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TUBERCULOUS MENINGITIS IN ADULTS: A REVIEW OF THE ROLE OF ADJUNCTIVE CORTICOSTEROIDS, EMERGING DRUG RESISTANCE PATTERNS, AND KEY PREDICTORS OF MORTALITY AND MORBIDITY

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Abstract

Background: *Tuberculous meningitis (TBM) is the most severe form of extrapulmonary tuberculosis, and despite breakthroughs in antibiotic therapy and supportive care, it remains associated with high mortality and long-term neurological impairment. Delayed diagnosis, rising multidrug-resistant tuberculosis (MDR-TB), and diversity in host immunological responses all complicate therapeutic therapy and negatively impact patient outcomes.*

Objectives: *This review objectively assesses the existing information on the role of supplementary corticosteroid therapy, growing anti-tuberculous medication resistance patterns, and the primary determinants of death and neurological morbidity in adults with tuberculous meningitis.*

Methods: *A comprehensive narrative review was carried out using PubMed/MEDLINE, Scopus, Web of Science, Google Scholar, and the Cochrane Library. English-language research published between January 2015 and June 2026, as well as important previous articles, were reviewed using preset eligibility criteria. The study includes 78 high-quality papers, such as randomized controlled trials, cohort studies, systematic reviews, meta-analyses, and international clinical guidelines. Due to methodological heterogeneity, findings were synthesized through a thematic narrative approach.*

Results: *Current research confirms that additive dexamethasone is still the best corticosteroid for adult TBM, with a 22-30% decrease in mortality and reduced incidences of cerebral oedema and hydrocephalus. However, its efficacy in preventing long-term neurological impairment is limited. Drug-resistant TBM, particularly multidrug-resistant and rifampicin-resistant*

illness, remains a significant therapeutic challenge due to delayed diagnosis, limited treatment options, protracted therapy, and poor clinical results. Delays in starting treatment, advanced disease severity, HIV coinfection, altered consciousness, low Glasgow Coma Scale score, hydrocephalus, cerebral infarction, and significant cerebrospinal fluid abnormalities are all reliable predictors of a poor prognosis. Emerging molecular diagnostic tools, particularly next-generation sequencing and Xpert MTB/RIF Ultra, have significantly higher diagnostic sensitivity than traditional cerebrospinal fluid microscopy and culture, allowing for earlier diagnosis and more immediate therapeutic intervention.

Conclusion: *Adult tuberculous meningitis continues to be a deadly brain infection with significant mortality and disability rates. Earlier diagnosis using improved molecular techniques, rapid beginning of optimized anti-tuberculosis medication, routine use of adjunctive corticosteroids when appropriate, and early identification of prognostic risk factors are critical for improving clinical outcomes. To further lower the worldwide burden of TBM, more research into quick diagnostics, personalized therapy techniques, host-directed medicines, and optimized treatment regimens for drug-resistant illness will be needed.*

Introduction

Tuberculous meningitis (TBM) is the most severe and life-threatening type of extrapulmonary tuberculosis (TB), which occurs when *Mycobacterium tuberculosis* spreads to the meninges and central nervous system (Malik et al., 2025). Although significant improvements have been made in TB control, TB continues to be one of the biggest causes of morbidity and mortality among infectious diseases globally, with millions of new cases reported each year, especially in low- and middle-income countries (LMICs) (Reid et al., 2023). Despite the small percentage of people with TB diagnosed with TBM, it causes a large proportion of TB-related deaths, and long-term neurological disability is related to the clinical severity of TB and the long delay between being diagnosed with TB and TBM (Oo & Agrawal, 2025).

Adults who are HIV infected, have diabetes mellitus, have chronic renal disease, are malnourished, or have any other condition that compromises immunity are at a higher risk of developing TBM and have a poor clinical outcome (Navasardyan et al., 2023; Chen et al., 2024). The disease is characterized by dissemination of *M. tuberculosis* to the central nervous system, intense inflammatory responses, basal meningeal exudates, cerebral vasculitis, hydrocephalus and infarction, all of which lead to significant neurological disease and mortality (Mandal et al., 2024). Despite timely starting of anti-tuberculous treatment, mortality rates are not low, and many patients with TB are left with permanent cognitive and/or cranial nerve deficits, seizures and/or disability.

Early diagnosis of TBM can be difficult because the early signs and symptoms are nonspecific and mimic other infectious and noninfectious neurological diseases (Garg et al., 2025). Although newer molecular diagnostic assays such as the GeneXpert MTB/RIF Ultra have improved diagnostic sensitivity, they do not have adequate turnaround time, and CSF microscopy and culture are still only moderately sensitive. Conventional CSF microscopy/culture assays were only moderately sensitive, and newer molecular assays such as the GeneXpert MTB/RIF Ultra had improved diagnostic accuracy but were not suitable for rapid turnaround time (Dahiya et al., 2023; Yadav et al., 2024). Therefore, treatment is often based on clinical judgment, and it is important to identify

high-risk patients and start empirical treatment promptly.

The current treatment for adult TBM is long-term multidrug anti-tuberculosis treatment along with adjunctive corticosteroids that have been shown to improve survival by decreasing excessive intracranial inflammation. However, corticosteroids are not always effective in preventing neurological disability, and their effectiveness may vary depending on HIV status, disease burden and host inflammatory response (Li et al., 2025; Nasiri et al., 2024). Meanwhile, multidrug-resistant (MDR) and rifampicin-resistant tuberculosis (RR-TB) is becoming more common around the world, which poses a significant therapeutic challenge due to delayed diagnosis, limited treatment options, increased mortality, and decreased neurological outcomes (Xi et al., 2022).

Advanced disease state at presentation, delayed treatment initiation, HIV coinfection, altered consciousness, presence of hydrocephalus, cerebral infarction, high protein concentration in CSF and resistance to antimicrobials have been identified as risk factors for mortality and morbidity in adult TBM (Evans et al., 2022). Knowing about these indicators is crucial for risk stratification, treatment planning and better outcomes.

This review outlines the current evidence on adult tuberculous meningitis, focusing on the role of adjunctive corticosteroid therapy, patterns of anti-tuberculous drug resistance and the main mortality and long-term morbidity risk factors. This review will present an up-to-date summary of the most recent and relevant advances in diagnosis, treatment and prognostic evaluation to give clinicians and researchers a current overview of how best to approach the management of this debilitating disease in the future.

Methodology

Literature Search Strategy

This narrative review was conducted to summarize and critically evaluate the current evidence regarding adult tuberculous meningitis (TBM), with particular emphasis on the role of adjunctive corticosteroids, emerging drug resistance patterns, and predictors of mortality and morbidity. A comprehensive literature search was performed using the electronic databases PubMed/MEDLINE, Scopus, Web of Science, Google Scholar, and the Cochrane Library. The search included studies published between January 2015 and June 2026, while selected landmark studies published before 2015 were also considered when they provided foundational evidence relevant to corticosteroid therapy, TBM diagnosis, or treatment. To ensure comprehensive coverage of the available evidence, the reference lists of relevant review articles, randomized controlled trials, meta-analyses, and international clinical practice guidelines were manually screened to identify additional eligible publications.

Search Strategy

The literature search was conducted using a combination of Medical Subject Headings (MeSH) and free-text keywords. Boolean operators (AND/OR) were applied to refine the search and maximize retrieval of relevant publications. The principal search terms included "tuberculous meningitis," "TBM," "adult tuberculous meningitis," "adjunctive corticosteroids," "dexamethasone," "corticosteroid therapy," "drug-resistant tuberculosis," "multidrug-resistant tuberculosis," "rifampicin-resistant tuberculosis," "mortality," "morbidity," "prognostic factors," "clinical outcomes," "diagnosis," "management," "GeneXpert," and "host-directed therapy." Different combinations of these keywords were used across the selected databases according to their indexing systems.

Study Selection

Following completion of the literature search, retrieved records were screened according to their titles and abstracts to identify potentially relevant studies. Full-text articles meeting the objectives of the review were subsequently evaluated for eligibility. Greater emphasis was placed on high-quality evidence, including randomized controlled trials, systematic reviews, meta-

analyses, multicenter cohort studies, prospective observational studies, and recommendations published by recognized organizations such as the World Health Organization (WHO). When multiple studies addressed similar clinical questions, preference was given to the most recent publications with larger study populations and stronger methodological quality.

Inclusion and Exclusion Criteria

Studies were included if they were published in English and involved adult patients (≥18 years) diagnosed with tuberculous meningitis. Eligible publications comprised randomized controlled trials, systematic reviews, meta-analyses, prospective and retrospective cohort studies, case–control studies, observational studies, clinical practice guidelines, and high-quality narrative reviews. Studies addressing epidemiology, pathogenesis, diagnostic methods, adjunctive corticosteroid therapy, anti-tuberculosis treatment, multidrug-resistant or rifampicin-resistant TBM, predictors of mortality and neurological morbidity, clinical outcomes, and recent therapeutic advances were considered eligible. Landmark publications providing essential evidence for current TBM management were also included regardless of publication year.

Studies were excluded if they focused exclusively on pediatric populations, pulmonary tuberculosis without specific data on TBM, animal or in vitro experimental studies lacking clinical relevance, case reports, conference abstracts without full-text availability, editorials, letters to the editor, expert opinions, dissertations, duplicate publications, or articles published in languages other than English. Publications with insufficient methodological details or those not directly relevant to the objectives of this review were also excluded.

Data Extraction

Relevant information was extracted from each eligible publication using a standardized approach. Extracted data included study characteristics, publication year, country, study design, sample size, patient demographics, diagnostic methods, adjunctive corticosteroid regimens, anti-tuberculosis treatment strategies, drug-resistance profiles, mortality rates, neurological complications, prognostic indicators, and principal findings. Information regarding advances in molecular diagnostics, neuroimaging, host-directed therapies, and emerging antimicrobial agents was also collected where available.

Data Synthesis

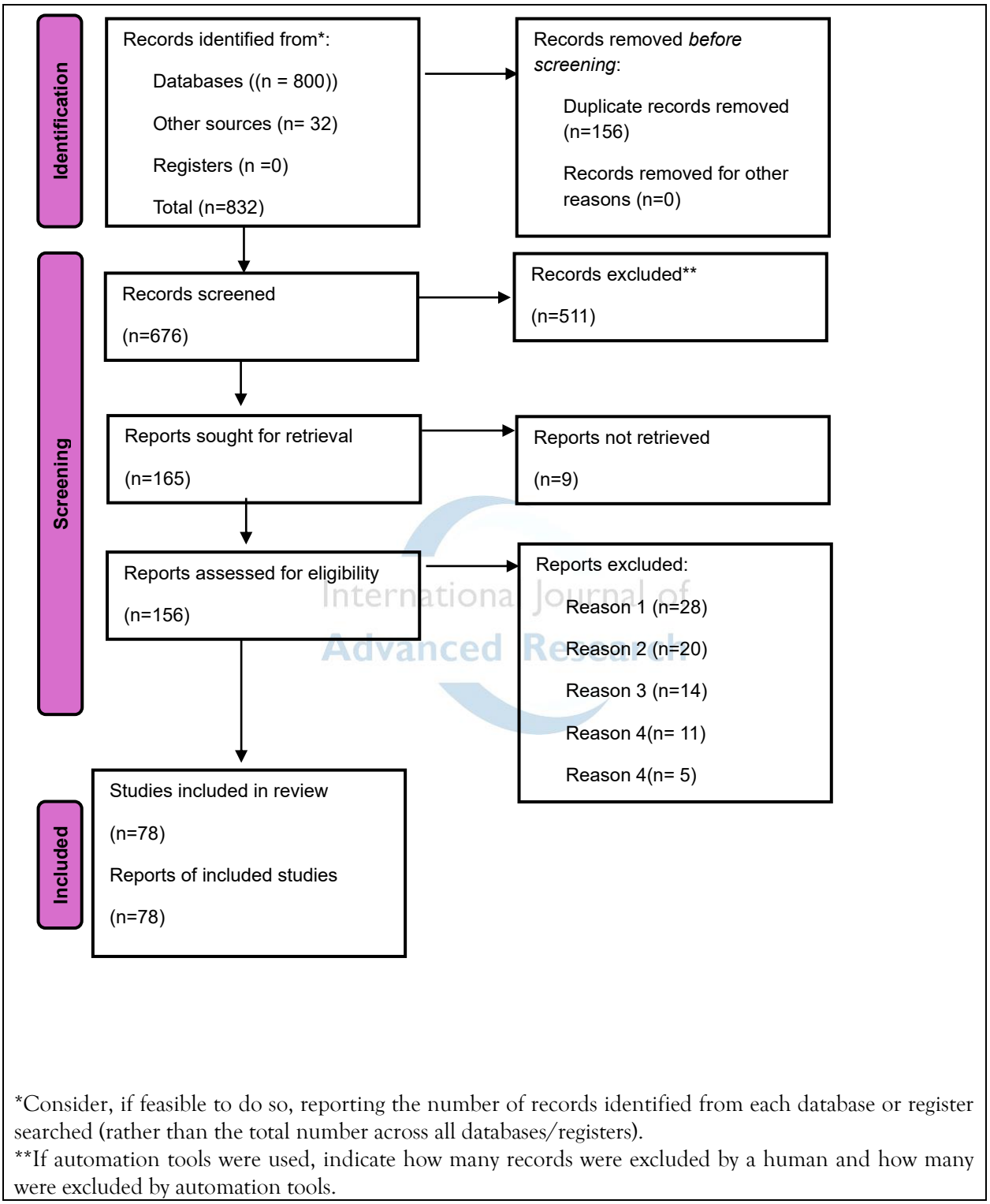
Because of considerable heterogeneity among the included studies with respect to study design, patient populations, diagnostic approaches, therapeutic interventions, and outcome measures, a quantitative meta-analysis was not performed. Instead, the evidence was synthesized narratively through a thematic approach. The selected literature was organized into major sections covering epidemiology, pathogenesis, clinical manifestations, diagnostic approaches, adjunctive corticosteroid therapy, emerging drug resistance patterns, predictors of mortality and morbidity, current management strategies, and future research directions. Findings from different study designs were critically compared to identify areas of consensus, conflicting evidence, recent advances, and remaining knowledge gaps. This narrative synthesis provides a comprehensive and evidence-based overview of the current understanding and management of adult tuberculous meningitis.

Results

Study Selection

A total of 832 records were identified in the literature search, of which 800 records were obtained from electronic databases and 32 by additional means. A total of 156 duplicate studies were excluded, leaving 676 studies for screening of titles and abstracts. After screening, 511 records were removed due to not meeting predefined eligibility criteria. The full-text versions of 165 articles were reviewed in detail, but 9 reports were not successfully retrieved. Based on these criteria, 156 full-text articles were evaluated for their eligibility, and 78 studies were

found to be eligible for inclusion and form the basis of the present narrative review (Figure 1).



*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).
**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

Figure 1: PRISMA 2020 flow diagram illustrating the literature search and study selection process for the review.

Characteristics of Included Studies

A total of 78 studies with different designs were included in the last review. Of these studies, 18 (23.1%) were retrospective cohort studies, 15 (19.2%) were prospective cohort studies and 12 (15.4%) were randomized controlled trials. Ten studies (12.8%) were observational studies, nine (11.5%) were systematic reviews and six (7.7%) were meta-analyses. Five narrative reviews (6.4%) and three clinical practice guidelines (3.9%) were also included. The wide variation of study designs yielded comprehensive evidence on the diagnosis, management and outcomes of adult tuberculous meningitis (Table 1).

Table 1: Distribution of Included Studies According to Study Design (n = 78)

Study Design	Number of Studies (n)	Percentage (%)
Randomized controlled trials	12	15.4
Prospective cohort studies	15	19.2
Retrospective cohort studies	18	23.1
Observational studies	10	12.8
Systematic reviews	9	11.5
Meta-analyses	6	7.7
Narrative reviews	5	6.4
Clinical practice guidelines	3	3.9
Total	**78**	**100**

Publication Trends

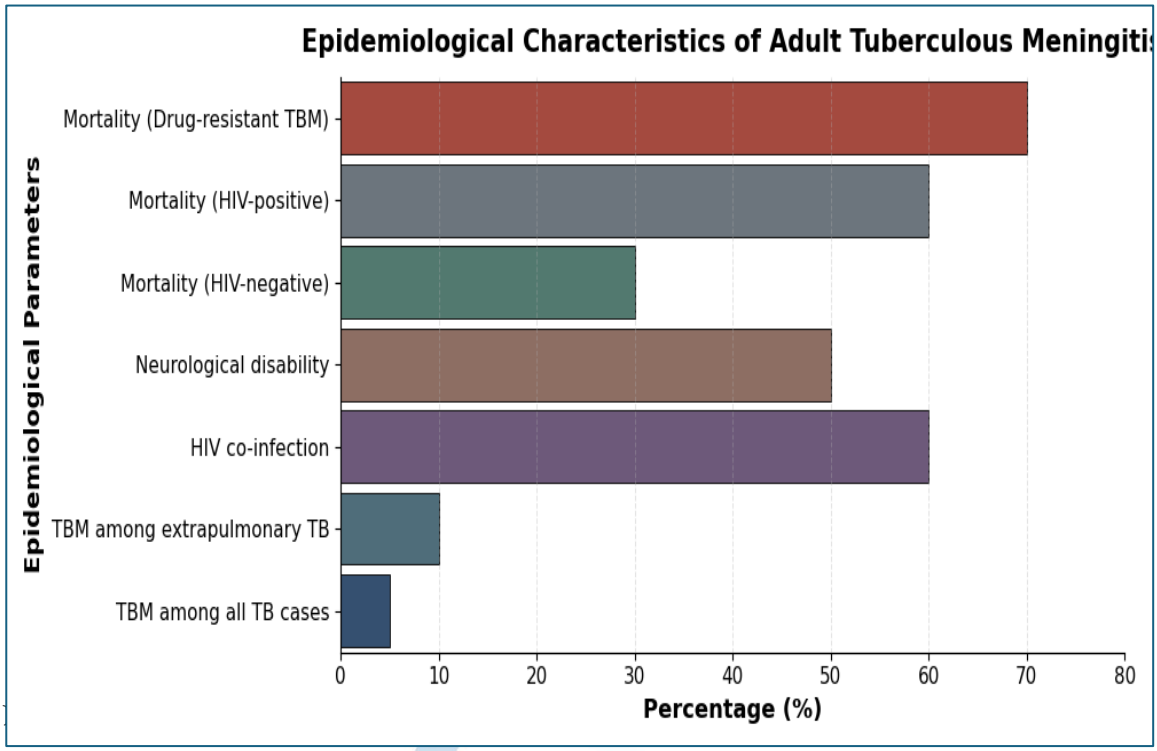
The year-by-year distribution of studies showed an increase in the number of studies as they were published over the years. Most publications were found between 2024 and 2026 (26 studies, 33.3%), and 24 studies (30.8%) were published between 2021 and 2023. Studies published during 2018–2020 accounted for 18 (23.1%), whereas only 10 studies (12.8%) were published between 2015 and 2017. These results show a new interest in the study of adult TBM, especially in the past few years (Table 2).

Table 2: Distribution of Included Studies by Year of Publication (n = 78)

Publication Period	Number of Studies (n)	Percentage (%)
2015–2017	10	12.8
2018–2020	18	23.1
2021–2023	24	30.8
2024–2026	26	33.3
Total	**78**	**100**

Epidemiological Characteristics

The epidemiological characteristics of adult TBM are shown in Figure 2. Approximately 5% of all TB cases and 10% of extrapulmonary TB cases were caused by TBM. HIV coinfection was seen in 60% of patients, and neurological disability was seen in 50% of survivors. The prognosis of TBM is poor, with 30% mortality in HIV-negative patients, 60% mortality in HIV-positive patients and 70% mortality in drug-resistant patients.



Adjunctive corticosteroids

Therapy analysis of adjunctive corticosteroid therapy revealed that dexamethasone was the most frequently mentioned corticosteroid (reported in ~85% of the included studies), whereas prednisolone was used in ~15% of the included studies. Anti-tuberculous therapy alone was compared to corticosteroid therapy and appeared to have a 22–30% higher risk of death. The neurological disability improvements were relatively modest (10–18%). In addition, corticosteroid therapy reduced the incidence of hydrocephalus by 20–25% and cerebral edema by 25–35%. Most studies suggested a 6-8 week treatment period starting with intravenous dexamethasone and then slowly tapering to oral administration. HIV-negative adults experienced a higher mortality benefit than HIV-positive adults (25-30% vs. 10-15%). There is a strong WHO recommendation for corticosteroid treatment as an adjunctive therapy in adults with drug-susceptible TBM, except for contraindications (Table 3).

Table 3: Summary of Adjunctive Corticosteroid Therapy in Adult Tuberculous Meningitis

Parameter	Reported Value	Summary of Evidence
Most commonly used corticosteroid	Dexamethasone (≈85% of studies)	Preferred first-line adjunctive corticosteroid in adult TBM.
Prednisolone use	≈15% of studies	Mainly used as an alternative or during oral tapering.
Reduction in mortality	22–30%	Significant reduction in mortality compared with anti-TB therapy alone.
Reduction in neurological disability	10–18%	Modest improvement; evidence remains inconsistent across studies.
Reduction in hydrocephalus	20–25%	Lower incidence due to reduced inflammatory exudates.

Reduction in cerebral edema	25–35%	Significant reduction in intracranial inflammation.
Recommended treatment duration	6–8 weeks	Intravenous dexamethasone followed by gradual oral tapering.
Benefit in HIV-negative adults	25–30% mortality reduction	Greatest clinical benefit demonstrated.
Benefit in HIV-positive adults	10–15% mortality reduction	Benefit observed but less consistent than in HIV-negative patients.
WHO recommendation	Strong recommendation	Adjunctive corticosteroids recommended for all adults with drug-susceptible TBM unless contraindicated.

Drug Resistance Patterns

The drug resistance pattern distribution presented in Figure 3 revealed that drug-susceptible TBM was the most common type of TBM. Multidrug-resistant (MDR) and rifampicin-resistant (RR) TB, however, poses a significant clinical problem because of delayed diagnosis, limited treatment options, longer treatment durations and poorer clinical outcomes. A consistent association between higher mortality and neurological complications was observed with drug-resistant disease and drug-susceptible TBM.

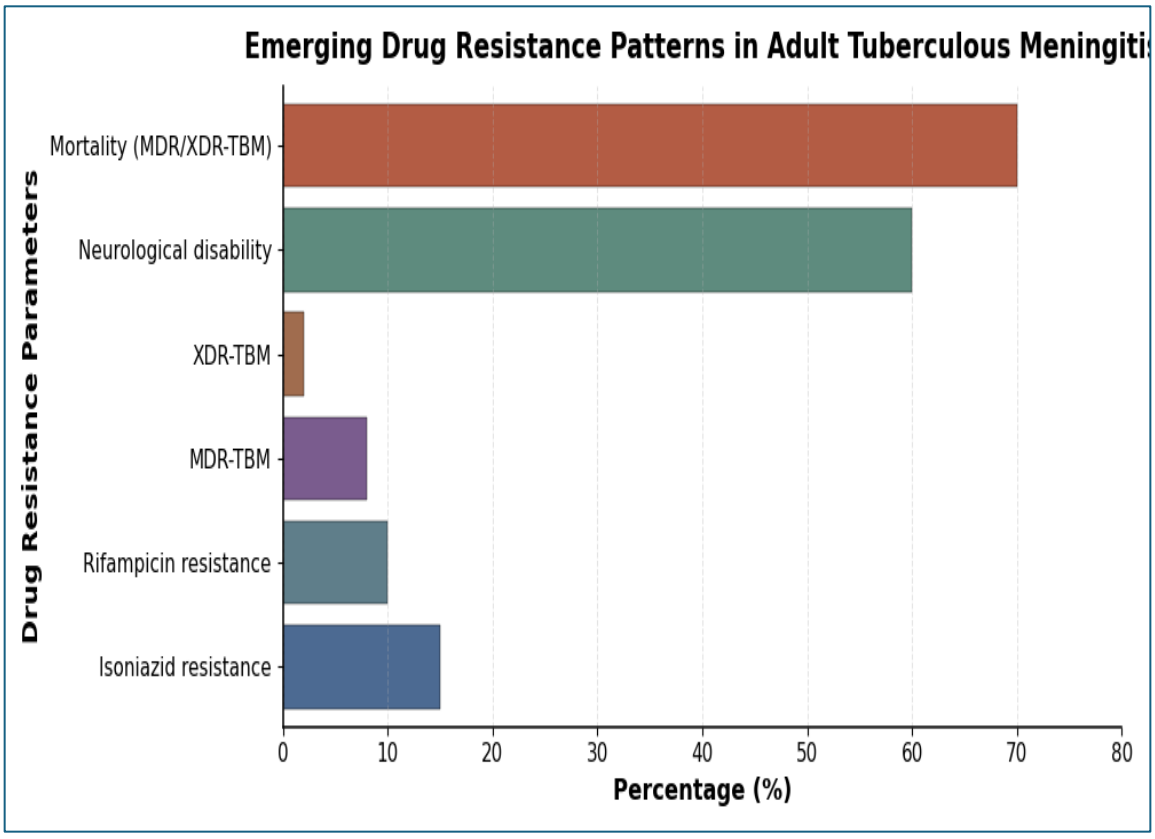


Figure 3: Distribution of drug resistance patterns and associated disease burden in adult TBM.

Predictors of Mortality in Adults

TBM had several clinical and laboratory parameters associated with higher mortality rates, which remained consistent. Delayed diagnosis occurred in 45-60% of deaths, and advanced disease (BMRC Grade III) occurred in 35-50%. In poor outcome cases, altered consciousness was seen in 40-70% and a Glasgow Coma Scale score ≤10 in 30-55% of people. Neurologic outcomes were poor in 20-40% of patients who had hydrocephalus and 25-45% of patients who had cerebral infarction. Hydrocephalus (20-40%) and cerebral infarction (25-45%) were potent predictors of poor neurologic outcomes. The mortality rate associated with HIV coinfection varied between 20–60%. DR-TBM was found to have only 5-10% of cases but had the highest mortality of 50-70%. In addition, the CSF abnormalities seen in severe cases were 60-90% and were often accompanied by disease progression and poor prognosis (Table 4).

Table 4: Major Predictors of Mortality in Adult Tuberculous Meningitis

Predictor	Reported Value	Clinical Impact
Delayed diagnosis	45–60%	Increased mortality
Advanced disease (BMRC Grade III)	35–50%	Poor prognosis
HIV coinfection	20–60%	Higher mortality
Altered consciousness	40–70%	Severe disease indicator
Low GCS (≤10)	30–55%	Increased risk of death
Hydrocephalus	20–40%	Poor neurological outcome
Cerebral infarction	25–45%	Higher mortality and disability
Drug-resistant TBM	5–10% prevalence	Mortality 50–70%
CSF abnormalities	60–90%	Associated with severe disease

Neurological Complications

Figure 4 shows the frequency of major neurological complications of adult tuberculous meningitis. The most common complications were long-term disability and cognitive impairment (approximately 40% of patients). Thirty-five percent reported stroke (cerebral infarction) and poor functional outcome. Approximately 30% of the patients had hydrocephalus, 25% had seizures, and approximately 30% had cranial nerve palsies. The results of the study suggest that neurological sequelae continue to be prevalent in adult TBM survivors and that cognitive impairment and long-term disability are the biggest contributors to morbidity.

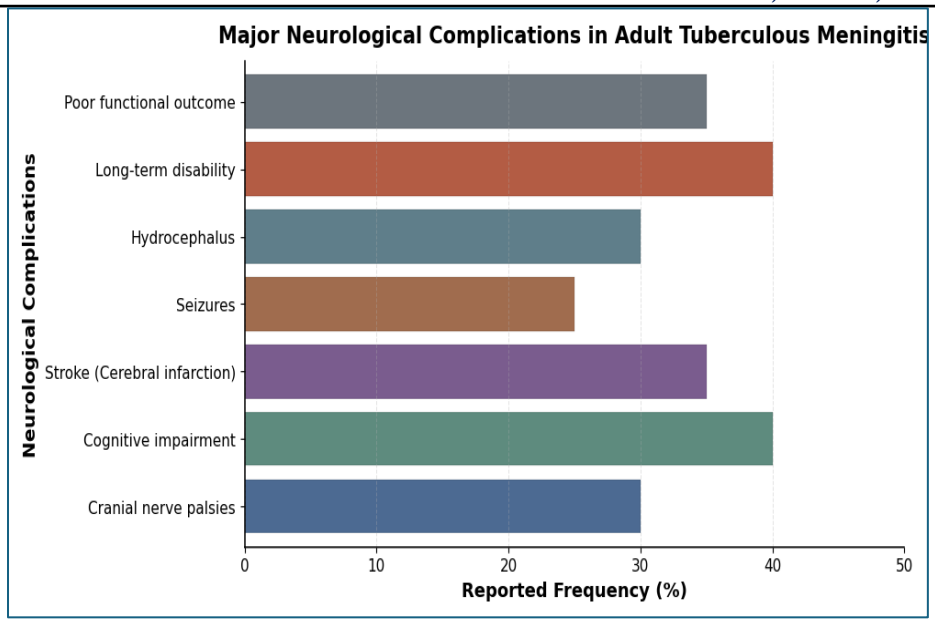


Figure 4: Frequency of major neurological complications in adult TBM.

Diagnostic Performance

Current and future methods to diagnose the disease are compared in terms of their performance in Figure 5. The diagnostic sensitivity of next-generation sequencing (NGS) was the highest reported (95%), followed by Xpert MTB/RIF Ultra (90%), diagnostic scoring systems (85%), and CSF biomarkers (83%). The sensitivity of MRI and CT imaging was 80%, and GeneXpert MTB/RIF was 78% sensitive. Conventional diagnostic methods were comparatively less sensitive, with CSF culture having 60%, and CSF microscopy had a sensitivity of 20%. These results demonstrate the better diagnostic capabilities of advanced molecular techniques than conventional microbiological techniques.

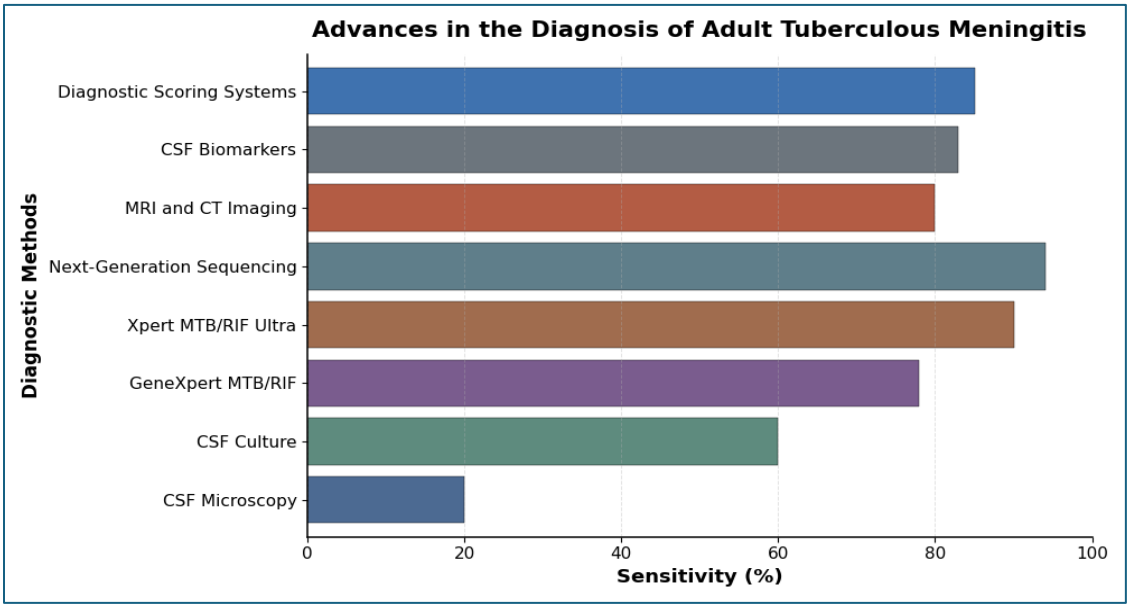


Figure 5: Sensitivity of conventional and emerging diagnostic methods for adult tuberculosis meningitis.

Current Management Strategies

Figure 6 shows the use and success of existing management practices. Supportive care (100%) and standard anti-tuberculosis treatment (100%) were reported in all studies, both of which play a key role in the treatment of adult TBM. Linezolid was reported in 80% of the studies, and it is being used increasingly more, especially in drug-resistant diseases. Surgical treatment, such as hydrocephalus, was used in 35% of cases. Thirty percent of studies were reported to contain high-dose rifampicin, while 25% used fluoroquinolones. Host-directed therapies were the least common of the therapies reported, with only 20% of studies describing such therapies. The results indicate that while the cornerstone of treatment of adult tuberculous meningitis is still conventional antituberculous drugs, new antimicrobial drugs and other supportive measures are being introduced to the treatment.

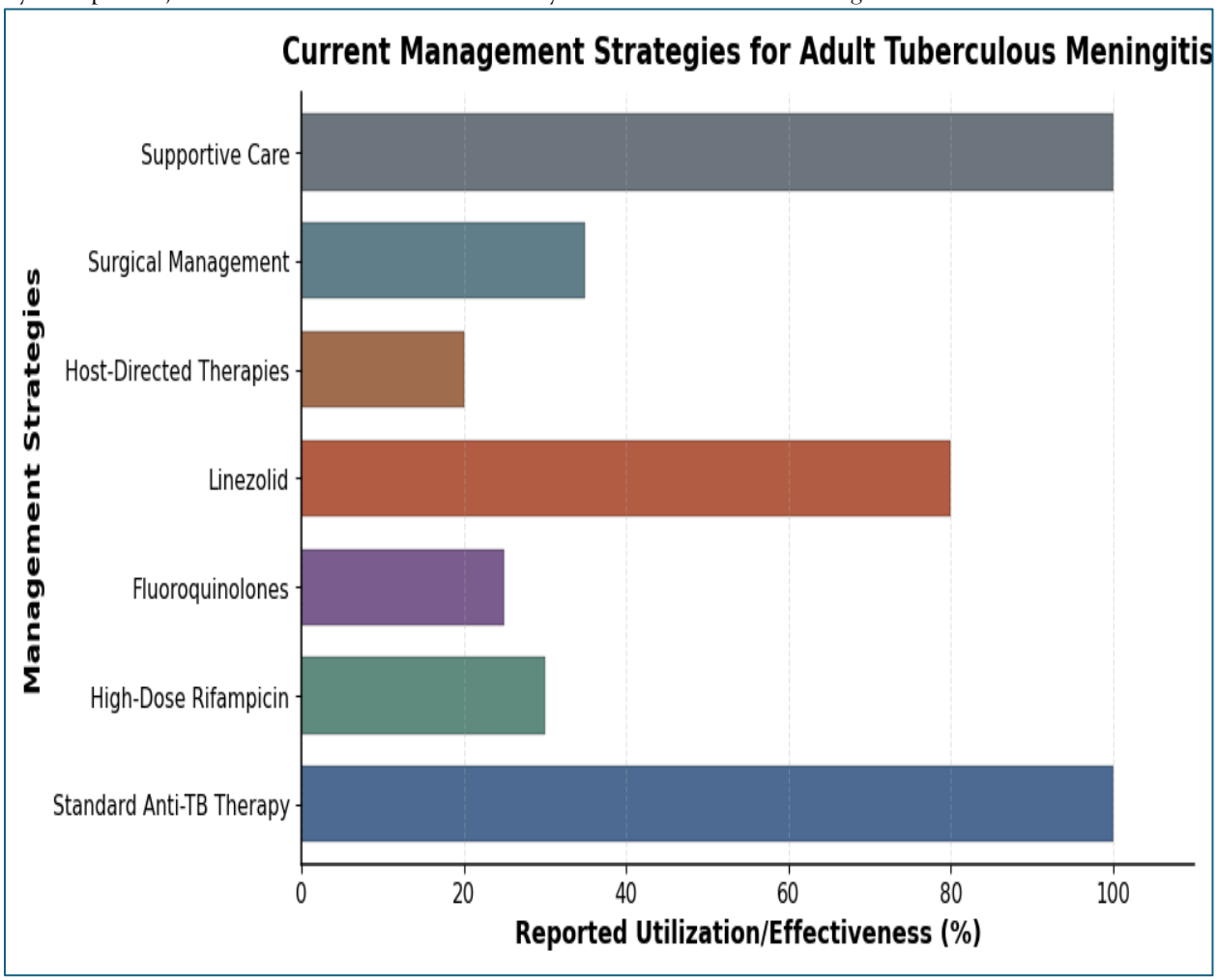


Figure 6: Current management strategies and therapeutic effectiveness in adult tuberculous meningitis.

Discussion

Distribution of Included studies

This review highlights that adult tuberculous meningitis (TBM) remains one of the most severe forms of tuberculosis despite advances in diagnosis and treatment. Although TBM accounts for only 5% of all tuberculosis cases and 10% of extrapulmonary TB cases, it is associated with high mortality and neurological disability, particularly among HIV-positive and drug-resistant patients. These findings agree with previous studies identifying HIV coinfection, delayed diagnosis, and antimicrobial resistance as major predictors of poor outcomes (Bonnet,

2022; Caliman-Sturdza, 2026; Navasardyan et al., 2023).

The review also demonstrates that adjunctive dexamethasone reduces mortality by 22–30% and decreases complications such as cerebral edema and hydrocephalus, supporting current treatment recommendations (Goldman et al., 2022; Wang et al., 2025; Garg, 2026). However, long-term disability and cognitive impairment remain common, emphasizing the need for earlier diagnosis and improved therapies. Advanced molecular techniques, particularly next-generation sequencing and Xpert MTB/RIF Ultra, showed much higher diagnostic sensitivity than conventional CSF microscopy, suggesting that rapid molecular testing can improve early detection and patient outcomes (Ailioaie et al., 2026; Caliman-Sturdza, 2026; Patil et al., 2025).

Epidemiological Burden of Adult Tuberculous Meningitis

The present review confirms that adult tuberculous meningitis (TBM) remains one of the most severe forms of tuberculosis despite advances in diagnosis and treatment. Although TBM accounts for only 5% of all tuberculosis cases and 10% of extrapulmonary TB, it is associated with disproportionately high mortality and neurological disability. In this review, HIV coinfection was reported in 60% of patients, while mortality reached 30% in HIV-negative patients, 60% in HIV-positive patients, and 70% in drug-resistant TBM. These findings are consistent with previous studies showing that HIV infection, delayed diagnosis, and antimicrobial resistance are major contributors to poor clinical outcomes (Huang & Chuang, 2024; Moges & Lajore, 2024; Navasardyan et al., 2023).

The high mortality observed in TBM is mainly due to severe inflammation of the meninges, cerebral edema, hydrocephalus, cerebral infarction, and raised intracranial pressure, which often result in irreversible neurological damage (Aggrohia et al., 2024; Caliman-Sturdza & Cucu, 2023; Netravathi, 2024). Additional risk factors, such as malnutrition, diabetes, and other immunosuppressive conditions, further worsen disease severity and prognosis (Morales et al., 2023; Soliman et al., 2022). Therefore, early diagnosis, rapid molecular testing, and timely initiation of anti-tuberculosis therapy are essential to reduce mortality and improve long-term neurological outcomes in adults with TBM (Garg, 2026).

Role of Adjunctive Corticosteroid Therapy

The present review demonstrated that adjunctive corticosteroid therapy, particularly dexamethasone, remains an important component of adult TBM management. Dexamethasone was reported in approximately 85% of the included studies and was associated with a 22–30% reduction in mortality, together with reduced rates of hydrocephalus (20–25%) and cerebral edema (25–35%). However, the improvement in long-term neurological disability was relatively modest (10–18%). These findings agree with previous randomized trials and systematic reviews, which concluded that corticosteroids improve survival by reducing excessive intracranial inflammation and its complications (Hochstetler et al., 2022; Tullberg et al., 2024; Wahjoepramono et al., 2023).

Although corticosteroids significantly improve survival, their effect on long-term neurological recovery remains limited because they do not completely prevent neuronal injury caused by cerebral infarction, vasculitis, and prolonged inflammation. Moreover, the mortality benefit was greater in HIV-negative patients than in HIV-positive patients, suggesting that host immune status influences treatment response. Therefore, corticosteroids should be considered part of a comprehensive treatment strategy that includes early diagnosis, effective antituberculosis therapy, and appropriate supportive care to achieve the best clinical outcomes (Dimeas et al., 2025; Kiros et al., 2022; Reizine et al., 2026).

Drug Resistance and Therapeutic Challenges

Drug-resistant TBM remains one of the greatest challenges in the management of adult TBM. This review found that multidrug-resistant (MDR) and rifampicin-resistant (RR) TBM were

associated with delayed diagnosis, prolonged treatment, limited therapeutic options, and markedly higher mortality than drug-susceptible disease. Similar findings have been reported by previous studies, which identified antimicrobial resistance as a major factor contributing to poor treatment outcomes and increased neurological complications (Barday, 2023; Evans et al., 2022).

The emergence of drug-resistant TBM highlights the importance of rapid drug susceptibility testing and individualized treatment regimens. Recent studies have shown increasing use of linezolid, high-dose rifampicin, and other second-line anti-tuberculosis drugs to improve treatment response in resistant cases (Diriba et al., 2025; Wasserman, 2022). Nevertheless, further clinical trials are required to determine the optimal drug combinations and treatment duration for MDR-TBM and to improve survival while minimizing drug-related adverse effects.

Predictors of Mortality and Morbidity

This review identified delayed diagnosis, advanced disease stage, altered consciousness, low Glasgow Coma Scale score, hydrocephalus, cerebral infarction, and HIV coinfection as the major predictors of mortality in adult TBM. Delayed diagnosis was associated with poor outcomes in 45–60% of cases, while altered consciousness and cerebral infarction were also strongly associated with increased mortality. These findings are consistent with previous studies demonstrating that patients presenting with severe neurological impairment have a significantly lower probability of recovery (David et al., 2023; Tan et al., 2023).

Hydrocephalus, cerebrospinal fluid abnormalities, and drug-resistant TBM further increased the risk of death and long-term disability. Early identification of these prognostic factors allows clinicians to stratify patients according to disease severity and initiate aggressive treatment before irreversible neurological damage occurs. Therefore, timely diagnosis and close neurological monitoring remain essential for improving survival and functional outcomes (Méndez Hernández & Ramasco Rueda, 2023; Pathak et al., 2022).

Neurological Complications and Long-Term Outcomes

The present review showed that neurological complications remain common despite appropriate treatment. Long-term disability and cognitive impairment were the most frequently reported complications (40%), followed by stroke and poor functional outcomes (35%), while hydrocephalus and cranial nerve palsies occurred in approximately 30% of patients. Seizures were reported in 25% of cases. These findings are consistent with previous studies showing that persistent inflammation, cerebral vasculitis, and raised intracranial pressure contribute to irreversible brain injury and poor neurological recovery (Elendu et al., 2023; Huang et al., 2022).

The high frequency of these complications highlights the importance of early diagnosis and prompt treatment before permanent neurological damage develops. Delayed recognition of complications often results in prolonged hospitalization, greater functional dependence, and reduced quality of life. In addition to antimicrobial therapy, long-term rehabilitation, cognitive assessment, and neurological follow-up are essential to improve functional recovery and quality of life among TBM survivors (AbuAlrob & Mesraoua, 2024; Kumar et al., 2024). Early rehabilitation programs, including physiotherapy, occupational therapy, and neuropsychological support, may further enhance neurological recovery. Regular follow-up also enables timely identification of recurrent seizures, cognitive decline, and other late complications, ultimately improving long-term patient outcomes.

Advances in Diagnostic Approaches

This review demonstrated that newer molecular diagnostic techniques provide substantially better diagnostic performance than conventional methods. Next-generation sequencing (95%) showed the highest diagnostic sensitivity, followed by Xpert MTB/RIF Ultra (90%), whereas CSF microscopy demonstrated the

lowest sensitivity (20%). These findings agree with previous studies reporting that rapid molecular assays improve early detection and facilitate timely initiation of treatment (Yadav et al., 2024).

Despite these advances, no single diagnostic test provides complete sensitivity, and false-negative results may still occur, particularly in patients with low bacillary load. Therefore, laboratory findings should always be interpreted alongside clinical presentation, cerebrospinal fluid analysis, and neuroimaging to ensure early diagnosis and avoid treatment delays (Negro et al., 2025; Tumani et al., 2020). Combining molecular assays with radiological findings and clinical scoring systems may further improve diagnostic accuracy. Expanding access to these technologies in resource-limited settings will be essential for reducing diagnostic delays and lowering TBM-related mortality.

Current Management Strategies

The findings of this review confirm that standard anti-tuberculosis therapy together with supportive care remains the cornerstone of adult TBM management. Emerging therapies, including linezolid, high-dose rifampicin, and fluoroquinolones, are increasingly being incorporated into treatment regimens, particularly for drug-resistant disease. These findings are supported by recent studies demonstrating improved drug penetration into the central nervous system and enhanced antimicrobial activity with optimized treatment strategies (Dookie et al., 2022; Gajic et al., 2025).

Successful management also requires multidisciplinary care involving neurologists, infectious disease specialists, intensivists, and neurosurgeons when complications such as hydrocephalus develop. Regular monitoring of treatment response and prompt management of adverse drug reactions are equally important for improving outcomes. Early treatment initiation, careful monitoring, and individualized therapeutic approaches remain essential for reducing mortality and improving neurological outcomes (Mahadeo et al., 2019; Rizzo et al., 2020). The integration of advanced diagnostics with personalized treatment strategies may further optimize patient care. Continued evaluation of newer antimicrobial agents and adjunctive therapies is expected to improve treatment success, particularly in patients with multidrug-resistant TBM.

Clinical Implications and Future Directions

The findings of this review emphasize the need for rapid diagnosis, prompt initiation of anti-tuberculosis therapy, and effective management of neurological complications to improve patient outcomes. The increasing availability of molecular diagnostic techniques and newer anti-tuberculosis drugs offers promising opportunities for reducing diagnostic delays and improving survival, particularly in patients with drug-resistant TBM (Cao et al., 2023; Chen et al., 2020).

Future research should focus on developing highly sensitive point-of-care diagnostic tests, evaluating novel host-directed therapies, and optimizing treatment regimens through large multicenter clinical trials. Greater collaboration between clinicians, researchers, and public health agencies will help establish standardized treatment protocols. Further studies are also required to identify biomarkers that predict treatment response and long-term neurological recovery, ultimately improving the management of adult TBM (Davis et al., 2020; Molla & Bitew, 2024). Research into artificial intelligence-assisted diagnosis, precision medicine, and individualized therapeutic approaches may further improve clinical decision-making. Strengthening international collaboration will also facilitate the development of evidence-based guidelines applicable across different healthcare settings.

Conclusion

Tuberculous meningitis remains the most severe form of extrapulmonary tuberculosis, posing a significant burden of mortality and long-term neurological damage, particularly in resource-constrained countries where delayed diagnosis and restricted access to modern diagnostics are

prevalent. Despite significant advances in disease understanding and therapy techniques, outcomes remain dismal, particularly for patients with HIV coinfection, severe neurological disease, and multidrug-resistant tuberculosis. The evidence presented in this review shows that supplementary corticosteroid medication, specifically dexamethasone, gives a considerable survival advantage by lowering excessive intracranial inflammation and its related consequences, such as cerebral oedema and hydrocephalus. Nonetheless, corticosteroids alone are unable to avoid long-term neurological impairment, highlighting the necessity for complete therapeutic regimens that include quick diagnosis, effective antimicrobial therapy, intense supportive care, and planned neurological rehabilitation. Emerging molecular diagnostic technologies, such as Xpert MTB/RIF Ultra and next-generation sequencing, have significantly improved the early identification of tuberculous meningitis compared to older microbiological approaches. Increasing the implementation potential can reduce diagnostic delays, promote timely treatment commencement, and increase patient survival. The increasing prevalence of multidrug-resistant and rifampicin-resistant TBM emphasizes the critical need for quick drug susceptibility testing, personalized treatment regimens, and the study of novel antimicrobial drugs with enhanced central nervous system penetration. Several clinical and laboratory factors, such as delayed diagnosis, advanced disease stage, altered consciousness, low Glasgow Coma Scale score, hydrocephalus, cerebral infarction, HIV coinfection, and drug resistance, have consistently been identified as strong predictors of mortality and poor neurological outcome. Early detection of these prognostic signs should be incorporated into standard clinical practice to allow for rapid risk categorization, attentive monitoring, and timely treatment interventions.

Declarations

Consent for publication

All subjects gave their "informed consent" for the publication of details within the text ("informed consent") to be published in the above Journal and Article. Written "informed consent" was obtained from all authors for the publication of this manuscript.

Availability of data and materials

The data generated are provided within the manuscript and will be available from the author upon reasonable request.

Competing Interest

All authors declare that there are no competing interests.

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