AUCTORES
Globalize your Research

Journal of Neuroscience and Neurological Surgery
Ildefonso Rodriguez-Leyva *

Open Access

Research Article

Clinical and Radiological Characteristics of Tuberculous Meningitis in the Central Hospital "Dr. Ignacio Morones Prieto," a public institution in Mexico

Moreno-Cortez Katia Mabiael [1,2], Roman-Guzman Rodolfo Manuel [1,2], Ortiz-Alvarez Arturo [1], Hernadez-Rodriguez Hector Gerardo [2], Rodriguez-Leyva Ildefonso [1,2]*

[1] Neurology Service, Hospital Central "Dr. Ignacio Morones Prieto".

[2] School of Medicine, Autonomous University of San Luis Potosí

***Corresponding Author:** Ildefonso Rodriguez-Leyva, Neurology Service, Hospital Central "Dr. Ignacio Morones Prieto".

Received date: Octobre 30, 2024; **Accepted date:** November 08, 2024; **Published date:** November 18, 2024

Citation: Katia Mabiael MC, Rodolfo Manuel RG, Ortiz-A. Arturo, Hector Gerardo HR, Rodriguez-L. Ildefonso, (2024), Clinical and Radiological Characteristics of Tuberculous Meningitis in the Central Hospital "Dr. Ignacio Morones Prieto," a Public Institution in Mexico, *J. Neuroscience and Neurological Surgery*, 16(4); **DOI:10.31579/2578-8868/345**

Abstract

Background: Tuberculosis (TB) manifests as tuberculous meningitis (TBM) in up to 5% of extrapulmonary cases, causing significant morbidity and mortality. In Mexico, the prevalence is 0.35 cases per 100,000. Diagnosis is challenging due to the gradual onset and low TB levels in CSF. Mortality is around 20%, higher in HIV patients.

Material and Methods: A cross-sectional, retrospective, descriptive study was performed with patients treated at the Central Hospital "Dr. Ignacio Morones Prieto" who were diagnosed with TBM from 2018 to 2023. Patient records that met the following criteria were included: a) age over 18 years, b) any gender, c) confirmed diagnosis of TBM through staining, bacteriological culture, molecular studies, or biopsy, and d) brain imaging study using CT or MRI.

Results: Thirty-three patient files were evaluated. GeneXpert PCR, which was positive (only) in 17 of the cases (51.5%), culture (Lowenstein-Jensen) positive (only) in 6 patients (18.2%), cranial meninges biopsy (only) in 2 of the cases (6.1%) and bacilloscopic study in 1 patient (3.0%). Two positive results (GeneXpert and culture) were obtained in 7 patients (21.2%). There was a statistically significant correlation for mortality in those patients who presented stupor (100%) vs. those who did not present drowsiness only (33.0%) or remained awake (0%) ($p<0.001$). On the other hand, the statistically significant correlation between the presentation of cerebral edema and mortality was very striking since 93.8% of the patients who did not present edema survived, and 100% of those who presented edema died ($p=0.001$). Lumbar puncture findings included pleocytosis, hypoglycorrhachia (<30 mg/dL), and elevated protein (0.2 to 5 g/dL). Severe hypoglycorrhachia (<25 mg/dL) was associated with hydrocephalus and altered consciousness.

Conclusions: This study provides a clinical and demographic overview of TBM in San Luis Potosí, Mexico, highlighting the need for more comprehensive data collection and larger sample sizes to better characterize the disease.

Keywords: tuberculous meningitis; meningitis; mycobacterium tuberculosis

Introduction

Tuberculosis, caused by Mycobacterium tuberculosis, manifests as tuberculous meningitis (TBM) in up to 5% of extrapulmonary cases[1]. The prevalence of TBM varies between 1% and 10%, depending on the country of study[2]. It is a significant cause of morbidity and mortality, with neurological sequelae and complications occurring in up to 50% of patients[1]. In Mexico, the prevalence is 0.35 cases per 100,000 inhabitants, according to a 2017 study conducted in Tijuana—one of the few demographic studies on meningeal tuberculosis in the country. The study concluded that TBM's clinical, imaging, and laboratory characteristics in Mexico are similar to those observed globally[3].

The risk of developing central nervous system (CNS) tuberculosis is higher in children and adults with human immunodeficiency virus (HIV) infection and other causes of immunosuppression, such as chronic steroid use or treatment with tumor necrosis factor-alpha (TNF-α) inhibitors[4].

Following inhalation of M. tuberculosis, an inflammatory reaction occurs, leading to the formation of a granuloma. This structure encapsulates the infected cells, slowing the bacilli replication and resulting in a latent infection. This immune response can progress to active primary tuberculosis in immunosuppressed patients, causing the bacilli to disseminate to other systems through lymphatic and blood routes. Once Mycobacterium tuberculosis enters the central nervous system, the limited innate immunity in this environment permits the bacillus to survive and replicate, resulting in latent tuberculous lesions. Known as Rich foci, these lesions are primarily located beneath the subcortical pia and adjacent to the ventricular system. When these lesions rupture, M. tuberculosis bacilli are released into the subarachnoid space, leading to granulomatous infection of the meninges and subsequent inflammation[5]. In the brain, microglial cells become infected and, along with infiltrating cells, produce inflammatory chemoattractants that damage the blood-brain barrier (BBB). This damage facilitates the penetration of innate immune system cells and specific B and T lymphocytes.[6]

The clinical presentation includes a prodromal period with nonspecific symptoms such as fatigue, malaise, myalgia, and fever. TBM consists of a subacute to a chronic process characterized by headache, fever, vomiting, photophobia, and nuchal rigidity, typically progressing slowly[6,7]. Among the main complications are cranial neuropathies, which occur in 25-50% of patients, primarily affecting cranial nerves VI and III[8]. Inflammatory infiltration in the subarachnoid space or ventricular system disrupts cerebrospinal fluid (CSF) flow, producing hydrocephalus, particularly of the communicating type[9]. Other causes of intracranial hypertension include encephalitis and obliterative vasculitis, which lead to cytotoxic and vasogenic edema[7]. Hyponatremia, due to cerebral salt-wasting or the syndrome of inappropriate antidiuretic hormone secretion (SIADH), is present in 40-50% of cases[10]. Another complication of TB infection in the CNS is the formation of tuberculomas. Tuberculomas may occur with or without TBM, presenting symptoms such as epileptic seizures, focal neurological deficits, or intracranial hypertension[11]. Cerebral infarction occurs in 15-57% of patients with TBM, predominantly affecting deep gray matter structures such as the caudate nucleus, anterior thalamus, genu, and anterior limb of the internal capsule. The mechanism of infarction involves vasculitis with direct inflammatory involvement from the meningitis[12]. Epileptic seizures occur in up to 34% of patients[13]. Other central nervous system manifestations include tuberculous abscesses, tuberculous spondylitis, and intradural spinal tuberculosis[4].

Diagnosing TBM is more challenging compared to other forms of bacterial meningitis. This difficulty arises partly because the symptoms usually develop more gradually than those of classic bacterial meningitis. TB leads to a paucibacillary infection that is hard to detect in the CSF. When detecting M. tuberculosis in CSF is not feasible, a presumptive diagnosis of TBM is often made based on a combination of clinical presentation and CSF findings.[14] Cerebrospinal fluid findings include pleocytosis (50 to 500 cells per microliter, with 50% or more being lymphocytes), increased protein levels (up to 1000 mg/L), and low glucose levels (<40 mg/dL)[15]. The opening pressure is greater than 25 cm H2O in 50% of patients[16].

Microbiological diagnostic methods include Ziehl-Neelsen staining of cerebrospinal fluid, a rapid and readily available technique, but its sensitivity varies between 10% and 20%. Mycobacterial cultures are currently the gold standard for diagnosis, with a sensitivity of up to 70%, although mycobacterial growth is slow and takes more than two weeks[16]. Detection of M. tuberculosis DNA is possible with molecular biology techniques such as GeneXpert MTB/RIF and GeneXpert MTB/RIF Ultra, which offer similar sensitivity to bacteriological culture but produce results more quickly. However, up to 50% of cases may lack bacteriological confirmation[14,17]. Adenosine deaminase determination has also been used as a marker of the disease, as its levels in cerebrospinal fluid are elevated in patients with the infection. However, false positives are common in patients with HIV infection[17]. Next-generation metagenomic sequencing is a recently developed technique with a sensitivity of 70% for detecting meningeal tuberculosis[18].

The most common radiological findings in tuberculosis meningitis are meningeal enhancement, tuberculomas, and hydrocephalus[19]. More extensive findings correlate with more significant clinical complications and cerebrospinal fluid abnormalities. Approximately 75% of patients present with hydrocephalus, 38% with basal meningeal enhancement, and 15-26% with cerebral infarcts4. The most sensitive feature is basal enhancement on CT or MRI with contrast. Advanced techniques like magnetization transfer imaging are also used. Basal enhancement is more common in HIV patients and advanced disease stages[20]. Hydrocephalus, usually communicating, is linked to basal exudates, tuberculomas, infarcts, and cranial nerve palsies and is the primary cause of intracranial hypertension in these patients[9].

In TBM, strokes are frequent and primarily affect the perforating and cortical branches[21]. It has been reported that up to 75% of cerebral infarctions occur in areas supplied by the lenticulostriate and thalamic-perforating arteries, with a smaller proportion in regions supplied by the lateral lenticulostriate, anterior choroidal, and thalamogeniculate arteries. However, findings vary across different studies, with some reporting different percentages and including other vascular territories, such as the cortical branches[22]. The pathogenesis is related to vasospasm in the early stages and an inflammatory reaction in the lumen of blood vessels, known as tuberculous vasculitis, in the later stages [23,24].

Treatment of tuberculosis involves a two-month intensive phase with isoniazid, rifampicin, ethambutol or streptomycin, and pyrazinamide, followed by a maintenance phase with rifampicin and isoniazid. Regimens last 6 to 9 months, but individualized management is recommended due to similar mortality rates. Intravenous or high-dose rifampicin with fluoroquinolones has not improved outcomes over standard therapy. Management is more complex with drug-resistant TB. For isoniazid resistance, levofloxacin and higher doses of rifampicin are suggested[25]. Second-line drugs include ethionamide, cycloserine, and linezolid[26]. Corticosteroids, like dexamethasone, are recommended to reduce brain and vessel inflammation, intracranial pressure, and mortality risk[27]. A Cochrane meta-analysis found reduced mortality but no impact on turning off neurological deficits[28].

Ventriculoperitoneal shunts and endoscopic ventriculostomies manage complications such as hydrocephalus. Intracranial hypertension may require mannitol or hypertonic solutions. Antiepileptic drugs treat symptomatic epileptic seizures. The treatment of hyponatremia depends on its cause: either a salt-losing brain or SIADH. Despite no therapeutic consensus, antiplatelet drugs are used for cerebral vasculitis and infarcts[29].

Approximately 20% of meningeal tuberculosis patients die, with higher risks in those over 18 and those co-infected with HIV[30].

Materials and Methods

A cross-sectional, retrospective, descriptive study was performed with patients treated at the Central Hospital "Dr. Ignacio Morones Prieto" who were diagnosed with TBM from 2018 to 2023. The study was approved by the Research Committee (COFEPRIS Registration Number 17 CI 24 028 093) and the Research Ethics Committee of the Central Hospital "Dr. Ignacio Morones Prieto" (Registration Number CONBIOETICA-24-CEI-001-20160427) with Registration Number 45-23.

Patient records that met the following criteria were included: a) age over 18 years, b) any gender, c) confirmed diagnosis of TBM through staining, bacteriological culture, molecular studies, or biopsy, and d) brain imaging study using computed tomography (CT) or magnetic resonance imaging (MRI). Exclusion criteria were: a) records that met the inclusion criteria, b) lack of a confirmatory study of the infection, and c) lack of a brain imaging study.

Statistical analyses were performed using IBM SPSS Statistics V.25 for Mac. The arithmetic mean, median (measures of central tendency), standard deviation, minimum, and maximum (measures of dispersion) were used for quantitative variables. For qualitative variables, relative frequency (percentages) and absolute frequency were used. Chi-square (X2) was used for qualitative variables. The student's T-test (in cases of normal distribution) or Wilcoxon signed-rank test (in cases of abnormal distribution) was used for quantitative variables. A 95% confidence b) interval was determined, with a p-value less than or equal to 0.05 in two directions for statistically significant values.

Results

The records of CSF samples sent for *M. tuberculosis* detection were obtained from the Epidemiology area of the hospital, with 147 suspected patients. Subsequently, the results were corroborated, obtaining 38 patients with a positive test for tuberculosis; 5 were discarded because they did not have a clinical record. Of the rest of the patients, 107 had a negative result, and 2 had a diagnosis of tuberculous meningitis due to cerebrospinal fluid findings and clinical correlation; however, they did not have a confirmatory test. Thirty-three patient files were evaluated (see Figure 1). Population characteristics are shown in table 1.

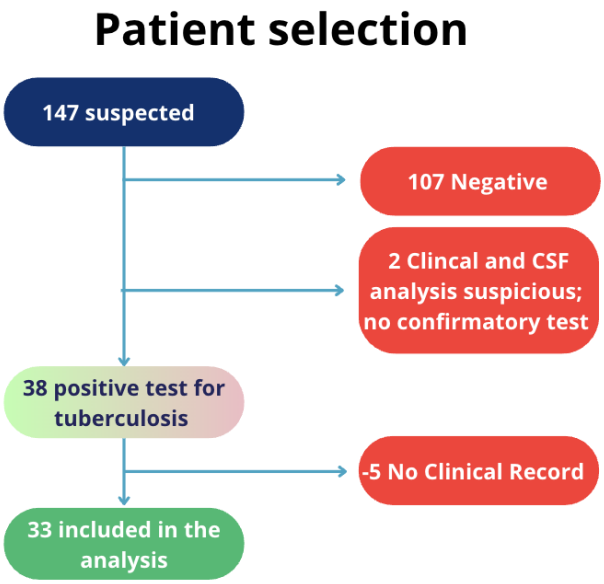


Figure 1: Patient selection

Table 1. Population characteristics	Total (*n* = 33)
Sex	
Male	23 (69.7%)
Female	10 (30.3%)
Age group, n (%)	
21-30	10 (30.3%)
31-40	11 (33.3%)
41-50	8 (24.2%)
51-60	0
61-70	3 (9.1%)
71-80	0
81-90	1 (3.1%)

The associated comorbidities in order of frequency were as follows: alcoholism 17 (51.5%), smoking 16 (48.5%), drug addiction 8 (24.2%), pulmonary tuberculosis 7 (21.2%), type 2 diabetes mellitus 6 (18.2%) and HIV 11 (33.3%). As for drug use, the most frequently used drugs were, in order of frequency: crystal meth, marijuana, and cocaine (see Table 2).

Table 2. Associated comorbidities	Total (*n* = 33)
Alcoholism	17 (51.5%)
Smoking	16 (48.5%)
Drug abuse	8 (24.2%)
- Crystal	- 4 (12.1%)
- Marijuana	- 3 (9.1%)
- Cocaine	- 1 (3.0%)
Pulmonary tuberculosis	7 (21.2%)
Diabetes mellitus type 2	6 (18.2%)
HIV	11 (33.3%)

Among the clinical manifestations, the frequency corresponded to the following: 21 patients presented headache (63.6%), 17 presented altered state of consciousness (51.5%), of which 15 corresponded to drowsiness (45.5%) and 2 to stupor (6.1%); fever was present in 17 patients (51.5%), nausea or vomiting (or both) in 10 patients (30.3%), epileptic seizures in 10 patients (30.3%).1%); fever was present in 17 patients (51.5%), nausea and vomiting in 10 patients (30.3%), epileptic seizures in 10 patients (30.3%), of which three patients presented focal status epilepticus, focal deficit in 3 patients (9.1%), nuchal rigidity in 2 patients (6.1%). Cranial nerve palsy was present in only one patient (3%), III cranial nerve palsy. General symptoms, such as asthenia, fatigue, and weight loss, were found in 12 patients (36.4%), and delirium was documented in 6 patients (18.1%), of which four were hyperactive (12.1%), and two were hypoactive (6.1%) (see Table 3).

Table 3. Clinical manifestations	Total (*n* = 33)
Headache	21 (63.6%)
Fever	17 (51.5%)
Altered state of consciousness	17 (51.5%)
Drowsiness	15 (45.5%)
Stupor	2 (6.1%)
Coma	0
Nausea or vomiting	10 (30.3%)
Epileptic seizures	10 (30.3%)
Focal deficit	3 (9.1%)
Nuchal rigidity	2 (6.1%)
Cranial nerve palsies	1 (3%)
General symptoms	12 (36.4%)
Delirium	6 (18.1%)
Hyperactive	4 (12.1%)
Hypoactive	2 (6.1%)

The imaging studies reviewed were computed tomography of the brain, performed in 28 patients. CT was performed in 28 patients (84.8%), and MRI was performed only in 12 patients (36.4%). Of the diagnostic methods required for inclusion in the study, the following were included: GeneXpert PCR, which was positive (only) in 17 of the cases (51.5%), culture (Lowenstein-Jensen) positive (only) in 6 patients (18.2%), cranial meninges biopsy (only) in 2 of the cases (6.1%) and bacilloscopic study in 1 patient (3.0%). Two positive results (GeneXpert and culture) were obtained in 7 patients (21.2%) (Table 4).

Table 4: Paraclinical studies	Total (*n* = 33)
Imaging studies	
Computed tomography of the brain	28 (84.8%)
Magnetic resonance imaging of the brain	12 (36.4%)
Microbiological studies	
GeneXpert	17 (51.5%)
Culture	6 (18.2%)
Biopsy	2 (6.1%)
Bacilloscopy	1 (3.3%)
GeneXpert/Culture	7 (21.2%)

The findings on imaging studies, in order of frequency, were as follows: tuberculoma or microabscesses in 9 patients (27.3%), hydrocephalus in 8 patients (24.2%), meningeal enhancement in 8 patients (24.2%), vasculitis in 6 patients (18.2%), ischemia in 5 patients (15.2%), and cerebral edema in 1 case (3.0%) (Table 5).

Table 5. Radiological findings	Total (*n* = 33)
Tuberculoma/micro abscess	9 (27.3%)
Hydrocephalus	8 (24.2%)
Meningeal enhancement	8 (24.2%)
Vasculitis	6 (18.2%)
Ischemia	5 (15.2%)
Cerebral edema	1 (3.3%

Secondary analysis:

In the secondary analysis, the Fisher exact Test was applied to establish the correlation between the patient's pre-existing conditions and the presentation of death (see Table 6). Similarly, using the Fisher exact Test (for variables with more than two items, Chi-squared was used), the clinical complications presented by the patients and their association with fatal outcomes were analyzed (See Table 7).

Table 6: Correlation of Pre-existing Conditions and Mortality
A 2X2 table with percentages per row is presented.

FEATURES	**n**	**NOT DEATH n (%)**	**DEATH n (%)**	***p***
GENRE				
Male	23	20 (87.0%)	3 (13.0%)	
Woman	10	10 **(**100%)	0 (0%)	0.536
DM2				
NO	27	24 (88.9%)	3 (11.1%)	
YES	6	6 (100%)	0 (0%)	1.000
HIV				
NO	22	21 (95.5%)	1 (4.5%)	
YES	11	9 (81.%8)	2 (18.2%)	0.252
Pulmonary Tuberculosis				
NO	26	23 (88.5%)	3 (11.5%)	
YES	7	7 (100%)	0 (0.0%)	1.00
Alcoholism				
NO	16	15 (93.8%)	1 (6.2%)	
YES	17	15 (88.2%)	2 (11.8%)	1.00
Smoking				
NO	17	16 (94.1%)	1 (5.9%)	
YES	16	14 (87.5%)	2 (12.5%)	0.601
Polydrug addictions				
NO	25	22 (88.0%)	3 (12%)	
YES	8	8 (100%)	0 (0%)	0.560

Table 7: Correlation of clinical complications and mortality.
A 2X2 table with percentages per row is presented.

FEATURE	**n**	**NOT DEATH n (%)**	**DEATH n (%)**	***p***
Alterations in awake state				
NO	16	16 (100%)	0 (0%)	
YES	17	14 (82.4%)	3 (17.6%)	0.227
Nuchal Rigidity				
NO	31	29 (93.5%)	2 (6.5%)	
YES	2	1 (50%)	1 (50%)	0.176
Focal deficit				
NO	30	28 (93.3%)	2 (6.7%)	
YES	3	2 (66.7%)	1 (33.3%)	0.256
State of consciousness*				
Awake	16	16 (100%)	0 (0%)	

Drowsiness	15	14 (93.3%)	1 (33.3%)	
Stupor	2	0 (0%)	2 (100%)	**<0.001**
Delirium*				
No Delirium	27	24 (88.9%)	3 (11.1%)	
Hypoactive	2	2 (100%)	0 (0%)	
Hyperactive	4	4 (100%)	0 (0%)	0.693
Epileptic seizures				
NO	23	22 (95.7%)	1 (4.3%)	
YES	10	8 (80.0%)	2 (20%)	0.212
Hydrocephalus				
NO	25	24 (96.0%)	1 (4.0%)	
YES	8	6 (75.0%)	2 (25.0%)	0.139
Cerebral Edema				
NO	32	30 (93.8%)	2 (6.3%)	
YES	1	0 (0%)	1 (100%)	0.091
Tuberculomas				
NO	24	23 (95.8%)	1 (4.2%)	
YES	9	7 (77.8%)	2 (22.2%)	0.174
Vasculitis				
NO	27	25 (92.6%)	2 (7.4%)	
YES	6	5 (83.3%)	1 (16.7%)	0.464
Ischemia				
NO	28	26 (92.9%)	2 (7.1%)	
YES	5	4 (80.0%)	1 (20.0%)	0.400

Chi-squared was applied due to more than two items.

There was a statistically significant correlation for mortality in those patients who presented stupor (100%) vs. those who did not present drowsiness only (33.0%) or remained awake (0%) ($p<0.001$). On the other hand, the statistically significant correlation between the presentation of cerebral edema and mortality was very striking since 93.8% of the patients who did not present edema survived, and 100% of those who presented edema died ($p=0.001$). Although 43.5% of the patients presented epileptic seizures, this complication did not have a statistically significant impact on mortality.

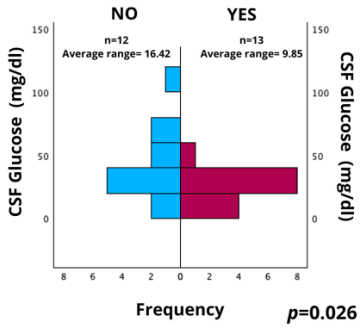
During data collection, it was decided to capture the values of the first lumbar puncture performed on the first day of admission to the emergency room. However, only 27 patients were found to be analyzed in this item. The data collected are shown in Table 8. Because of a lack of information, only 24 cases were counted with protein information and only 25 with glucose levels.

Table 8. CSF findings	Total (*n* = 27) (%)
Leukocytes (range) (mm^3/ml)	
10-100	15 (55.5%)
100-300	9 (33.3%)
300-500	2 (5.4%)
>500	1 (2.7%)
Mononuclear (range) (%)	
10-50	4 (14.8%)
50-100	23 (85.1%)
Protein (range) (g/dL)	
0-100	2 (7.4%)
101-200	7 (25.9%)
201-300	8 (29.6%)
301-400	2 (7.4%)
401-500	1 (2.7%)
>500	4 (5.4%)
Pandy +	3 (11.1%)
Glucose (range) (mg/dL)	
0-10	3 (11.1%)
11-20	5 (18.5%)
21-30	11 (40.7%)

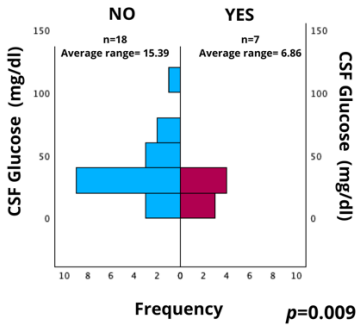
31-40	3 (11.1%)
41-50	1 (2.7%)
>50	4 (5.4%)

The Kolmogorov-Smirnov test assessed whether the CSF parameter results followed a normal distribution. The test indicated that the absolute leukocyte count (p=0.00), percentage of mononuclear cells (p=0.000), protein levels (p=0.000), and glucose levels (p=0.001) all exhibited a non-normal distribution. Based on this finding, the Mann-Whitney U test for independent samples was then utilized to analyze the association between these CSF parameters and specific clinical complications, including altered wakefulness, nuchal rigidity, focal deficits, epileptic seizures, hydrocephalus, cerebral edema, tuberculomas, vasculitis, and ischemia. Altered wakefulness and the development of hydrocephalus showed a significant correlation with low glucose levels (see Figures 2a and 2b). No significant correlation was found between CSF features and nuchal rigidity, focal deficits, epileptic seizures, cerebral edema, tuberculomas, vasculitis, or ischemia.

2a. Altered wakefulness / Glucose level



2b. Hydrocephalus / Glucose level



Therefore, taking these results into account, the decision was made to add a univariate analysis with a CSF glucose cutoff point ≤25 mg/dl (such cutoff comes out of the mean glucose associated with hydrocephalus <17> + 1 standard deviation <8.103>) to analyze its correlation with the different clinical complications, Fisher exact Test was applied, and the results of this are shown in Table 9.

Table 9: Correlation of clinical complications and CSF glucose level ≤25 mg/dl.
A 2X2 table with percentages per row is presented.

FEATURE	**n**	**Glucose >25 mg/dl n (%)**	**Glucose ≤25 mg/dl n (%)**	***p***
Altered wakefulness				
NO	12	9 (75%)	3 (25.0%)	
YES	13	3 (23.1%)	10 (76.9%)	**0.017**
Headache				
NO	6	5 (83.3%)	1 (16.7%)	
YES	19	7 (36.8%)	12 (63.2%)	0.073
Fever				
NO	11	8 (72.7%)	3 (27.3%)	
YES	14	4 (28.6%)	10 (71.4%)	**0.047**
Nuchal Rigidity				
NO	23	12 (52.1%)	11 (47.8%)	
YES	2	0 (0%)	2 (100%)	0.480

Focal deficit				
NO	23	11 (47.8%)	12 (52.2%)	
YES	2	1 (50.0%)	1 (50.0%)	1.00
State of consciousness*				
Awake	12	9 (75.0%)	3 (25.0%)	
Drowsiness	11	2 (18.2%)	9 (81.8%)	
Stupor	2	1 (50.0%)	1 (50.5%)	**0.024**
Delirium*				
No Delirium	21	11 (52.4%)	10 (47.6%)	
Hypoactive	1	0 (0%)	1 (100%)	
Hyperactive	3	1 (33.3%)	2 (66.7%)	0.511
Epileptic seizures				
NO	17	8 (47.1%)	9 (52.9%)	
YES	8	4 (50.0%)	4 (50%)	1.000
Hydrocephaly				
NO	18	12 (66.7%)	6 (33.3%)	
YES	7	0 (0%)	7 (100%)	**0.005**
Cerebral Edema				
NO	24	12 (50.0%)	12(50.0%)	
YES	1	0 (0%)	1 (100%)	1.000
Tuberculomas				
NO	18	9 (50.0%)	9 (50.0%)	
SI	7	3 (42.9%)	4 (57.1%)	1.000
Vasculitis				
NO	19	11 (57.9%)	8 (42.1%)	
YES	6	5 (16.7%)	5 (83.3%)	0.160
Ischemia				
NO	21	11 (52.4%)	10 (47.6%)	
YES	4	1 (25.0%)	3 (75.0%)	0.593

Chi-squared was applied due to more than two items.

Discussion

TBM represents 5-10% of extrapulmonary tuberculosis cases globally [31], aligning with its rarity but severe prognosis. The study by Garcia-Grimshaw et al. (2019) in Tijuana reported a young demographic, with 63.4% of male cases primarily between 18 and 40 years old [3]. In contrast, our study finds an older mean age, 31 to 47 years, which may reflect regional differences or a variation in risk factors, such as comorbidities.

Our study and other reports found that headache, fever, and altered consciousness were typical symptoms of TBM, reaffirming their central role in TBM presentations [32]. What sets our study apart is the unique finding of a higher prevalence of seizures, which could be an indicator of more advanced or cerebral-complicated cases. This observation aligns with findings suggesting that neurologic sequelae, like seizures, may be prevalent in advanced disease stages. The common comorbidities in our sample, such as alcoholism, type 2 diabetes, and HIV, are also recognized as risk factors that compromise immune response, potentially exacerbating TBM susceptibility [33]. These unique findings provide a deeper understanding of TBM and its clinical implications.

The association of stupor with higher mortality rates found in our research may underscore the role of early mental status changes as a predictive indicator for outcomes in TBM.

Meningeal enhancement and hydrocephalus were radiologically prevalent, consistent with TBM's classic presentation in imaging [31]. Our finding of cerebral edema as a predictor of mortality aligns with the literature, noting that brain swelling complicates outcomes in TBM due to increased intracranial pressure. Additionally, the high frequency of tuberculomas or microabscesses in our sample suggests a progressive form of TBM that may require aggressive treatment approaches.

Like many others, our study acknowledges the challenges of TBM diagnosis and treatment. GeneXpert, despite its sensitivity challenges, has significantly improved TBM detection rates, particularly in resource-limited settings [31]. Our study's observed mortality rate of 9.1%, notably lower than that of other studies, could reflect differences in early diagnosis, access to care, or treatment protocols [32]. Acknowledging the challenges and the potential for improvement in TBM diagnosis and treatment is crucial for advancing patient care.

Consistent with other studies, cerebrospinal fluid findings in our sample showed pleocytosis, hypoglycorrhachia, and elevated protein levels. Severe hypoglycorrhachia (under 25 mg/dL), associated with hydrocephalus and altered consciousness in our data, highlights the importance of monitoring glucose levels as a marker of disease severity in TBM. Hypoglycorrhachia correlates with poor outcomes, as lower CSF glucose often indicates a more aggressive inflammatory response, which may be linked to increased mortality risks.

Limitations and New Perspectives

Limitations:

- Some records were unavailable, making it impossible to include more patients in the study.
- MRI is more effective for identifying brain and posterior fossa lesions, but due to cost, it was only sometimes used.
- Patient follow-up needed to be more consistent, leading to incomplete evolution data.
- The initial lumbar puncture data did not account for the number of days since symptom onset or modifications due to empirical treatments.
- Data were derived from reports and clinical notes, which may be influenced by interobserver variability.

Perspectives:

- The database can facilitate future analytical and correlation studies, providing more comprehensive data for analyzing and identifying tuberculous meningitis. This can help address the scarcity of published results on the Mexican population.
- Future proposals include collecting clinical history from emergency department admission to obtain significant data for a larger sample.

Conclusions

This study collected the most frequent clinical and radiological findings in the Central Hospital "Dr. Ignacio Morones Prieto population," providing a demographic and clinical overview of the epidemiological state in San Luis Potosí, Mexico. The data aim to improve prompt disease identification in our unit and the region. More analytical studies, comprehensive data collection, and larger sample sizes are necessary for better disease characterization.

References

1. Manyelo CM, Solomons RS, Walzl G, Chegou NN. (2021). Tuberculous Meningitis: Pathogenesis, Immune Responses, Diagnostic Challenges, and the Potential of Biomarker-Based Approaches. J Clin Microbiol. 59(3):e01771-20. doi:10.1128/JCM.01771-20
2. Dodd PJ, Osman M, Cresswell FV, et al. (2021). The global burden of tuberculous meningitis in adults: A modelling study. PLOS Glob Public Health. 1(12):e0000069. doi:10.1371/journal.pgph.0000069
3. García-Grimshaw M, Gutiérrez-Manjarrez FA, Navarro-Álvarez S, González-Duarte A. (2020). Clinical, Imaging, and Laboratory Characteristics of Adult Mexican Patients with Tuberculous Meningitis: A Retrospective Cohort Study. J Epidemiol Glob Health. 10(1):59-64. doi:10.2991/jegh.k.191023.001
4. Schaller MA, Wicke F, Foerch C, Weidauer S. (2019). Central Nervous System Tuberculosis. Clin Neuroradiol. 29(1):3-18. doi:10.1007/s00062-018-0726-9
5. Davis AG, Rohlwink UK, Proust A, Figaji AA, Wilkinson RJ. (2019). The Pathogenesis of Tuberculous Meningitis. J Leukoc Biol. 105(2):267-280. doi:10.1002/JLB.MR0318-102R
6. Wilkinson RJ, Rohlwink U, Misra UK, et al. (2017). Tuberculous meningitis. Nat Rev Neurol. 13(10):581-598. doi:10.1038/nrneurol.2017.120
7. Wen L, Li M, Xu T, Yu X, Wang L, Li K. (2019). Clinical features, outcomes and prognostic factors of tuberculous meningitis in adults worldwide: systematic review and meta-analysis. J Neurol. 266(12):3009-3021. doi:10.1007/s00415-019-09523-6
8. Shibuya K, Tsuneyama A, Misawa S, et al. (2020). Cranial nerve involvement in typical and atypical chronic inflammatory demyelinating polyneuropathies. Eur J Neurol. 27(12):2658-2661. doi:10.1111/ene.14497
9. Raut T, Garg RK, Jain A, et al. (2013). Hydrocephalus in tuberculous meningitis: Incidence, its predictive factors and impact on the prognosis. J Infect. 66(4):330-337. doi:10.1016/j.jinf.2012.12.009
10. Misra UK, Kalita J, Bhoi SK, Singh RK. (2016). A study of hyponatremia in tuberculous meningitis. J Neurol Sci. 367:152-157. doi:10.1016/j.jns.2016.06.004
11. Perez-Malagon CD, Barrera-Rodriguez R, Lopez-Gonzalez MA, Alva-Lopez LF. Diagnostic and Neurological Overview of Brain Tuberculomas: A Review of Literature. Cureus. 13(12):e20133. doi:10.7759/cureus.20133
12. Zhang L, Zhang X, Li H, Chen G, Zhu M. (2019). Acute ischemic stroke in young adults with tuberculous meningitis. BMC Infect Dis. 19:362. doi:10.1186/s12879-019-4004-5
13. Misra UK, Kumar M, Kalita J. (2018). Seizures in tuberculous meningitis. Epilepsy Res. 148:90-95. doi:10.1016/j.eplepsyres.2018.10.005
14. Metcalf T, Soria J, Montano SM, et al. (2018). Evaluation of the GeneXpert MTB/RIF in patients with presumptive tuberculous meningitis. Mokrousov I, ed. PLOS ONE. 13(6):e0198695. doi:10.1371/journal.pone.0198695
15. Ahlawat S, Chaudhary R, Dangi M, Bala K, Singh M, Chhillar AK. (2020). Advances in tuberculous meningitis diagnosis. Expert Rev Mol Diagn. 20(12):1229-1241. doi:10.1080/14737159.2020.1858805
16. Foppiano Palacios C, Saleeb PG. (2020). Challenges in the diagnosis of tuberculous meningitis. J Clin Tuberc Mycobact Dis. 20:100164. doi:10.1016/j.jctube.2020.100164
17. Luo Y, Xue Y, Lin Q, et al. (2021). Diagnostic Model for Discrimination Between Tuberculous Meningitis and Bacterial Meningitis. Front Immunol. 12:731876. doi:10.3389/fimmu.2021.731876
18. Lin Y, Zhang W, Xiong Y, et al. (2023). Comparative performance of microbiological methods for the detection of tuberculous meningitis pathogens in cerebrospinal fluid. Diagn Microbiol Infect Dis. 107(2):116025. doi:10.1016/j.diagmicrobio.2023.116025
19. Tai MLS, Nor HM, Rahmat K, et al. Neuroimaging findings are sensitive and specific in diagnosis of tuberculous meningitis. Neurol Asia. Published online 2017.
20. Kumar S, Gutch M. (2020). Advanced Magnetic Resonance Imaging Techniques in Tuberculous Meningitis. Adv Biomed Res. 9:20. doi:10.4103/abr.abr_222_19
21. Soni N, Kumar S, Shimle A, Ora M, Bathla G, Mishra P. (2020). Cerebrovascular complications in tuberculous meningitis—A magnetic resonance imaging study in 90 patients from a tertiary care hospital. Neuroradiol J. 33(1):3-16. doi:10.1177/1971400919881188
22. Tai MLS, Viswanathan S, Rahmat K, et al. (2016). Cerebral infarction pattern in tuberculous meningitis. Sci Rep. 6:38802. doi:10.1038/srep38802
23. Verma R, Chakraborty R. (2023). Extensive Vasculitis in Tuberculous Meningitis. J Glob Infect Dis. 15(4):169. doi:10.4103/jgid.jgid_24_23
24. Vanjare HA, Gunasekaran K, Manesh A, et al. (2021). Evaluation of Intracranial Vasculitis in Tuberculous Meningitis using Magnetic Resonance Vessel Wall Imaging Technique. Int J Mycobacteriology. 10(3):228. doi:10.4103/ijmy.ijmy_117_21
25. Arshad A, Dayal S, Gadhe R, et al. (2020). Analysis of Tuberculosis Meningitis Pathogenesis, Diagnosis, and Treatment. J Clin Med. 9(9):2962. doi:10.3390/jcm9092962

26. Kempker RR, Smith AGC, Avaliani T, et al. (2022). Cycloserine and Linezolid for Tuberculosis Meningitis: Pharmacokinetic Evidence of Potential Usefulness. Clin Infect Dis. 75(4):682-689. doi:10.1093/cid/ciab992
27. Donald PR, Toorn RV. (2016). Use of corticosteroids in tuberculous meningitis. The Lancet. 387(10038):2585-2587. doi:10.1016/S0140-6736(16)30770-X
28. Prasad K, Singh MB, Ryan H. (2016). Corticosteroids for managing tuberculous meningitis. Cochrane Database Syst Rev. 2016(4):CD002244. doi:10.1002/14651858.CD002244.pub4
29. Davis A, Meintjes G, Wilkinson RJ. (2018). Treatment of Tuberculous Meningitis and Its Complications in Adults. Curr Treat Options Neurol. 20(3):5. doi:10.1007/s11940-018-0490-9
30. Seid G, Alemu A, Dagne B, Gamtesa DF. (2023). Microbiological diagnosis and mortality of tuberculosis meningitis: Systematic review and meta-analysis. PLOS ONE. 18(2):e0279203. doi:10.1371/journal.pone.0279203
31. Barnacle, James R., Angharad G. Davis, and Robert J. Wilkinson. "Recent advances in understanding the human host immune response in tuberculous meningitis." Frontiers in Immunology 14 (2024): 1326651.
32. https://academic.oup.com/bmb/article-abstract/113/1/117/284995
33. Manyelo CM, Solomons RS, Walzl G, Chegou NN. (2021). Tuberculous Meningitis: Pathogenesis, Immune Responses, Diagnostic Challenges, and the Potential of Biomarker-Based Approaches. J Clin Microbiol59:10.1128/jcm.01771-20.https://doi.org/10.1128/jcm.01771-20

DOI:10.31579/2578-8868/345