e-ISSN: 0975-9506, p-ISSN: 2961-6093

Available online on www.ijpqa.com doi: 10.25258/ijpqa.16.10.41

International Journal of Pharmaceutical Quality Assurance 2025; 16(10); 249-256

Original Research Article

# Clinical and Microbiological Profile of Central Nervous System Infections

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**Received: 11-08-2025 / Revised: 15-09-2025 / Accepted: 24-10-2025**

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**Conflict of interest: Nil**

**Abstract:**

**Background:** Central nervous system (CNS) infections remain a major public health challenge globally, particularly in developing nations. These infections, including meningitis, encephalitis, and brain abscess, are associated with high morbidity and mortality. Their clinical and microbiological patterns vary according to geography, patient demographics, and immune status.

**Objectives:** The present study aimed to determine the clinical spectrum, laboratory characteristics, microbial etiology, and antimicrobial resistance patterns among patients diagnosed with CNS infections.

**Materials and Methods:** A hospital-based cross-sectional study was conducted on 160 patients with clinically and laboratory-confirmed CNS infections at Sir Sunder Lal Hospital, Varanasi, between June 2017 and May 2019. Cerebrospinal fluid (CSF) samples were analyzed for cytological, biochemical, and microbiological parameters. Statistical analysis was performed using SPSS version 21.0, with $p < 0.05$ considered significant.

**Results:** Of 160 patients, 58% were males and 42% females, with the majority aged 21–40 years. Tubercular meningitis was the most common infection (53.1%), followed by viral (26.9%) and bacterial meningitis (8.8%). Fever (97.5%), headache (95.6%), and altered sensorium (75%) were the predominant symptoms. CSF findings revealed elevated protein and ADA levels in tubercular meningitis, neutrophilic predominance in bacterial, and lymphocytic predominance in viral infections. Streptococcus species (41.7%) and *E. coli* (33.3%) were the most frequent bacterial isolates.

**Conclusion:** Tubercular meningitis remains the leading CNS infection in this region. CSF analysis remains pivotal for diagnosis, and early microbiological identification can guide prompt, targeted therapy, reducing complications and mortality.

**Keywords:** CNS Infections, Meningitis, Microbiological Profile, Cerebrospinal Fluid, Tubercular Meningitis, Streptococcus Species.

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## Introduction

Central nervous system (CNS) infections constitute a significant cause of morbidity and mortality worldwide, affecting both developed and developing nations. These infections comprise a broad spectrum of clinical syndromes, such as meningitis, encephalitis, brain abscess, and ventriculitis, with inflammation of all different parts of the CNS. The causative agents differ according to geographical area, climate, age group, immune condition, and healthcare facilities. Though the antimicrobial therapy and neuroimaging advances have been made, CNS infections still remain a challenging diagnosis and treatment issue mainly because of the nonspecific clinical manifestations and constraints in the traditional diagnostic techniques [1,2]. Timely detection and diagnosis of causative pathogen is the key to proper treatment and prevention of complications and mortality rates, however, the challenge in distinguishing between bacterial and viral etiologies often postpones the process of targeted treatment.

Bacterial meningitis is considered one of the most dangerous types of CNS infection, and most cases in adults in the world are caused by Streptococcus pneumoniae and Neisseria meningitidis [3]. On the contrary, viral diseases like herpes simple virus, enteroviruses and Japanese encephalitis virus are the major ones in most of the Asian countries as the

disease patterns are also regional. Parasitic and fungal infections, especially the Cryptococcus neoformans and Toxoplasma gondii are becoming common in immunocompromised patients, especially HIV/AIDS patients and organ transplant recipients [4]. In addition, CNS-related nosocomial infections, neurosurgical surgeries, and external ventricular drains have become the leading causes of morbidity, with the involvement of multidrug-resistant organisms like Acinetobacter baumannii and methicillin-resistant Staphylococcus aureus (MRSA) being implicated more than others [5]. The increasing number of CNS pathogens with antimicrobial resistance complicated empirical treatment and required region-specific microbiological monitoring.

The patients may be unable to distinguish between various etiologies as the clinical manifestations of CNS infections may be mild, febrile based illness up to life-threatening neurological dysfunction. The typical characteristics are fever, headache, neck stiffness, changes in consciousness, and seizures. Nevertheless, abnormal presentations are not rare particularly in older or immunocompromised patients and this complicates early clinical diagnosis. CSF study will continue to form the basis of diagnosis by giving details on the nature of the infection in terms of cytological, biochemical, and microbiological parameters. However, the conventional culture methods are not sensitive enough particularly in patients who have had previous antibiotics. Polymerase chain reaction (PCR) and next-generation sequencing (NGS) as the methods of diagnostic approach have transformed the method of diagnosis and increased the detection rate of pathogens in the CSF and improved clinical decision-making [6,7]. Nevertheless, such molecular tools are not available in most resource limited environments and it is clear that classic microbiological methods can be used with extensive clinical correlation.

CNS infection is a complex, diverse phenomenon; hence, the essentials needed to comprehend the regional clinical spectrum, etiology, and local antimicrobial susceptibility patterns are region-specific studies. This type of information can be useful in developing empirical treatment guidelines and putting into practice infection control strategies, especially in tertiary care hospitals and neurosurgical units. This study aims to delineate the clinical characteristics, laboratory findings, microbiological profile, and antimicrobial resistance trends among patients diagnosed with CNS infections. Understanding these parameters will not only help clinicians improve diagnostic accuracy and therapeutic efficacy but also contribute to epidemiological data necessary for public health planning and preventive strategies.

## Material and Methods

**Study Design and Setting:** This cross-sectional study was conducted on 160 patients diagnosed with central nervous system (CNS) infections in the Department of General Medicine, Institute of Medical Sciences Banaras Hindu University, Varanasi, Uttar Pradesh, India. This was conducted between June 2017 and May 2019. Ethical approval of the study was secured with the Institutional Ethics Committee before the study began. The inclusion and exclusion criteria were stipulated and all participants were selected based on them. Each case was subjected to detailed clinical history, physical and neurological examination and all other investigations relevant to the case to provide diagnosis and evaluate clinical and microbiological results.

**Study Population:** The study included patients aged 14 years and above presenting with signs and symptoms suggestive of meningitis or other CNS infections. Patients who were discharged or died within 24 hours of admission, as well as those who refused to provide informed consent, were excluded from the study. Thus, only patients fulfilling both clinical and laboratory criteria for CNS infection were enrolled for evaluation.

**Method and Procedure:** Informed consent was given to all the participants, or those who could sign on behalf of their clients, especially those who were very ill and could not sign informed consent. The information was obtained during admission and consisted of age, gender, and medical history. A thorough clinical assessment of meningitis was conducted on all patients based on the hospital protocol, and then a systemic as well as a neurological examination was conducted.

Lumbar puncture (LP) was done as soon as admission was done and before the administration of antibiotics unless otherwise. The samples of cerebrospinal fluid (CSF) were examined upon cytological, biochemical, and microbiological parameters, such as white blood cell (WBC) count and differential, protein and glucose levels, Gram stain, and culture. Additional tests like India ink preparation, cryptococcal antigen assay were conducted whenever noted in the clinical. Computer tomography (CT) of the head was used to exclude space-occupying lesions or increased intracranial pressure in patients with altered mental status or with focal neurological deficits before LP was done or within 2448 hours of hospitalization.

Sputum analysis of the acid-fast bacilli (AFB), culture and chest radiography was performed on patients suspected of having TB meningitis or HIV infection to identify active tuberculosis. All patients were subjected to routine biochemical tests, such as complete blood count and liver and renal function tests, electrolyte estimates. A maningitis diagnosis

was made through the combination of clinical presentation, CSF analysis, and microbiological results.

**Diagnostic Criteria:** Bacterial meningitis was diagnosed when the CSF Gram stain or culture was positive, or when bacterial antigen tests (BAT) were reactive, along with typical CSF findings such as pleocytosis with polymorphonuclear predominance, elevated protein, and decreased glucose levels. CSF cultures for bacterial pathogens were performed using blood agar, MacConkey agar, and chocolate agar media. Cryptococcal meningitis was diagnosed when India ink staining or CSF cryptococcal antigen testing yielded positive results. The Cryptococcal Latex Agglutination System (CLAGS) was used as a qualitative and semi-quantitative test to detect capsular polysaccharide antigens of Cryptococcus neoformans in CSF and serum samples.

Tubercular meningitis (TBM) was diagnosed in patients with negative CSF Gram stain and bacterial cultures, negative cryptococcal antigen test, and at least one of the following: characteristic CSF findings (lymphocytic pleocytosis, low glucose, and high protein levels), evidence of active tuberculosis at another site such as the lungs, or brain CT findings suggestive of TBM including basal meningeal enhancement or hydrocephalus. CSF AFB smear and GeneXpert testing were also performed whenever possible. Viral meningitis was considered when patients presented with typical meningitic features, negative bacterial and cryptococcal tests, and characteristic CSF findings such as lymphocytic predominance, normal or mildly elevated protein, and normal glucose levels, after exclusion of other non-viral causes.

**Statistical Analysis:** All collected data were entered and analyzed using SPSS statistical software (version 21.0). Quantitative variables were expressed as mean ± standard deviation, and categorical variables as percentages. Comparative analyses of adenosine deaminase (ADA) levels and other parameters between groups were performed using appropriate statistical tests. A p value of less than 0.05 was considered statistically significant.

## Results

This cross-sectional study involved 160 patients with central nervous system (CNS) infections. The literature examined demographic data, clinical picture, hematological and biochemical indicators, results of cerebral spinal fluid (CSF), microbiological trends, and neuroimaging to identify the clinical and microbial picture of CNS infections. The age distribution showed that the CNS infections cut across all ages although the highest proportion of CNS infections were among young adults and middle-aged adults. The group of 2130 years old had the highest level of prevalence of the disease with 28.7 per cent cases, 4150 years old with 19.3per cent, and 1020 year of age with 20.6per cent cases. Cases among the patients aged above 60 years were only 9.4% and this suggests that CNS infections are mainly diseases of the young and middle-aged young population. Gender analysis indicated the study was more male dominated with 93 (58 percent) males and 67 (42 percent) females giving male-to-female ratio of about 1.4:1. This gender gap could be explained by an increased occupational exposure, immunosuppression by lifestyle, and differences in healthcare seeking among the males in this area.

**Table 1: Demographic Distribution of Patients (n = 160)**

| Parameter | Subcategory | No. of Patients | Percentage (%) |
|---|---|---|---|
| **Age (years)** | 10–20 | 33 | 20.6 |
| | 21–30 | 46 | 28.7 |
| | 31–40 | 31 | 19.3 |
| | 41–50 | 35 | 21.8 |
| | >60 | 15 | 9.4 |
| **Gender** | Male | 93 | 58.0 |
| | Female | 67 | 42.0 |

Among the 160 cases, tubercular meningitis was the most common CNS infection, accounting for 53% of total cases. This was followed by viral meningitis (27%), bacterial meningitis (9%), aseptic meningitis (7%), septic meningitis (3%), and fungal meningitis (1%). Tubercular meningitis dominated in the 21–40-year age group, whereas bacterial meningitis was relatively more frequent in older patients (41–50 years). The high proportion of tubercular meningitis may reflect endemic tuberculosis prevalence and late presentation of patients with chronic symptoms. Viral meningitis was commonly observed during the monsoon months, correlating with seasonal viral outbreaks.

**Table 2: Distribution of CNS Infections by Type**

| Type of CNS Infection | No. of Patients | Percentage (%) |
|---|---|---|
| Tubercular Meningitis | 85 | 53.1 |
| Viral Meningitis | 43 | 26.9 |
| Bacterial Meningitis | 14 | 8.8 |
| Aseptic Meningitis | 11 | 6.9 |
| Septic Meningitis | 5 | 3.1 |
| Fungal Meningitis | 2 | 1.2 |

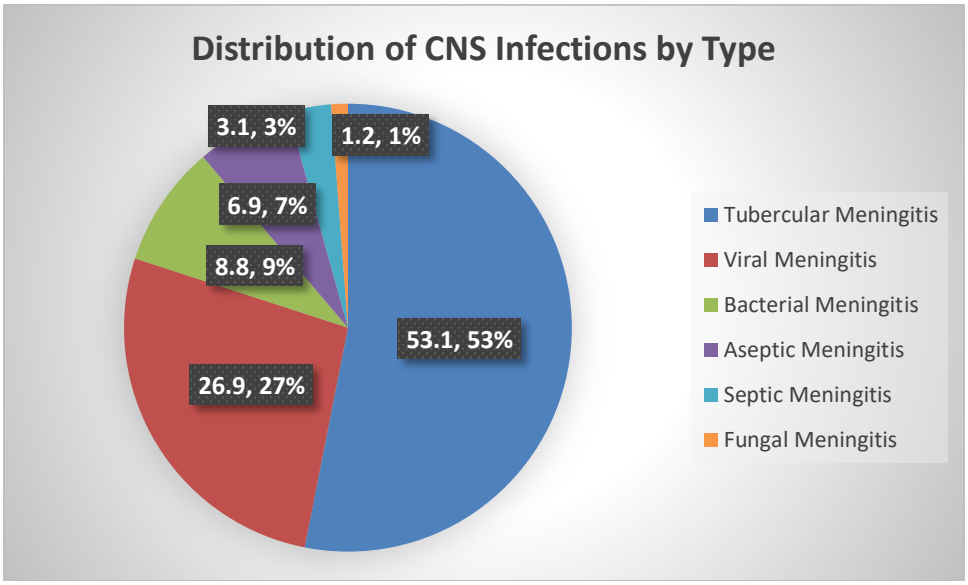


**Figure 1: Distribution of CNS Infections by Type**

The clinical picture was non-homogenous and was predominated by typical signs of meningitis. The most reliable symptom was also fever in 97.5 percent of the cases, followed by headache (95.6 percent), altered sensorium (75 percent), neck stiffness (67.5 percent), and seizures (40 percent). Others were vomiting (32%), photophobia (18%), and focal neurological deficits (14%). The symptoms patients with tubercular meningitis took a longer period to manifest compared to bacterial meningitis which in most cases showed up acutely after 2-5 days. Cases of viral meningitis were less severe and self-limiting in nature. In compliance with comorbid illnesses, 6.8% of patients were diagnosed with diabetes mellitus and hypertension, 3 individuals had previously been in contact with tuberculosis at home, and 1 individual had a history of antitubercular treatment (ATT).

Laboratory showed hemoglobin of 6.6 to 15.5 g/dL with mild anemia being identified in 45 percent of the cases particularly in chronic tuberculosis infection. The meningitis of bacteria (11,00025,000/mm 3 ) and septic meningitis were featured by the increased total leukocyte count (TLC), whereas a normal or slightly elevated count was observed in viral cases. In bacterial meningitis, neutrophil pre-eminence was the feature (average 78%), whereas in viral and tubercular meningitis, lymphocytic pre-eminence (up to 90%) was the feature. Aseptic meningitis had slightly high (1.2-1.5 mg/dl) serum creatinine, whereas liver enzymes (SGOT, SGPT) were slightly elevated in tuberculosis and septic meningitis, probably by the reason of the general infection.

The basis of diagnosis was CSF examination. In bacterial meningitis whose polymorphonuclear cells predominated, the mean CSF total cell count was 730 cells/mm 3 whereas in viral meningitis, the mean was 180 cells/mm 3 where the lymphocytic cells dominated. The protein levels were significantly elevated in tubercular and septic meningitis (average 445 mg/dL) and glucose levels decreased (average 35 mg/dL) in the majority of bacterial and tubercular meningitis. The level of adenosine deaminase (ADA) was also found to be quite high in the cases of tuberculosis meningitis, and could be used as a supportive diagnostic marker.

There was 60 percent culture positivity of bacterial meningitis. Streptococcus species (41.7%), E. coli (33.3%), Staphylococcus aureus (16.7%) and Pseudomonas aeruginosa (8.3) were the most commonly isolated organisms. Aseptic or viral meningitis did not show any bacterial growth. GeneXpert detected Mycobacterium tuberculosis in 4.7% in tubercular meningitis, and 2 cases of fungal meningitis were found using India ink and cryptococcal antigen test as Cryptococcus neoformans.

**Table 3: CSF Microbiological Findings**

| Pathogen Identified | Type of Infection | No. of Positive Cases | Percentage (%) |
|---|---|---|---|
| Streptococcus spp. | Bacterial meningitis | 5 | 41.7 |
| Staphylococcus aureus | Bacterial meningitis | 2 | 16.7 |
| E. coli | Bacterial meningitis | 4 | 33.3 |
| Pseudomonas aeruginosa | Bacterial meningitis | 1 | 8.3 |
| Mycobacterium tuberculosis (GeneXpert) | Tubercular meningitis | 4 | 4.7 |
| Cryptococcus neoformans | Fungal meningitis | 2 | 1.2 |

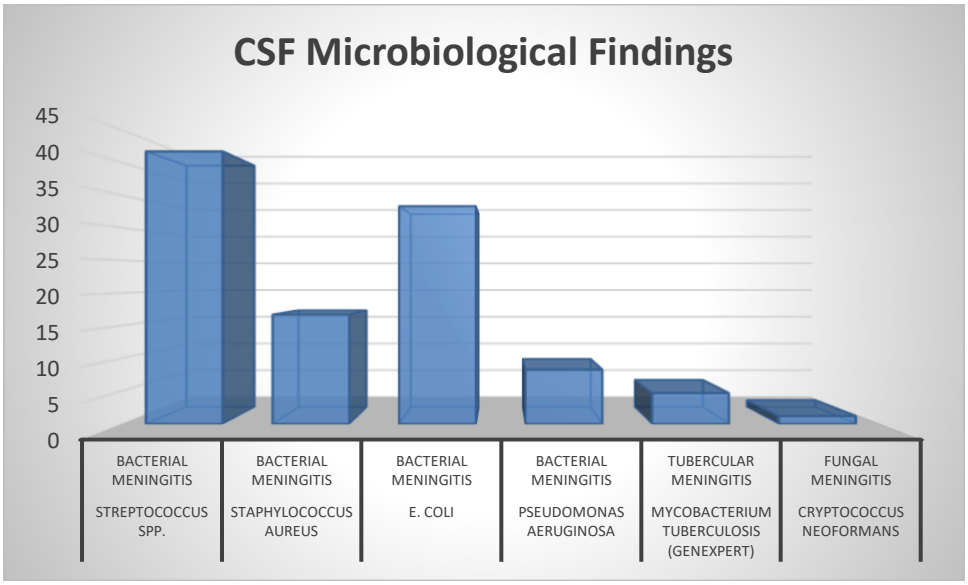


**Figure 2: CSF Microbiological Findings**

Computed tomography (CT) of the brain revealed significant abnormalities in 38% of cases. Hydrocephalus was seen in 34% of tubercular and 27% of bacterial meningitis cases. Basal meningeal enhancement, infarction, and tuberculoma formation were key findings in tubercular meningitis. Vascular infarcts were reported in 14% of cases, with some patients showing both hydrocephalus and infarction. Viral meningitis cases generally demonstrated normal imaging, except for mild cerebral edema in a few patients. HIV seropositivity was detected in 23 patients (14.3%), most commonly associated with tubercular (21%) and viral meningitis (9.3%) cases. These patients tended to have longer hospital stays and poorer outcomes. Overall, mortality was 8.7%, predominantly among tubercular and septic meningitis patients, while recovery with neurological sequelae such as cranial nerve palsy and cognitive deficits occurred in approximately 12% of survivors.

## Discussion

This hospital-based study provides valuable insights into the clinical and microbiological profile of central nervous system (CNS) infections among febrile hospitalized patients. CNS infections, particularly meningitis and encephalitis, continue to be a major cause of morbidity and mortality worldwide, especially in developing countries where diagnostic resources and preventive measures remain limited. The current results not only show the persistence of bacterial and viral pathogens as a major etiologic agent but also demonstrate diagnostic issues arising because of previous exposure to antibiotics and the inadequacy of the traditional microbiologic methods. We have found that the most common bacterial pathogens in meningitis in our data were Staphylococcus aureus, Streptococci, Pseudomonas aeruginosa and Escherichia coli. This is in accordance with the world statistics of such species of bacteria being the leading causes of adult meningitis caused by bacteria [8]. Our level of positive bacterial culture was however limited to 7.5 percent which could be attributable to the action of using empirical antibiotics prior to the patient seeking hospital care. Pre-treatment with antibiotics has been reported to significantly reduce culture yield especially when lumbar puncture is not administered promptly with the beginning of treatment [9].

The low rate of pathogen detection using the traditional techniques highlights the need to use molecular diagnostic techniques, including PCR and GeneXpert, in the diagnostic algorithm of the CNS infections. There is a chance that the use of molecular assays would enhance the rate of pathogen identification, particularly in tuberculosis

meningitis (TBM), where the sensitivity of the smear and culture is infamously low. However, regardless of the presence of GeneXpert and TB-PCR in this work, the detection of the pathogen was small, which could be due to a low content of bacteria or the presence of organisms that were not included in the test panel. Other Indian and international studies have presented similar low rates of detection, highlighting that the yield of diagnosis is affected by the amount of specimen, when it was collected and the way it has been handled by the laboratory [10].

Comparison of the clinical diagnosis made during admission with that of laboratory confirmation was an important part of our study. The inconsistencies that were noted on clinical and laboratory diagnoses suggest that a considerable number of cases are misdefined using clinical presentation only. This underlines the clinical overlap of bacterial, viral and tubercular meningitis. An example is that all types of meningitis were the prevalent of fever, headache, and altered sensorium, and neck stiffness and vomiting were seen in different percentages, as well as Rowlinson and others [11].

The case in this cohort was mostly of 1030-years (49) with a majority of the males (58). These results are consistent with the studies conducted by other researchers who have reported a higher occurrence of meningitis in younger adults, which may have been due to more exposure to infectious agents and their immunological susceptibility to this group of the population [12]. It is also within the same gender distribution with slight male dominance, which is reflected in earlier epidemiological reports, which might be because of increased occupational exposure and disparity in health-seeking behavior between the males and the females. Most patients (95 percent) came in presenting with fever and headache (95 percent), altered sensorium (75 percent) and neck stiffness (67 percent). These results can be compared to Rowlinson et al. [11], who found that in 98 percent of the cases they found fever, headache and in 69 percent of cases they found to have neck stiffness, which confirms them as typical manifestations of CNS infections. Nevertheless, lack of specificity of these symptoms still makes it difficult to clinicians to tell bacterial and viral or tubercular meningitis without the support of laboratory.

Various CNS infection diagnosis depends on bio-chemical analysis of cerebrospinal fluid (CSF). The mean CSF glucose levels were minimum in bacterial meningitis (24.8 mg/dl) and maximum in viral meningitis (45.5mg/dl) and tubercular meningitis (48.6mg/dl). Those results refer to the typical scheme of hypoglycorrhachia in bacterial infections owing to a rise in glucose windowing by neutrophils and pathogens. Rowlinson et al. [11] have found mean glucose level at 44 mg/dl with bacterial meningitis, 69 mg/dl with viral meningitis, and 39 mg/dl with tubercular meningitis, which is widely similar to our findings. All forms of meningitis were found to have elevated CSF protein levels (>200 mg/dl) with the highest levels in septic meningitis (445 mg/dl). The hyperproteinemia of the CSF indicates the greater permeability of blood-brain barrier when the inflammation occurs. Though Rowlinson et al. [11] showed relatively reduced levels of proteins, the differences can be attributed to the duration and time of sampling. CSF cytological picture was also useful as a diagnostic clue. Viral and tubercular meningitis was lymphocytic and neutrophilic was bacterial and aseptic. The results are in tandem to the known diagnostic trends and support the prior investigation [13].

These results were positive in CSF culture after nine cases of bacterial meningitis (60), two cases of tuberculosis meningitis, and one case of septic meningitis. Among them, five patients yielded Streptococcus species, two yielded S. aureus, one Pseudomonas aeruginosa and four E. coli. The prevalence of bacterial pathogens in this research is partly similar to that of the world in which S. pneumoniae is the most frequent pathogen of bacterial meningitis (58%), then Streptococcus agalactiae (18.1%), Neisseria meningitidis (13.9%), Haemophilus influenzae (6.7), and Listeria monocytogenes (3.4) [14]. The high presence of E. coli and S. aureus in our research is probably indicative of nosocomial infections or secondary invasion by bacteria especially in immunocompromised patients or those who have undergone a surgery. Radiological results also added to the diagnostic image. In all bacterial meningitis, the normal chest X-rays were found whereas in 4 viral, 1 fungal and 2 aseptic meningitis cases, abnormalities were detected. It is interesting to note that 18 cases of tuberculular meningitis showed the results of the X-rays of the chest which were associated with pulmonary tuberculosis. These findings are similar to those of the previous researchers who also reported that up to a third of TBM patients develop pulmonary lesion on radiography.

The ADA activity on CSF has been extensively studied as a biological indicator of the tuberculous meningitis. In our research the mean ADA levels were high mainly in TBM cases and at the same time they were in normal levels in other cases. The joint interpretation of ADA and clinical-radiological characteristics improved the confidence of the diagnosis. GeneXpert positivity in 4.7% and TB-PCR confirmation were also positive evidence in the etiology of tuberculosis in the selective patients. The GeneXpert MTB/RIF assay is a potential revolution in the field of TB diagnostics; it is rapid, sensitive and specific and can be used in paucibacillary

specimens, including CSF. In the past studies have indicated such utility of GeneXpert in the diagnosis of TBM with sensitivity of about 60-80% as a result of the volume of sample and pre- treatment. Centrifuged large-volume CSF samples (810 ml) have been suggested to enhance the diagnostic yield [15].

Our research also remarkably showed a high rate of co-infection by HIV. The number of patients who were HIV reactive was 23 (14.3). Opposite to opportunistic infections, those with HIV are susceptible to Cryptococcal neoformans, Toxoplasma gondii, cytomegalovirus and Mycobacterium tuberculosis, which lead to CNS infections due to case of immunocompromised state. The neuroimpairments in HIV may also be similar to the classical amyotrophic lateral sclerosis (ALS) but the symptoms may be reversed with the beginning of antiretroviral therapy [16]. This association points to the significance of integrated HIV testing and management procedures in CNS-infected patients. When combined, these results prove again that CNS infections is a multi-factor, and is preconditioned by the host immunity, the conditions in the environment, and access to the healthcare. Low yield of bacteria culture, close clinical presentation, and ineffective molecular diagnosis are the diagnostic pitfalls observed in this case, which are indicative of syndrome approach that incorporates clinical, biochemical, molecular, and imaging histories. Increased surveillance and proximate diagnostic measures may matter to trim the weight of complications, such as hydrocephalus, seizures, and permanent neurological downsides.

The findings of our work on the international research, it is possible to mention that the etiology of bacterial meningitis differs according to the geography. H. influenzae and N. meningitidis are rare in the developed countries due to vaccination; they are present in low- and middle-income countries with Mycobacterium tuberculosis. Also, viral and fungal etiologies are also increasing partly due to the better diagnostic modalities. The relatively high prevalence of tuberculosis and viral meningitis within our cohort explains the necessity of the further awareness of the population of the health problem under consideration in the regions where tuberculosis and HIV are prevalent.

## Conclusion

In conclusion, tubercular meningitis emerged as the most prevalent form of CNS infection, followed by viral and bacterial meningitis. Fever, headache, and altered sensorium were the most common clinical presentations. CSF analysis proved essential for diagnosis, with elevated protein and ADA levels serving as key indicators in specific meningitis types. Streptococcus species were identified as the predominant bacterial pathogen. The study emphasizes the importance of early detection and accurate microbiological evaluation to ensure timely and effective management of meningitis cases.

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