors before ischemic events, standardized MRI-based infarction definitions, longitudinal inflammatory profiling, and external validation across adult populations with differing clinical severity and vascular comorbidity.

Neuroimaging Assessment, Therapeutic Interventions, and Clinical Implications of Cerebral Infarction in Adult Tuberculous Meningitis

Neuroimaging assessment constitutes a central component of cerebral infarction identification in adult tuberculous meningitis (TBM), particularly because neurological manifestations do not consistently correspond to the anatomical extent or temporal development of ischemic injury. Conventional magnetic resonance imaging (MRI) enables the identification of cerebral parenchymal abnormalities, while diffusion-weighted sequences contribute to recognizing ischemic lesions that may remain clinically unrecognized during neurological examination. The retrospective investigation by Deng et al. (2025) identified patients with radiologically confirmed ischemic stroke who lacked clearly recognizable stroke manifestations, demonstrating the limitations of symptom-based detection in selected adult populations. Advances in neurological imaging have consequently increased attention to the complementary evaluation of cerebral tissue, vascular structures, and regional perfusion rather than reliance on a single imaging modality (Mertiri et al., 2024; Wang et al., 2026).

The anatomical characterization of cerebrovascular abnormalities requires differentiation between arterial involvement, venous complications, and ischemic damage affecting cerebral parenchyma. Magnetic resonance angiography (MRA) provides information concerning arterial luminal abnormalities, whereas magnetic resonance venography (MRV) evaluates venous structures that may be affected by distinct pathological processes during TBM. Naik et al. (2022) reported arterial abnormalities in 13 of 30 patients and cerebral infarction in 10 patients, while cerebral venous sinus thrombosis was identified in two participants, indicating that intracranial vascular involvement may extend beyond arterial ischemia. These observations support the interpretation that vascular imaging abnormalities should not automatically be classified as cerebral infarction or attributed to a uniform mechanism of inflammatory vasculitis without additional diagnostic evidence (Lamb et al., 2026).

Advanced MRI techniques have introduced additional opportunities to characterize the physiological consequences of cerebrovascular abnormalities by examining cerebral perfusion and tissue integrity beyond conventional structural imaging. Kumar and Gutch (2020) investigated arterial spin labeling (ASL), diffusion tensor imaging, and magnetization transfer techniques in adults with TBM, identifying perfusion abnormalities that were not necessarily restricted to regions with established cerebral infarction. Such findings suggest that reduced cerebral blood flow and

irreversible ischemic injury represent related but nonidentical physiological phenomena, requiring careful distinction when interpreting imaging abnormalities. More recent investigations incorporating quantitative ASL perfusion and vessel wall imaging have expanded the methodological possibilities for evaluating vascular involvement and treatment-associated imaging changes, although their clinical applicability requires consideration of study populations, examination timing, and outcome definitions (Wang et al., 2026).

The diagnostic value of neuroimaging is also influenced by the timing of assessment relative to infection progression, clinical deterioration, and therapeutic intervention. Cross-sectional imaging can demonstrate established cerebral infarction but cannot independently determine the exact sequence of vascular inflammation, perfusion impairment, and tissue injury when baseline examination is unavailable. Prospective neuroimaging investigations have therefore contributed to understanding how neurological abnormalities may evolve during treatment, although differences in follow-up schedules limit comparisons between studies (Pandey et al., 2024). This methodological limitation becomes particularly relevant when infarction detected at follow-up is interpreted as a newly developed complication, since consistent baseline and subsequent imaging are required to establish the temporal status of ischemic lesions (Deng et al., 2025).

The included studies employed distinct imaging approaches and therapeutic outcome assessments, producing evidence that requires separation according to the clinical questions addressed by each investigation. Structural MRI, angiographic examination, venous imaging, and perfusion techniques were used to characterize different components of cerebral vascular involvement, whereas randomized therapeutic investigations evaluated whether adjunctive antiplatelet treatment altered ischemic or composite clinical outcomes. Table 3 summarizes the principal imaging findings and intervention-related outcomes reported in the included primary studies, preserving differences in study design, diagnostic procedures, and outcome definitions. The comparative presentation facilitates interpretation of diagnostic observations separately from evidence concerning therapeutic effectiveness, avoiding the assumption that improved visualization of vascular abnormalities necessarily indicates an effective preventive intervention (Mai et al., 2018; Bhatia et al., 2025).

Table 3. Neuroimaging Characteristics and Therapeutic Outcomes in Adult Tuberculous Meningitis

Study	Investigation or intervention	Reported findings	Clinical interpretation
Naik et al. (2022)	MRI, MRA, and MRV	Cerebral infarction in 10/30 patients (33.3%); arterial abnormalities in 13/30 (43.3%); venous sinus thrombosis in two patients	Arterial, venous, and parenchymal abnormalities require separate diagnostic interpretation
Kumar & Gutch (2020)	Advanced MRI including ASL, DTI, and MTR	Cerebral infarction approximately 27%; reduced basal ganglia cerebral blood flow compared with controls ($p < 0.05$)	Perfusion abnormalities may provide information beyond established structural infarction
Deng et al. (2025)	MRI assessment of ischemic stroke	Stroke in 49/176 patients (27.8%); 10/49 patients (20.4%) lacked clear clinical stroke manifestations	Imaging may identify ischemic lesions without overt clinical manifestations
Cantier et al. (2018)	MRI in critically ill adults	Infarction in 38/75 imaged patients (50.7%)	Findings reflect a selected intensive-care population and incomplete cohort imaging
Mai et al. (2018)	Aspirin 81 mg, aspirin 1,000 mg, or placebo	New infarction or death: 22.2%, 15.8%, and 28.9%, respectively; $p = 0.40$	Numerical differences did not demonstrate statistically established treatment benefit
Bhatia et	Aspirin 75 mg,	Primary outcome at one month:	No definitive difference

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al. (2025)	clopidogrel 75 mg, or standard treatment	9.1%, 11.1%, and 14.3%, respectively; p = 0.60	between treatment groups was established

The findings presented in Table 3 demonstrate that neuroimaging contributes to identifying cerebral vascular involvement through several complementary modalities, although their diagnostic information cannot be treated as interchangeable. The identification of arterial abnormalities in 43.3% of participants in the investigation by Naik et al. (2022), compared with cerebral infarction in 33.3%, illustrates that abnormal vascular findings and established ischemic lesions do not necessarily occur in identical proportions. The perfusion abnormalities described by Kumar and Gutch (2020) further suggest that physiological disturbances may be detectable beyond regions exhibiting conventional imaging evidence of infarction, although their small study population limits conclusions concerning diagnostic accuracy or prognostic value. These observations are consistent with contemporary neuroimaging approaches that emphasize the distinction between vascular morphology, regional blood flow, and irreversible cerebral tissue injury (Mertiri et al., 2024; Wang et al., 2026).

Therapeutic investigations have examined whether modulation of platelet activity or inflammatory processes can reduce cerebrovascular complications associated with TBM, although the available randomized evidence remains insufficient to establish a definitive antiplatelet strategy. Mai et al. (2018) evaluated adjunctive aspirin at doses of 81 mg and 1,000 mg against placebo, reporting numerically lower proportions of the composite outcome of new cerebral infarction or death in the aspirin groups without a statistically significant overall difference. The subsequent ACT-TBM trial compared aspirin 75 mg, clopidogrel 75 mg, and standard medical treatment, similarly failing to demonstrate a conclusive difference in the primary vascular outcome despite numerical variation between groups (Bhatia et al., 2025). Differences in drug exposure, comparator groups, clinical characteristics, endpoint definitions, and follow-up procedures prevent the numerical results of these trials from being interpreted as equivalent estimates of treatment effectiveness.

The interpretation of therapeutic efficacy is further complicated by the biological distinction between controlling meningeal inflammation and preventing established cerebral ischemic injury. Adjunctive corticosteroid treatment has been investigated as a strategy for improving outcomes in TBM, but evidence concerning mortality or broader neurological endpoints cannot automatically establish a specific reduction in cerebral infarction. Donovan et al. (2023) evaluated adjunctive dexamethasone in adults with HIV-associated TBM, while Saluja et al. (2023) investigated different dexamethasone regimens, contributing evidence concerning treatment strategies without providing a directly interchangeable basis for infarction-specific conclusions. Investigations of linezolid pharmacokinetics and clinical effectiveness similarly inform antimicrobial treatment considerations, although pharmacological exposure and general therapeutic outcomes should be distinguished from demonstrated cerebrovascular protection (Abdelgawad et al., 2024; Fei et al., 2025).

Clinical interpretation also requires attention to methodological limitations that may influence the apparent effectiveness of antiplatelet interventions, particularly missing follow-up imaging, incomplete outcome ascertainment, and the competing consequences of severe neurological disease. The randomized investigation by Bhatia et al. (2025) reported incomplete follow-up assessments, creating uncertainty because patients with severe illness or death may be less likely to undergo scheduled neuroimaging. A statistically nonsignificant comparison should not be interpreted as proof of therapeutic equivalence, especially when confidence intervals remain compatible with clinically relevant benefit or an absence of meaningful treatment effect. Contemporary clinical management literature consequently supports cautious interpretation of adjunctive therapies while maintaining the distinction between established TBM treatment, management of neurological complications, and interventions specifically intended to prevent cerebral infarction (Garg, 2026; Donovan et al., 2026).

The available evidence indicates that cerebral infarction assessment in adult TBM requires integration of neurological examination with appropriately selected structural and vascular neuroimaging, while recognizing that diagnostic abnormalities, inflammatory activity, and therapeutic outcomes represent distinct dimensions of the disease. MRI and complementary vascular techniques provide clinically relevant information concerning ischemic lesions and intracranial vascular involvement, but the reviewed studies do not establish a universally applicable imaging schedule or demonstrate that advanced imaging independently improves long-term functional outcomes (Naik et al., 2022; Kumar & Gutch, 2020; Deng et al., 2025). Randomized trials have not established a

definitive benefit from routine adjunctive antiplatelet administration for preventing cerebrovascular complications, and current findings do not justify extrapolating treatment effectiveness from numerical differences or composite endpoints alone (Mai et al., 2018; Bhatia et al., 2025). Future investigations should prioritize standardized definitions of imaging-confirmed cerebral infarction, prospective vascular assessment, consistent reporting of neurological and functional outcomes, and adequately powered therapeutic evaluations capable of distinguishing infarction prevention from improvements in general TBM prognosis.

CONCLUSION

Cerebral infarction represents a clinically significant cerebrovascular complication of tuberculous meningitis in adults, with considerable variation in its reported frequency, anatomical distribution, and associated clinical characteristics. The systematic review of 11 primary studies demonstrated that cerebral infarction frequency ranged from 20.0% to 81.0% across selected observational populations, although differences in participant selection, disease severity, age distribution, and neuroimaging procedures prevented the calculation of a reliable pooled estimate. Ischemic lesions frequently involved the basal ganglia and other vascular territories, supporting an association between meningeal inflammation and cerebrovascular injury without establishing a uniform causal mechanism. Clinical and inflammatory factors, including older age, focal neurological deficits, cerebrospinal fluid neutrophil percentages, and meningeal enhancement, demonstrated associations with cerebral infarction, but their predictive utility remained constrained by limited sample sizes, temporal ambiguity, potential confounding, and insufficient external validation. Structural magnetic resonance imaging, magnetic resonance angiography, venography, and advanced perfusion techniques provided complementary information concerning cerebral tissue injury, vascular abnormalities, and regional blood flow, particularly when ischemic lesions occurred without recognizable clinical stroke manifestations. These findings establish the importance of distinguishing radiologically confirmed infarction from clinical stroke, vascular abnormalities, and broader neurological outcomes when interpreting cerebrovascular complications in adult tuberculous meningitis.

Therapeutic evidence from two randomized controlled trials did not demonstrate a definitive benefit of adjunctive antiplatelet treatment for preventing cerebral infarction or improving the assessed vascular outcomes, although differences in intervention regimens, composite endpoints, and incomplete follow-up limited the certainty of interpretation. The findings do not support a general recommendation for routine antiplatelet administration specifically to prevent TBM-associated cerebral infarction, nor do they establish an optimal drug or dosage for this purpose. The principal scientific contribution of this review lies in integrating evidence concerning infarction patterns, associated clinical and inflammatory factors, neuroimaging assessment, and therapeutic interventions while distinguishing observational associations from causal or prognostic conclusions. Its clinical implications support coordinated neurological evaluation and appropriately selected neuroimaging, with laboratory and inflammatory markers interpreted as supplementary rather than independently validated diagnostic indicators. Interpretation remains limited by the exclusive use of PubMed for systematic searching, the unavailability of 31 potentially relevant full-text reports, heterogeneous study methodologies, possible cohort overlap, and the absence of formal certainty-of-evidence assessment. Future investigations should prioritize prospective multicenter designs, standardized infarction definitions, consistent baseline and follow-up imaging, independent validation of proposed predictive factors, and adequately powered randomized trials employing clearly defined cerebrovascular and functional outcomes. These priorities may strengthen the reliability of cerebral infarction identification, improve risk assessment, and provide a more rigorous foundation for evaluating preventive interventions in adults with tuberculous meningitis.

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