

**ARSI UNIVERSITY COLLEGE OF HEALTH SCIENCES
SCHOOL OF MEDICINE**



**CHARACTERISTICS AND HOSPITAL OUTCOMES OF ADULTS WITH
CENTRAL NERVOUS SYSTEM TUBERCULOSIS AT ASELLA
REFFERAL AND TEACHING HOSPITAL**

**A Research Paper to be Submitted to Department of Internal Medicine,
College of Health Sciences, Arsi University for Partial Fulfilment of The
Requirement of Specialty Training Program in Internal Medicine**

JANUARY, 2026

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**Characteristics and Hospital Outcomes of Central Nervous System
Tuberculosis among Adults at Asella Referral and Teaching Hospital**

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LIST OF FIGURES

Figure 1: Conceptual frame work for Characteristics,hospital outcome and its associated factors among adult central nervous system tuberculosis patients at Asella referral and teaching hospital	15
Figure 2: Types of CNS Tuberculosis Diagnoses Among Participants with Central Nervous System Tuberculosis at Asella Referral and Teaching Hospital	25
Figure 3: Glasgow Coma Scale (GCS) Scores at Admission and Discharge of Participants with Central Nervous System Tuberculosis.....	27
Figure 4: Types of Complications Among Participants with Central Nervous System Tuberculosis	29
Figure 5:MRS Status of Patients with Central Nervous System Tuberculosis	30

LIST OF TABLES

Table 1:Socio-Demographic Characteristics of Participants with Central Nervous System Tuberculosis Among Adults at Asella Referral and Teaching Hospital.....	22
Table 2:Clinical Characteristics of Participants with Central Nervous System Tuberculosis Among Adults at Asella Referral and Teaching Hospital.	23
Table 3: Clinical Characteristics of Participants with Central Nervous System Tuberculosis Among Adults at Asella Referral and Teaching Hospital.....	24
Table 4:Laboratory Characteristics of Participants with Central Nervous System Tuberculosis at Asella Referral and Teaching Hospital.	26
Table 5: In hospital course and Treatment Outcomes of Participants with Central Nervous System Tuberculosis at Asella Referral and Teaching Hospital.....	27
Table 6:Factors associated with the poor treatment outcome of MRS Status of Patients with CNS TB	31

ABBREVIATIONS AND ACRONYMS

AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Therapy
ARTH	Asella Referral and Teaching Hospital
CD4	Cluster of differentiation
CSF	Cerebrospinal Fluid
CNS	Central nervous system
CN	Cranial nerve
CPT	Cotrimoxazole Prophylactic Therapy
EPTB	Extra pulmonary Tuberculosis
GCS	Glasgow Comma Scale
HIV	Human Immunodeficiency Virus
IPT	Isoniazid Preventive Therapy
MDR/RR-TB	multidrug-resistant or rifampicin-resistant tuberculosis
MDR-TB	Multidrug-Resistant Tuberculosis
MRS	modified Rankin score
TB	Tuberculosis
TBM	Tuberculous meningitis
WHO	World Health organization

ABSTRACT

Background

Central nervous system (CNS) tuberculosis (TB) is among the relatively uncommon yet most devastating forms of human mycobacterial infection. The estimated mortality of CNS-TB is approximately 42% in hospitalized patients (based on meningitis related deaths). However, hospital outcomes of CNS-TB and its predictors are not well studied in the study area.

Objectives

To Assess Clinical Characteristics, treatment outcomes and its associated factors of central nervous system tuberculosis among adults at Asella referral and teaching hospital.

Methodology: Institutional based Cross-sectional study was conducted on CNS TB Patients who presented to Asella referral and teaching hospital during the study period. Data were collected from the patient's medical records using a checklist created on kobo toolbox. A total sample size of 130 was included and analyzed using Statistical Package for Social Science (SPSS) version 27. Bivariate and multivariate logistic regression analysis was applied to assess associations between dependent and independent variables. The odds ratio with a 95% confidence interval was used to declare the strength of associations between dependent and independent variables. P values less than 0.05 was considered statistically significant.

Results: A total of 130 participants were included in the study. Among them, 74 (56.9%) were male. The mean age of participants was 43.22 ± 14.98 years. The clinical presentation of CNS TB revealed that headache, fever, and neck rigidity were reported by 125 participants (96.15%). Regarding treatment, only 4 participants (3.08%) did not receive TB treatment, while 126 (96.92%) did. The initiation of drug therapy occurred in less than two weeks for 60 participants (46.2%). At discharge, 111 participants (85.38%) showed improvement, although there were 11 deaths (8.46%), and 3 referrals (2.31%). In the multivariable logistic regression models, age, duration of drug initiation, and HIV status were statistically significant predictors of poor treatment outcomes for CNS TB. Age emerged as a critical risk factor, especially for those over 65 years, who faced a significantly increased risk of poor treatment outcomes (AOR 3.23, 95% CI 2.62-7.21, $p < 0.001$). Patients whose treatments initiated after more than two weeks had poor treatment outcomes (AOR 4.56, $p < 0.001$), and those with reactive HIV tests faced a higher risk of poor treatment outcomes (AOR 2.66, $p = 0.002$).

Conclusion: A significant majority of the participants were male, with an average age of around 43 years. Notably, classic symptoms such as headache, fever, and neck rigidity were predominant among patients, with severe neurological complications like seizures and cognitive impairments documented. The diagnosis of TB meningitis was the most common. However, a concerning 8.46% of cases resulted in death. Age, timing of drug initiation, and HIV status as significant predictors of poor treatment outcomes. Particularly alarming was the increased risk in patients over 65 years and those who delayed treatment.

Key words: clinical characteristics, Central Nerve system TB and treatment outcome

TABLE CONTENTS

Acknowledgement	
List of Figures	i
List of tables.....	ii
Abbreviations and Acronyms	iii
ABSTRACT.....	iv
TABLE CONTENTS.....	vi
1.INTRODUCTION	8
1.1 Background	8
1.2 Statement of problem	10
1.3 Significance of the study	11
2.LITERATURE REVIEW	12
2.1 Overview of Central Nervous System Tuberculosis.....	12
2.2 Associated factors of CNS TB infections	13
2.2.1 Socio-demographic factors	13
2.2.2 Behavioral factors	13
2.2.3 Clinical factors	14
2.3 Conceptual frame work	15
3.OBJECTIVES OF THE STUDY	16
3.1 General objectives	16
3.2 Specific objectives.....	16
3.3 Research questions	17
4. RESEARCH METHODOLOGY.....	18
4.1 Study Period and Area.....	18
4.2 Study design	18
4.3 Source population.....	18
4.4 Study Population	18
4.5 Eligibility Criteria	19
4.5.1 Inclusion criteria	19
4.5.2 Exclusion criteria	19
4.6 Sample size and sampling technique.....	19

4.7	Sampling procedure.....	19
4.8	Measurement	19
4.8.1	Study Variables	19
4.9	Operational definitions.....	20
4.10	Data collection procedure.....	20
4.11	Data processing and Analysis	20
4.12	Ethical considerations	21
4.13	Dissemination plan.....	21
5.	RESULT	22
5.1	Socio-Demographic Characteristics of Participants with Central Nervous System Tuberculosis	22
5.2	Clinical Presentation and Diagnosis.....	22
5.3	TB Contact History and Comorbidity	23
5.4	Laboratory Characteristics of Participants with Central Nervous System Tuberculosis	25
5.5	Glasgow Coma Scale (GCS) scores for participants with Central Nervous System Tuberculosis	26
5.6	Treatment Outcomes of Participants with Central Nervous System Tuberculosis	27
5.7	Types of Complications Among Participants with Central Nervous System Tuberculosis	28
5.8	MRS Status of Patients among Participants with Central Nervous System Tuberculosis..	29
5.9	Factors Associated with the poor treatment outcome of MRS Status of Patients with CNS TB.....	30
6.	DISCUSSION	32
6.1	Conclusion.....	36
6.2	Limitations of the Study.....	37
6.3	Recommendations	38
	REFERENCES	39
	ANNEXES	42
	Annex-1. Data extraction checklist	42
	Annex 2: DECLARATIONS	46

1.INTRODUCTION

1.1 Background

CNS tuberculosis (TB) refers to granulomatous inflammation of the central nervous system caused by *Mycobacterium tuberculosis* which can affect the meninges, brain, spinal cord, and the bones surrounding the brain and spinal cord and its manifestations vary depending on the specific location of the disease(1).

In individuals with a healthy immune system, clinical CNS TB develops in 1 to 2% of all patients with active tuberculosis and makes up around 8% of all reported extra-pulmonary TB cases in those who are immunocompetent(2). Although the main manifestation of TB is pulmonary, cases of extra pulmonary TB (EPTB) are not rare, representing 15% of all TB reported case(3).

CNS TB is categorized based on its anatomical location (intracranial and spinal), with tuberculosis meningitis (TBM) being the most common and severe form where without treatment, the majority of patients with TBM die within 5 to 8 weeks of the onset of the disease (4). It may manifest in a variety of forms including parenchymal and leptomeningeal tuberculomas, abscesses, cerebritis, vasculitis, infarction, meningitis, and osteomyelitis(5).

The diagnosis of TBM was established as per Ahuja et al criteria, which include clinical, CSF examination, radiological and evidence of extra-neural tuberculosis(6). TBM is staged as Stage I - alert, no deficits; Stage II - GCS 11-14 or 15 with deficits; Stage III - GCS 10 or less, with or without deficits(7).

WHO states tuberculosis treatment outcome as the end result of TB treatment and categorized as successful (cure and treatment completion), unsuccessful (death, default, and failure)(8). Treatment success is an important aspect in the TB control(9).

Treatment for tuberculosis requires the patient to take a combination of different medications over several months to ensure a successful cure, which is a critical and valuable aspect of post-TB treatment (10).

The World Health Organization (WHO) guidelines for the treatment of Tuberculous Meningitis (TBM) are derived from those established for pulmonary tuberculosis. The recommended regimen includes an initial treatment of two months with rifampicin (RMP), isoniazid (INH), pyrazinamide (PZE), and ethambutol (ETB), followed by an additional 7 to 10 months of RMP and INH for all patients (2).

Adjunctive glucocorticoid therapy, such as dexamethasone or prednisone, is beneficial for adults with tuberculous meningitis (11). In Tikur Anbessa Specialized Hospital, Ethiopia, the prevalence of CNS TB was higher among HIV-infected adults with TB-HIV co-infection and TB meningitis was the most common type of CNS TB(12). It is known that CNS TB is worst type of extra-pulmonary TB and it is one of the reasons for TB hospitalization and yet there is no adequate research on this issue in Ethiopia.

1.2 Statement of problem

Central nervous system TB (CNS-TB) is one of the most challenging clinical diagnoses, and it is associated with a high morbidity and mortality. The relative shortage and protean nature of its symptoms makes tuberculosis of the CNS a difficult diagnostic challenge(13). The proportion of people with a new episode of TB who were co-infected with HIV is highest in countries in the WHO African Region exceeding 50% in parts of southern Africa(14).

Several studies have been done to find out presentation, diagnosis, treatment and outcomes of Tuberculous Meningitis (TBM) cases in various countries of the world, but to my best knowledge, various aspects of CNS TB as a whole are yet to be studied in Ethiopia in general and specifically in Asella. Thus, this study comprehensively will attempt to assess the Characteristics and prognostic outcomes of CNS tuberculosis among adult patients treated at ARTH.

1.3 Significance of the study

This study will be devoted to assess Characteristics and prognostic outcomes of CNS tuberculosis among adult patients treated at ARTH. It will come up with the expected final finding capable of serving all the stakeholders including the researcher, general public health, policy makers and to the supervisors and health institution.

Determining the characteristics and prognostic outcomes of CNS tuberculosis has implications in improving patients' response to treatment. It assists health care practitioners, policymakers and health care managers to identify the variations in treatment success rate and to focus on the area that fuels increased mortality and morbidity of TB patients. The study can also contribute as literature for those who are planning to conduct research on this topic or on a similar one.

2.LITERATURE REVIEW

2.1 Overview of Central Nervous System Tuberculosis

Tuberculosis (TB) of the central nervous system (CNS) is classically described as meningitis. However, altered mental status, including encephalitis, is within the spectrum of clinical manifestations. Because early treatment can dramatically improve outcomes, consideration of TB as a potential pathogen in CNS infections, including encephalitis, is vital(13).

Central nervous system tuberculosis (CNS-TB) comprises a variety of neurological syndromes with a relatively high mortality and morbidity caused by *Mycobacterium tuberculosis*. The most common presentation of CNS-TB is meningitis, followed by tuberculomas, tuberculous brain abscess, and Pott's disease(Zalalem Kaba Babure et al).

From a systematic review and meta-analysis done in 2022 which included 53 studies from 28 countries, representing 12,621 patients with CNS-TB the global prevalence of CNS-TB in the general population is 2 cases per 100,000 inhabitant(16). In hospitalized patients, it is present in approximately 9%. This frequency is around 14% in patients with meningitis and 5% in patients with TB. Tuberculomas was reported in few studies with a frequency of < 1%. The estimated mortality of CNS-TB was approximately 42% in hospitalized patients (based on meningitis related deaths)(16).

A systematic review of patients in Africa reported that TB meningitis represented on average 15.3% of all patients with meningitis, associated with a higher mortality in settings with a prevalence higher than 20%(12).

A single-center observational cross-sectional study conducted on Ninety-five HIV infected adults with presumptive TB-HIV co-infection on combination antiretroviral therapy for median of 144 months were assessed at Tikur Anbessa Specialized Hospital and showed a prevalence of CNS tuberculosis of 56.8% (TB meningitis 53.7%, tuberculomas 2.1%, and spinal TB 1.1%). patients with CNS TB were younger compared to those with extra CNS TB (38.6 vs. 43.6 years, $p = 0.04$)(12).

2.2 Associated factors of CNS TB infections

2.2.1 Socio-demographic factors

Different studies at different places have showed an association with socio demographic variables and CNS TB. These variables are Age category, sex, educational status and number of rooms in residency.

The study conducted in India on Fifty-six patients with newly diagnosed CNS tuberculosis were registered and followed up. A total of 56 patients between the ages of 18 to 65 were enrolled in this study. The mean age was 35 ± 11 years and it showed that increasing age was associated with higher mRS (($p=0.002$)(17) . Patients with either isolated TBM or tuberculomas had improvement in outcomes(17). On multivariate analysis, it was found that CN palsy (HR=0.38, $p=0.003$), duration of illness (HR=0.35, $p=0.005$) and age (HR=0.33, $p=0.008$) were the most significant predictor of worse outcomes.

Patients with CNS TB were younger compared to those with extra CNS TB (38.6 vs. 43.6 years, $p = 0.04$); no gender difference was observed between the two groups ($p = 0.9$)(12).

A retrospective chart review of CNS TB patients done in Bangkok showed that CNS TB affected males more than females, mainly middle-aged adults (mean age, 43.64 years) and Fever, headache, signs of meningeal irritation, and impaired cognitive function were common clinical manifestations of CNS TB (17).

2.2.2 Behavioral factors

Behavior related factor like smoking alcohol drinking habit and History of imprisonment have showed association. A study conducted in Belarus and Sudan reveal that those respondents with history of smoking have significant association with MDR – TB with (95% CI: 1.1–2.0), history of imprisonment (95% CI: 1.1–2.0) and history of alcohol abuse (95% CI: 1.0–1.8) showed association(18)(19). Study conducted in Brazil reveled that due to immune pathological relation of smoking with TB, studies have shown that smoking was associated with higher prevalence of PTB(20).

2.2.3 Clinical factors

In a study done at Tikur Anbessa high prevalence of CNS TB among treatment experienced HIV-infected adults with dual TB-HIV infection was shown and advanced HIV disease stages, deferred CPT, and IPT were independent predictors of CNS tuberculosis(12).

A study done in Thailand on Clinical factors predictive of functional outcomes in tuberculous meningitis showed shorter duration of TBM symptoms was correlated with good outcomes with respect to both short- and long-term functional status(21).

isoniazid resistance on initial susceptibility testing was associated with subsequent death among those with a positive cerebrospinal fluid culture for MTB(22).

A prospective observational study conducted at V.S. Hospital, Ahmedabad, which assessed the socio-demographic profile as well as outcomes in patients with various forms of CNS TB showed that a long duration of illness was associated with poor outcomes (HR of 0.35 and $p=0.005$)(17).

2.3 Conceptual frame work

This conceptual frame work is adapted and modified accordingly from different studies done(21)(12)(17).

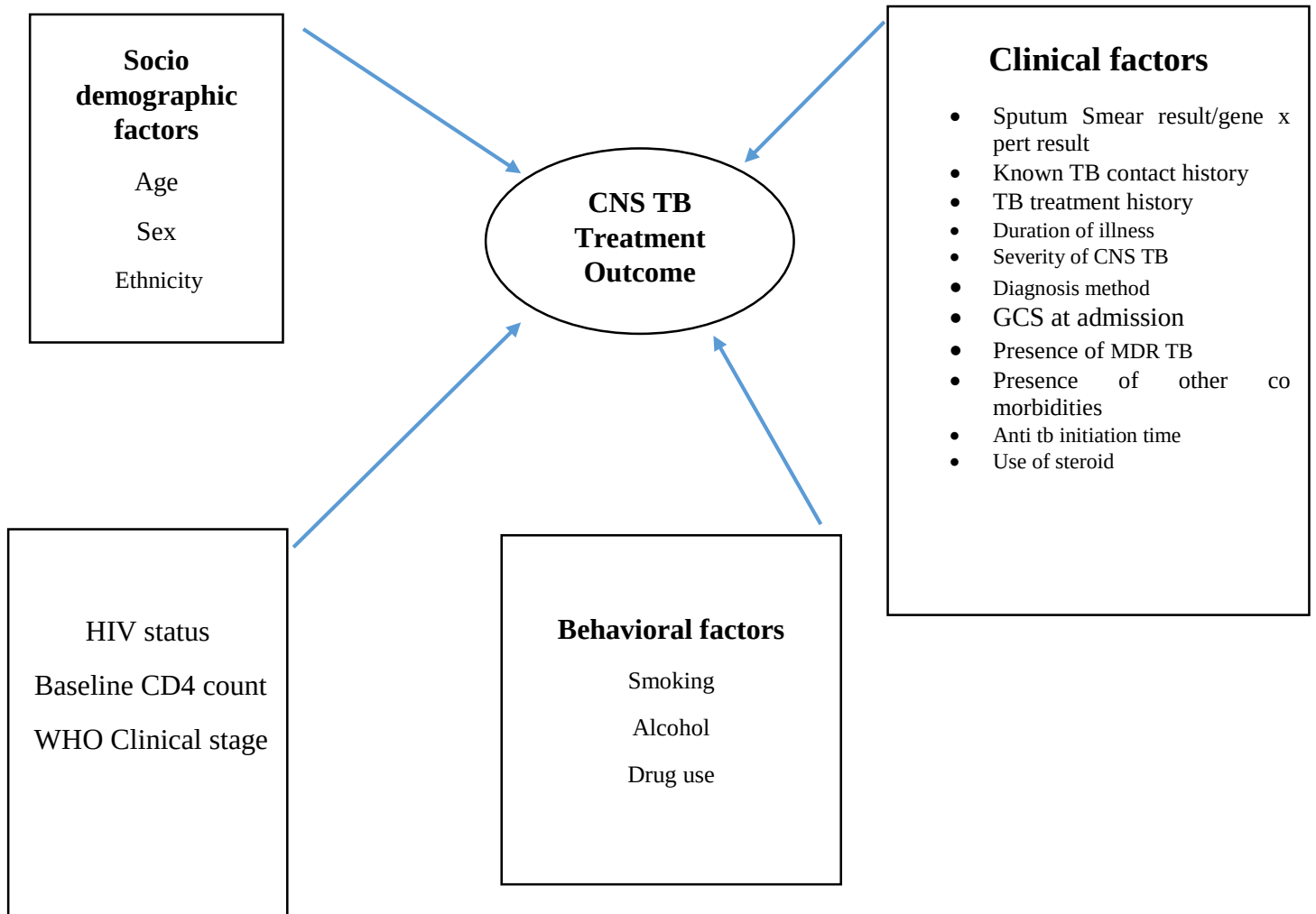


Figure 1: Conceptual frame work for Clinical Characteristics, treatment outcome and its associated factors among adult central nervous system tuberculosis patients at Asella referral and teaching hospital. (Source cited above)

3.OBJECTIVES OF THE STUDY

3.1 General objectives

- To Assess Clinical Characteristics, hospital outcomes and its factors associated among adult central nervous system tuberculosis patients at Asella referral and teaching hospital.

3.2 Specific objectives

- ✓ To examine the clinical characteristics of adult patients with central nervous system tuberculosis at Asella referral and teaching hospital.
- ✓ To evaluate treatment outcome of adult patients with CNS tuberculosis at Asella Referral and Teaching Hospital.
- ✓ To Assess factors associated with treatment outcome with central nervous system tuberculosis at Asella referral and teaching hospital.

3.3 Research questions

1. What are the sociodemographic, clinical and behavioral characteristics of hospitalized CNS Tuberculosis patients in Asella referral and teaching hospital during the study period?
2. What are factors associated with prognosis and hospital outcome of central nervous system tuberculosis among adults at Asella referral and teaching hospital during the study period?

4. RESEARCH METHODOLOGY

4.1 Study Period and Area

This study was conducted at Asella teaching and referral hospital (ATRH), from 2019 to 2025. ATRH is located in Asella town, Arsi zone, Oromia Regional State, Ethiopia. Asella town is located at 165 KM to southeast of Addis Ababa, the capital city of Ethiopia.

The hospital has 321 beds with more than 6 departments (, Internal Medicine Pediatrics and Child Health, Gynecology and Obstetrics, Surgery, Orthopedics and Oncology, ICU) and involved in training undergraduate and postgraduates in different specialties in 04 major departments (Internal Medicine Pediatrics and Child Health, Gynecology and Obstetrics, and Surgery)

The department of Internal medicine has inpatient service of 54 beds with highly dependent unit (HDU) constitutes 04 beds, one general Emergency room and 01 General ICU. For patients on follow up for chronic diseases there are diabetic clinic, neurology clinic, and general medical follow up clinics, ART clinic and TB clinic. The department has more than 20 seniors, 1 Cardiologist and 2 neurologists, 36 residents of different level, 6 General Practitioners and 18 nurses. The TB clinic provides services for those patients diagnosed with TB.

4.2 Study design

Intuition based Cross-sectional study was conducted in ARTH

4.3 Source population

All CNS TB patients presented to ARTH.

4.4 Study Population

Those selected patients' medical chart who was diagnosed with CNS TB presented to ARTH during the study Period and fulfil the inclusion criteria

4.5 Eligibility Criteria

4.5.1 Inclusion criteria

Patients with Completed medical charts with the diagnosis of CNS TB

Patients whose age is 15 and above were included in the study.

4.5.2 Exclusion criteria

Patient charts with incomplete information

Alternative CNS infection (bacterial, viral meningitis confirmed by CSF analysis)

4.6 Sample size and sampling technique

All eligible records of CNS TB patients found during the study period was included in the study.

4.7 Sampling procedure

All medical records for patients who were admitted with the diagnosis of CNS TB in Asella Teaching and Referral Hospitals ward from January 1, 2020 to December 31, 2026 was listed based on the sequence of their card numbers from registration book, and Census of those who meet inclusion criteria during the study period was included in the study and data were collected using structured checklist on kobo toolbox from their medical records history, physical examination, laboratory investigation, and diagnosis. convenience sampling technique was used.

4.8 Measurement

4.8.1 Study Variables

4.8.1.1 Dependent variable:

Prognostic outcome of CNS-TB (classified as good, bad outcomes based on functional status on discharge defined by MRS score)

4.8.1.2 Independent variables:

Socio-demographic factors: Age and Sex

Behavioral factors: Smoking, Alcohol drinking habit, drug use habit

Clinical factors: Known TB contact history, previous TB treatment history, Smear result at the time of diagnosis, duration of illness, Presence of comorbidities, GCS at admission, diagnosis method, Severity of CNS TB, time to anti tb initiation, use of steroid, presence of MDR TB,

HIV status of the patient; positive or negative, WHO Stage, baseline CD4 count,

4.9 Operational definitions

Central Nervous System (CNS) Tuberculosis-infection the brain and spinal cord by MTB confirmed by clinical, radiological, and/or microbiological criteria.

Prognostic Outcome; measurable result related to a patient's hospital stay.

Favorable(good) outcomes in this study is discharge with mild or no disability (mRS <2)

Unfavorable(bad) outcomes include severe disability (mRS >3), death, neurologic complications like stroke, seizure

Clinically diagnosed: when a person who does not fulfil the criteria for bacteriological confirmation has been diagnosed with TB disease by a physician who has decided to give the person a full course of TB treatment(23).

4.10 Data collection procedure

Data was collected using kobo toolbox by a check list from patient's medical record of adult CNS TB patients. 2 nurses from medical ward were selected for data collection since they have a medical background.

The data collected were also cross-checked for its completeness, consistency, accuracy and clarity on a daily basis. The principal investigator carried out close supervision during the whole data collection period to monitor over all data collecting quality.

4.11 Data processing and Analysis

Data was collected by Kobo toolbox and exported to SPSS version 27. Descriptive, bivariate, and multivariable logistic regression analyses were performed. The odds ratio with a 95% confidence interval was used to declare the strength of associations between dependent and independent variables. P values less than 0.05 were considered statistically significant.

4.12 Ethical considerations

Ethical clearance was obtained from post graduate programs coordinating office of college of health sciences of Asella University to conduct research. Permission request letter was written to ARTH administration to get access to patient's charts. The study was conducted through a review of records. To ensure confidentiality, the name and other identifiers of patients, physicians, and other health care members who examined the patients is not be recorded on the data abstraction format.

4.13 Dissemination plan

After research completion and finalizing report, this study will be presented to the department of Internal medicine and public health, as part of Internal medicine specialty thesis at Arsi University and submitted to post graduate programs coordinating office of college of health sciences of Arsi University and other stake holders for possible use of this proposal as a baseline study for future studies on similar tittle and for possible publication of the study.

5. RESULT

5.1 Socio-Demographic Characteristics of Participants with Central Nervous System Tuberculosis

A total of 130 participants were included in the study. Among them, 74 (56.9%) were male, indicating that a majority of the participants diagnosed with Central Nervous System Tuberculosis (CNS TB) are male. In contrast, 55 participants (42.3%) were female. The mean age of participants was 43.22 ± 14.98 years. The age group of 35-44 years had 28 participants (21.5%), reflecting a higher number of cases in this category. Additionally, the age group of 55-64 years included 27 participants (20.8%). Regarding substance use history, 106 participants (81.54%) did not report a history of substance use, while 24 participants (18.46%) reported such a history. Among those with a history of substance use, 15 participants (11.54%) indicated alcohol use. (Table 1.)

Table 1: Socio-Demographic Characteristics of Participants with Central Nervous System Tuberculosis Among Adults at Asella Referral and Teaching Hospital.

Variable	Category	Frequency	Percentage
Sex	Male	74	56.9
	Female	55	42.3
Age	Mean $\pm$ Std. Deviation	43.22 $\pm$ 14.98	
	15-24	14	10.8
	25-34	25	19.2
	35-44	28	21.5
	45-54	24	18.5
	55-64	27	20.8
	=>65	12	9.2
Substance uses history	No	106	81.54
	Yes	24	18.46
Types of substance	Alcohol	15	11.54
	Cigarette smoking	9	6.92

5.2 Clinical Presentation and Diagnosis

The clinical presentation of Central Nervous System Tuberculosis (CNS TB) revealed that headache, fever, and neck rigidity were reported by 125 participants (96.15%), making these the predominant symptoms of the disease. This underscores the frequent manifestation of CNS TB with these classic symptoms. Additionally, 99 participants (76.50%) exhibited behavioral changes, indicating the disease's impact on cognitive functions. Seizures affected 50 participants (38.50%),

highlighting a significant neurological involvement, while 33 participants (25.40%) experienced physical weakness. Altered mental status was observed in 40 participants (30.8%). Furthermore, 16 participants (12.30%) had cranial nerve palsies, reflecting specific neurological deficits. In terms of diagnosis, TB meningitis was the most commonly identified form of CNS TB, affecting 82 individuals (63.09%), followed by tuberculomas in 23 participants (17.69%), tubercular abscesses in 12 participants (9.22%), and spinal TB in 9 participants (6.90%). **(Table.2)**

5.3 TB Contact History and Comorbidity

Regarding TB contact history, 105 participants (80.77%) reported no known exposure to tuberculosis, while 25 participants (19.23%) indicated they had previously been in contact with someone infected with the disease. The Glasgow Coma Scale (GCS) at admission showed that 76 participants (58.5%) were in a mild state of consciousness impairment. A moderate level of impairment was observed in 40 participants (30.8%), with 14 participants (10.8%) presenting with severe impairment. In terms of comorbidity, 114 individuals (87.69%) did not report any additional conditions, whereas 16 participants (12.31%) had comorbidities, including 8 participants (6.15%) with cardiac issues and 3 participants (2.31%) with liver problems that could complicate their treatment. Most patients 104 participants (80.00%) were admitted to the general ward, while 26 participants (20.00%) required care in the intensive care unit (ICU). Of 104 individuals (80.00%) were admitted to the ward, while 26 (20.00%) required intensive care unit (ICU) support. Complications occurred in 62 participants (47.69%), with the primary reasons for ICU admission being respiratory support (10.00%), sedation (3.10%), low Glasgow Coma Scale (GCS) scores (2.3%), and coma (4.62%). Most participants were classified as WHO Stage 1 (1.54%) or Stage 4 (3.10%). **(Table.2 and 3)**

Table 2: Clinical Characteristics of Participants with Central Nervous System Tuberculosis Among Adults at Asella Referral and Teaching Hospital.

Variable	Category	Frequency	Percentage
Clinical presentation of CNS TB	Headache, fever, neck rigidity	125	96.15
	Seizure	50	38.50
	Change in Behavior	99	76.50
	Cranial nerve palsy	16	12.30
	Body weakness	33	25.40
	Visual complication	7	5.00

	Change in mentation	40	30.8
	Others	5	3.85
Symptoms of pulmonary TB	Cough more than 2 weeks	55	42.30
	Night sweating	43	33.10
	Weight loss	32	24.60
Types of CNS TB diagnosis	TB meningitis	82	63.09
	Tuberculomas	23	17.69
	Tubercular abscess	12	9.22
	Spinal TB	9	6.90
	Others	4	3.10
TB contact history	No	105	80.77
	Yes	25	19.23

Table 3: Clinical Characteristics of Participants with Central Nervous System Tuberculosis Among Adults at Asella Referral and Teaching Hospital.

Variable	Category	Frequency	Percentage
Glasgow Coma Scale (GCS) at admission	Mild (13-15)	76	58.5
	Moderate (9-12)	40	30.8
	Severe (3-8)	14	10.8
Having comorbidity	No	114	87.69
	Yes	16	12.31
Type of Comorbidity	Cardiac disease	8	6.15
	Liver disease	3	2.31
	Diabetes	5	3.85
Place of admission	Ward	104	80.00
	ICU	26	20.00
Complication	No	68	52.31
	Yes	62	47.69
Reason for ICU	For respiratory support	13	10.00
	For Sedation	4	3.10
	Due to low GCS	9	6.92
Length of hospital Stay (mean± Std. Deviation)	15.13±8.86		

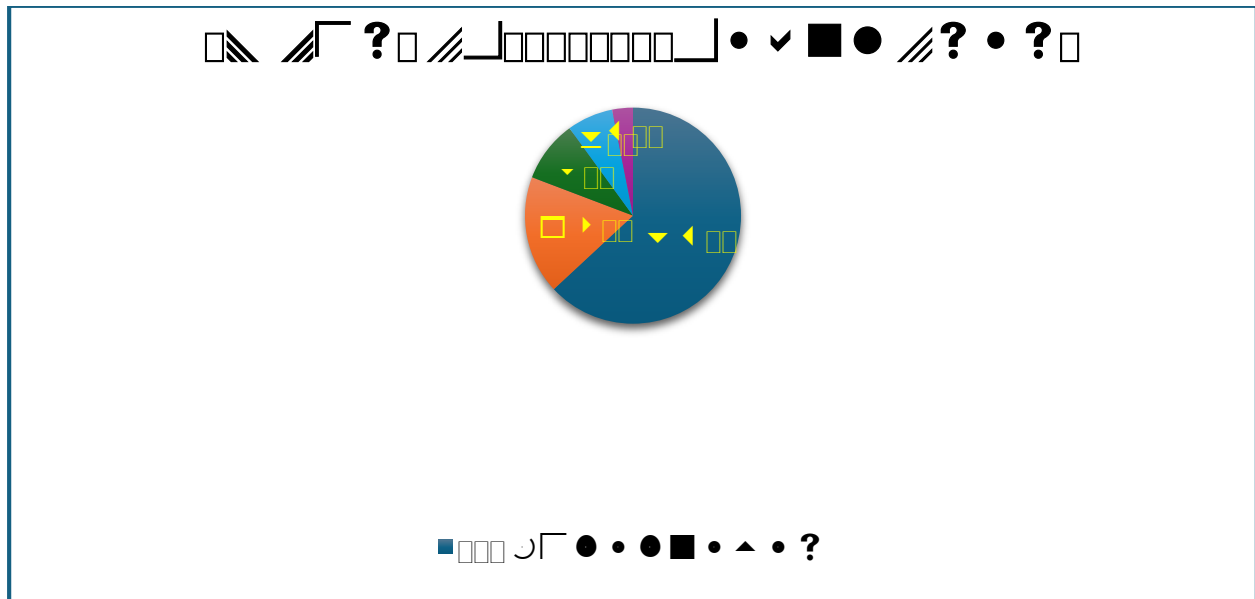


Figure 2: Types of CNS Tuberculosis Diagnoses Among Participants with Central Nervous System Tuberculosis at Asella Referral and Teaching Hospital.

5.4 Laboratory Characteristics of Participants with Central Nervous System Tuberculosis

In the study of participants with Central Nervous System Tuberculosis at Asella Referral and Teaching Hospital, laboratory characteristics revealed several important findings. CSF analysis was performed on 49 participants (37.69%). Regarding the GeneXpert test for CSF, 104 participants (80.00%) did not have it done, 6 participants (4.62%) were detected, and 20 participants (15.38%) were not detected. For sputum GeneXpert, 106 participants (81.54%) did not have the test, with 4 participants (3.10%) testing positive and 20 participants (15.38%) testing negative. A chest X-ray was conducted on 55 participants (42.31%), while 75 participants (57.69%) did not have one. Computed Tomography (CT) scans were performed on 44 participants (33.85%), with 86 participants (66.15%) not undergoing the procedure. Magnetic Resonance Imaging (MRI) rarely performed, with 9 participants (6.90%) undergoing the scan, leaving 121 participants (93.10%) without one. Finally, in terms of HIV screening, 124 participants (95.38%) tested negative, whereas 6 participants (4.62%) tested positive. (**Table.4**)

Table 4: Laboratory Characteristics of Participants with Central Nervous System Tuberculosis at Asella Referral and Teaching Hospital.

Variable	Category	Frequency	Percentage
CSF analysis done	No	81	62.31
	Yes	49	37.69
Gene Xpert For CSF	Not done	104	80.00
	Detected	6	4.62
	Not detected	20	15.38
Sputum gene Xpert	Not done	106	81.54
	Detected	4	3.10
	Not detected	20	15.38
Chest X ray Done	No	75	57.69
	Yes	55	42.31
CT done	No	86	66.15
	Yes	44	33.85
CT done with contrast	No	26	20.00
	Yes	18	13.85
MRI Done	No	121	93.10
	Yes	9	6.90
HIV screening	Not Reactive	124	95.38
	Reactive	6	4.62

5.5 Glasgow Coma Scale (GCS) scores for participants with Central Nervous System Tuberculosis

At admission, 78.5% of participants were in the mild range (GCS 13-15), but this percentage dropped to 58.5% by discharge, indicating a significant improvement in consciousness levels. Conversely, the moderate category (GCS 9-12) decreased from 30.8% at admission to 13.8% at discharge. In the severe range (GCS 3-8), 10.8% of participants were critically impaired at admission, with only a slight decrease to 10.7% by discharge, reflecting that a small number remained in a severely compromised state. Overall, the data highlights a positive trend in GCS scores.

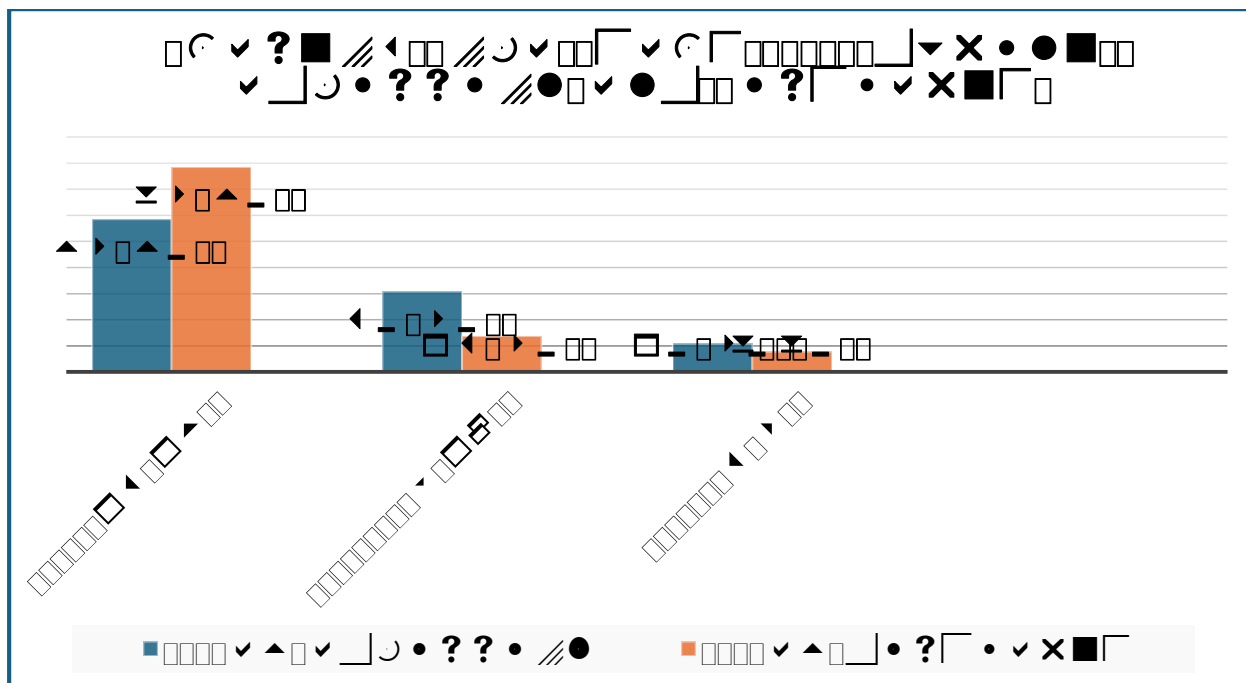


Figure 3: Glasgow Coma Scale (GCS) Scores at Admission and Discharge of Participants with Central Nervous System Tuberculosis Asella Referral and Teaching Hospital.

5.6 Treatment Outcomes of Participants with Central Nervous System Tuberculosis

Regarding treatment, only 4 participants (3.08%) did not receive tuberculosis (TB) treatment, while 126 (96.92%) did. Steroids were administered to 104 participants (80.00%), with the majority receiving both types of steroids (60.00%). The initiation of drug therapy occurred in less than two weeks for 60 participants (46.2%). At discharge, 111 participants (85.38%) showed improvement, although there were 11 deaths (8.46%), and 3 referrals (2.31%). The GCS at discharge reflected positive outcomes, with 102 participants (78.5%) classified as mild, 18 (13.8%) as moderate, and 10 (7.7%) as severe. The mean length of hospital stay was 15.13 days (± 8.86). (Table 5.)

Table 5: In hospital course and Treatment Outcomes of Participants with Central Nervous System Tuberculosis at Asella Referral and Teaching Hospital.

Variable	Category	Frequency	Percentage
HAART regimen	Fist line treatment	1	0.77
	Third line treatment	5	3.85
TB treatment given	No	4	3.08
	Yes	126	96.92

Steroid given	No	26	20.00
	Yes	104	80.00
Types of steroids	Both	78	60.00
	Dexamethasone	18	13.85
	Prednisolone	8	6.15
Another medication given	No	86	66.15
	Yes	44	33.85
Duration of drug initiation	Less than two weeks	60	46.2
	Greater than two weeks	70	53.8
Discharge outcome	Improved	111	85.38
	Death	11	8.46
	Refers	3	2.31
	Left against medical advice	5	3.85
GCS at discharge	Mild (13-15)	102	78.5
	Moderate (9-12)	18	13.8
	Severe (3-8)	10	7.7

5.7 Types of Complications Among Participants with Central Nervous System Tuberculosis

The most common complication was seizures, reported by 45.16% of participants, highlighting the significant impact of CNS TB on neurological function. Hydrocephalus was noted in 24.19% of participants, indicating a burden on cerebrospinal fluid dynamics. Focal neurologic deficits affected 19.45% of participants. Additionally, strokes occurred in 6.45% of cases, reflecting the severity of complications arising from CNS TB. Lastly, vision impairment was reported in 4.84% of participants, emphasizing the varied neurological impact of the condition. **(Figure 4.)**

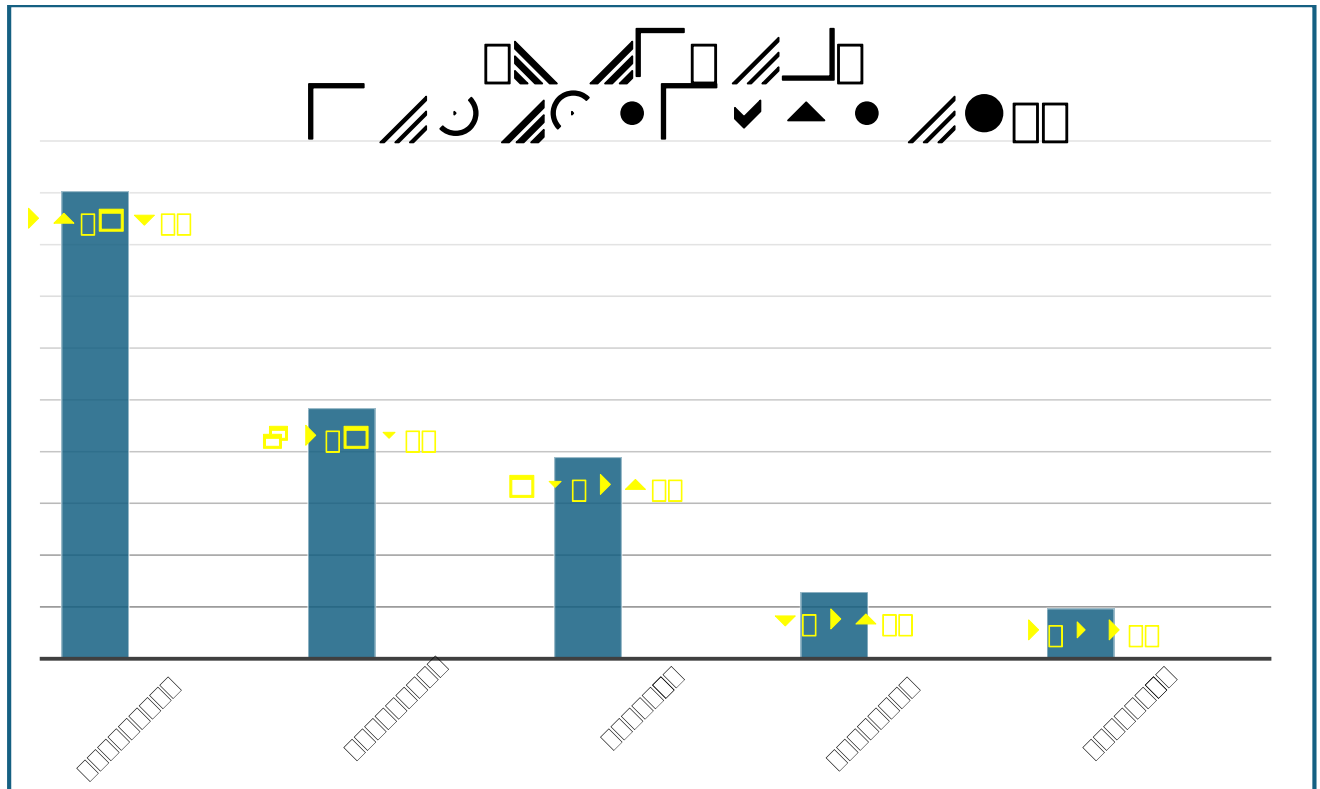


Figure 4: Types of Complications Among Participants with Central Nervous System Tuberculosis

5.8 MRS Status of Patients among Participants with Central Nervous System Tuberculosis

The pie chart illustrates the Modified Rankin Scale (MRS) status of patients, highlighting their outcomes following treatment. A significant majority, comprising 74% of patients, achieved a good outcome (MRS score of 0-2). In contrast, 26% of patients faced a poor outcome (MRS score greater than 3). **(Figure 5.)**

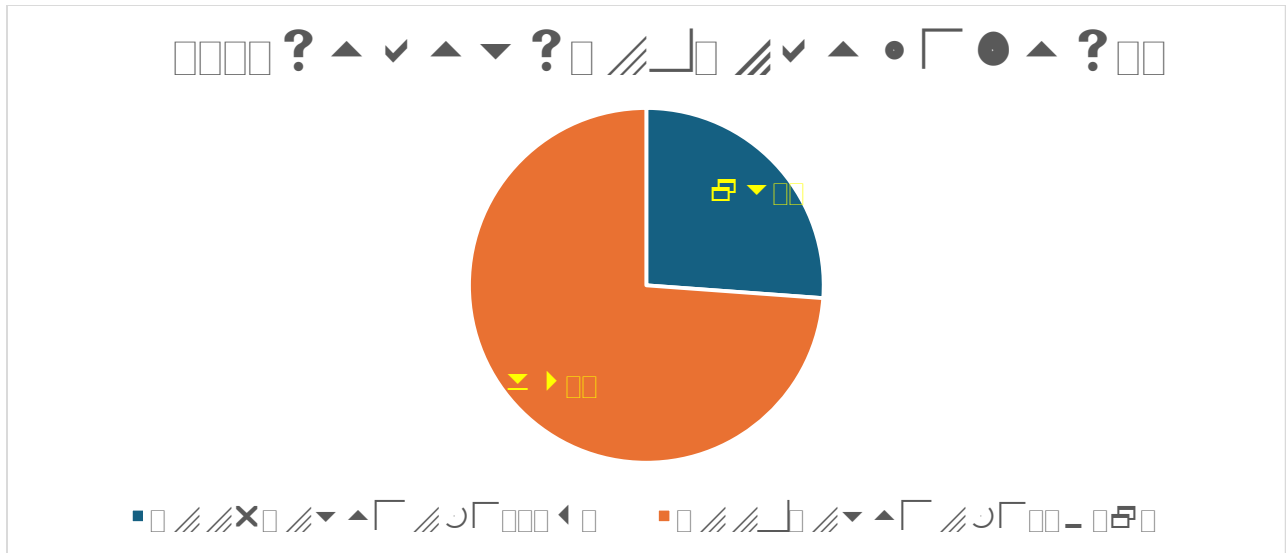


Figure 5: MRS Status of Patients with Central Nervous System Tuberculosis

5.9 Factors Associated with the poor treatment outcome of MRS Status of Patients with CNS TB

The study provides a thorough analysis of the factors influencing the Modified Rankin Scale (MRS) status in patients with central nervous system tuberculosis (CNS TB). Notably, in the bivariate logistic regression analysis, sex, age, substance use, symptoms of pulmonary TB, comorbidities, HIV status, complications, and the duration of drug initiation were identified as factors associated with poor treatment outcomes for CNS TB.

In the multivariable logistic regression models, age, duration of drug initiation, and HIV status were statistically significant predictors of poor treatment outcomes for CNS TB. Age emerged as a critical risk factor, especially for those over 65 years, who faced a significantly increased risk of poor treatment outcomes (AOR 3.23, 95% CI 2.62-7.21, $p < 0.001$). Patients who initiated treatment after more than two weeks had poor treatment outcomes (AOR 4.56, $p < 0.001$), and those with reactive HIV tests faced a higher risk of poor treatment outcomes (AOR 2.66, $p = 0.002$).

Table 6: Factors associated with the poor treatment outcome of MRS Status of Patients with CNS TB

MRS Status of Patients with CNS TB							
Category	Variables	Good outcome N (%)	Poor outcome N (%)	COR (95%CI)	P-value	AOR (95%CI)	P-value
sex	Male	32(43.20)	24(42.9)	0.13(1.09-1.34)	<0.001	0.68(0.36-4.77)	0.056
	Female	42(56.8)	32(57.1)	1		1	
Age	15-24	13(17.6)	1(1.8)	1		1	
	25-34	14(18.9)	11(19.6)	0.31(0.16-0.63)	0.031	0.05(0.08-0.37)	0.302
	35-44	12(16.2)	16(28.6)	2.44(1.12-5.33)	0.086	0.71(0.12-4.45)	0.351
	45-54	14(18.9)	10(17.9)	0.47(0.22-0.98)	0.046	2.86(0.64-12.84)	0.163
	55-64	15(20.3)	12(21.4)	0.38(0.10-1.40)	0.145	0.17(0.10-1.40)	0.165
	=>65	6(8.1)	6(10.7)	1.63(0.3-1.58)	0.018	3.23(2.62-7.21)	<0.001*
Substance uses	No	59(79.73)	47(83.93)	1		1	
	Yes	15(20.27)	9(16.07)	2.55(1.19-5.46)	0.16	1.91(0.68-5.34)	0.198
Symptoms of pulmonary TB	Cough more than 2 weeks	32(43.24)	23(41.07)	1		1	
	Night sweating	27(36.49)	16(28.57)	1.51(0.32-4.59)	0.014	0.18(0.23-1.40)	0.132
	Weight loss	17(22.97)	17(30.36)	1.88(0.86-4.12)	0.23	1.91(0.68-5.34)	0.245
Having comorbidity	No	62(83.78)	52(92.86)	1		1	
	Yes	12(16.22)	4(7.14)	1.61(1.45-4.60)	0.019	0.32(0.10-1.60)	0.067
Duration of drug initiation	Less than two weeks	39(52.7)	21(37.5)	1		1	
	Greater than two weeks	35(47.3)	35(62.5)	1.26(1.17-5.86)	0.008	4.56(3.05-9.05)	<0.001*
HIV screening	Not Reactive	71(95.9)	53(94.64)	1		1	
	Reactive	3(4.1)	3(5.36)	0.28(0.12-0.62)	0.002	2.66(2.35-12.69)	0.002*
Complication	No	38(51.35)	42(75.00)	1		1	
	Yes	36(48.65)	14(25.00)	0.56(0.27-1.15)	0.083	4.28 (0.25-0.53)	0.702

6. DISCUSSION

A total of 130 participants were included in the study. Among them, 74 (56.9%) were male, indicating that a majority of the participants diagnosed with Central Nervous System Tuberculosis (CNS TB) are male. In contrast, 55 participants (42.3%) were female. The mean age of participants was 43.22 ± 14.98 years, indicating that the average age is approximately 43 years, with a standard deviation of about 15 years. The age group of 35-44 years had 28 participants (21.5%), reflecting a higher number of cases in this category. Additionally, the age group of 55-64 years included 27 participants (20.8%). Regarding substance use history, 106 participants (81.54%) did not report a history of substance use, while 24 participants (18.46%) reported such a history. Among those with a history of substance use, 15 participants (11.54%) indicated alcohol use. Similar study conducted in Ethiopia a total of 95 participants, the mean age (1SD) age of the participants was 40.8 (± 12.4) years and another similar study was done in Thailand A total of 114 patients received a provisional diagnosis of CNS-TB during the study period. A median (interquartile range) age was 40.8 (31.7–55.4) years, and 75 patients (65.8%) were male(24,25)

In terms of diagnosis, TB meningitis was the most commonly identified form of CNS TB, affecting 82 individuals (63.09%), followed by tuberculomas in 23 participants (17.69%), tubercular abscesses in 12 participants (9.22%), and spinal TB in 9 participants (6.90%). Similar study conducted in Ethiopia a total of 144 participants, the prevalence of CNS tuberculosis was 56.8% (TB meningitis 53.7%, tuberculomas 2.1%, and spinal TB 1.1%). Patients with CNS TB were younger compared to those with extra CNS TB (38.6 vs. 43.6 years, $p = 0.04$). A higher proportion of patients with CNS TB had undetectable HIV RNA compared to those with extra CNS TB (55.8% vs. 36.8% $p = 0.04$) another similar study was done in Thailand, a total of 114 patients Presumptive diagnoses included 95 cases (83.3%) of TB meningitis, 19 cases (16.7%) of tuberculomas/abscess, and 4 (3.5%) of spinal TB. Some patients had more than one diagnosis(24,25).

The clinical presentation of Central Nervous System Tuberculosis (CNS TB) revealed that headache, fever, and neck rigidity were reported by 125 participants (96.15%), making these the predominant symptoms of the disease. This underscores the frequent manifestation of CNS TB with these classic symptoms. Additionally, 99 participants (76.50%) exhibited behavioral changes. Seizures affected 50 participants (38.50%), highlighting a significant neurological involvement,

while 33 participants (25.40%) experienced physical weakness. Altered mental status was observed in 40 participants (30.8%). Furthermore, 16 participants (12.30%) had cranial nerve palsies. Similar study in Thailand A total of 114 patients was done in Common presenting symptoms included fever in 91 (80.5%), headache in 71 (62.8%), and weight loss in 48 (44%). Median body temperature at presentation was 37.9°C (IQR 37-38.5), and GCS score was 6 (IQR 5-6). Frequent neurological signs included altered mental status in 63 (55.8%), neck stiffness in 53 (46.9%), and motor weakness in 38 (33.6%). Another study conducted in Saudi Arabia the most common signs found by clinical examination were weakness (45%) followed by sensory impairment. 23% of the patients were reported to have encephalopathy and impaired level of consciousness. Documented fever upon presentation was found in 35% of patients but meningeal signs were uncommon and only found in 12% of them Tuberculin skin test was not performed routinely for our patients(26).

In this study CSF analysis was performed on 49 participants (37.69%), while 81 participants (62.31%) did not undergo this test. Regarding the GeneXpert test for CSF, 104 participants (80.00%) did not have it done, 6 participants (4.62%) were detected, and 20 participants (15.38%) were not detected. For sputum GeneXpert, 106 participants (81.54%) did not have the test, with 4 participants (3.10%) testing positive and 20 participants (15.38%) testing negative. A chest X-ray was conducted on 55 participants (42.31%), while 75 participants (57.69%) did not have one. Computed Tomography (CT) scans were performed on 44 participants (33.85%), with 86 participants (66.15%) not undergoing the procedure. Furthermore, 18 participants (13.85%) had a CT scan with contrast, while 26 participants (20.00%) did not. Magnetic Resonance Imaging (MRI) rarely performed, with 9 participants (6.90%) undergoing the scan, leaving 121 participants (93.10%) without one. Finally, in terms of HIV screening, 124 participants (95.38%) tested negative, whereas 6 participants (4.62%) tested positive. Different study done in Thailand A total of 114 patients Evidence of TB was as follows. CSF acid-fast bacilli were positive in only 1 of 101 specimens (1.0%). For CSF specimens, molecular assays and isolation of MTB were positive in 19 of 101 cases (18.8%) and 12 of 101 specimens (11.9%), respectively. Both molecular assays and isolation of MTB were positive in five patients. Twenty-two of 105 cases (21.0%) had positive blood culture for MTB. Chest radiography and chest CT were consistent with active pulmonary TB in 45 of 104 patients (43.3%) and 11 of 19 patients (57.9%), respectively. Sputum AFB and

isolation of MTB were positive in 16 of 90 specimens (17.8%) and 8 of 87 specimens (9.2%), respectively. Pulmonary TB was diagnosed in 56 cases (52.3%)(25).

Of 104 individuals (80.00%) were admitted to the ward, while 26 (20.00%) required intensive care unit (ICU) support. Complications occurred in 62 participants (47.69%), with the primary reasons for ICU admission being respiratory support (10.00%), sedation (3.10%), low Glasgow Coma Scale (GCS) scores (2.3%), and coma (4.62%). Regarding treatment, only 4 participants (3.08%) did not receive tuberculosis (TB) treatment, while 126 (96.92%) did. The initiation of drug therapy occurred in less than two weeks for 60 participants (46.2%). At discharge, 111 participants (85.38%) showed improvement, although there were 11 deaths (8.46%), and 3 referrals (2.31%). The GCS at discharge reflected positive outcomes, with 102 participants (78.5%) classified as mild, 18 (13.8%) as moderate, and 10 (7.7%) as severe. The mean length of hospital stay was 15.13 days (± 8.86). similar study done in Saudi Arabia, the Average hospital length of stay was 39 days. About a third of patients require Intensive Care Unit (ICU) admission with an average of 20 days spent in the ICU. Post discharge patients were followed in the outpatient clinics for at least 12 months. 68 patients (83%) had favorable outcome. 45 patients (55%) had complete or good recovery, and 23 patients (28%) had partial recovery. However, 12 patients (15%) had poor or no improvement. 2 patients (2%) lost their follow up. 30 day mortality rate was 8.5% (7 patients had died)(26). Different study done in different countries, the mortality rate of CNS-TB is high and 17.8% of patients died, which is comparable to other studies, Previous studies showed that poor outcome of CNS-TB was correlated with old age, neurological impairment at presentation, the presence of headache, fever or hydrocephalus, the presence of MTB in CSF, and delayed treatment(25,27–29).

In the multivariable logistic regression models, age, duration of drug initiation, and HIV status were statistically significant predictors of poor treatment outcomes for CNS TB. Age emerged as a critical risk factor, especially for those over 65 years, who faced a significantly increased risk of poor treatment outcomes (AOR 3.23, 95% CI 2.62-7.21, $p < 0.001$). Patients who initiated treatment after more than two weeks had poor treatment outcomes (AOR 4.56, $p < 0.001$), and those with reactive HIV tests faced a higher risk of poor treatment outcomes (AOR 2.66, $p = 0.002$). Similar study done in Thailand, age, confusion, and nausea/vomiting were associated with

definite CNS-TB (OR 0.96, 95% CI 0.93–0.99; $p = 0.015$, OR 2.86, 95% CI 1.03–7.94; $p = 0.044$, and OR 0.30, 95% CI 0.11–0.82; $p = 0.019$, respectively(25).

6.1 Conclusion

In this study, epidemiological and clinical findings related to Central Nervous System Tuberculosis (CNS TB) were evaluated among 130 participants. A significant majority of the participants were male, with an average age of around 43 years. Notably, classic symptoms such as headache, fever, and neck rigidity were predominant among patients, with severe neurological complications like seizures and cognitive impairments documented. The diagnosis of TB meningitis was the most common. However, a concerning 8.46% of cases resulted in death. Multivariable logistic regression analysis identified age, timing of drug initiation, and HIV status as significant predictors of poor treatment outcomes. Particularly alarming was the increased risk in patients over 65 years and those who delayed treatment.

6.2 Limitations of the Study

The study's cross-sectional nature limits the ability to establish causality between predictors and outcomes, making it challenging to draw definitive conclusions about temporal relationships. Data on history of substance use and TB contact may be subject to recall bias, as participants might not accurately remember or report past experiences. If conducted at a single center, the findings may not fully represent the broader population affected by CNS TB in different geographical or socioeconomic contexts. The study does not provide extended follow-up data, limiting insights into long-term outcomes and the sustained impact of treatment. Potential gaps in data collection regarding comorbidities and other health conditions could affect the interpretation of the results and the overall understanding of patient health status. The absence of a control group limits comparative analysis, making it difficult to assess the effectiveness of interventions relative to a baseline population.

6.3 Recommendations

Timely diagnosis and Treatment Initiation:

- ✓ Establish protocols to ensure early consideration of the diagnosis for appropriate patients and timely initiation of treatment, ideally up on diagnosis. This could include developing pathways to streamline diagnostic testing and treatment planning.

Training for Healthcare Providers:

- ✓ Provide training for healthcare practitioners on recognizing the early signs of CNS TB and the critical role of timely treatment in improving patient prognosis.

Research Initiatives:

- ✓ Promote further research into the pathophysiology of CNS TB, particularly among older adults and those with HIV, to develop specialized treatment protocols that could improve outcomes in these vulnerable populations

✓ .

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ANNEXES

Annex-1. Data extraction checklist

Patient Medical Record number_____

Part I: Socio-demographic factors

Number	Variables	Answers
1	Gender	1, Male 2, Female
2	Age/years	_____
3	Ethnicity	_____
4	Address	_____

Part II; Clinical characteristics and laboratory finding

Number	Variable/Question	Answer
1	Clinical presentation of CNS TB	1). Headache, fever, seizure 2). Focal neurologic deficit (A, CNs abnormality B, body weakness Abnormal body movement). 3)symptoms of Pulmonary TB 4.Other_____
2	Type of CNS TB diagnosed	1, TB meningitis 2, CNS tuberculomas 3, spinal TB 4.Other_____
3	Diagnosis method	1, brain imaging 2, CSF analysis and GeneXpert 3.Clinical diagnosis 3, Other supportive evidences
4	GCS at admission	
5	GCS At discharge	
6	CSF analysis done	1.yes 2.no
7	If yes to the above question	1.protien_____ 2.wbc_____(neutrophils%__lymphocytes %__) 3.glucose _____

		4.genexpert a. Detected b. Not detected 5.other_____
8	Sputum Smear result	1.Detected 2.Not detected 3.Not done
9	gene xpert result	1.detected 2.Not detected 3.not done
10	Known household TB contact history	1.Yes 2.No
11	If yes specify when	yy-mm--dd
12	TB treatment history	1.yes 2.no
13	If “Yes” to Q9 above, specify when_____	
12	What was the Duration between symptom onset and treatment initiation	_____
13	Serostatus for HIV	1, Positive 2, Negative 3 not done
	If yes to the above question answer question number 15 to 17	
14	what was the WHO clinical stage?	
15	What was the CD4 count (cell/mm ³)?	1, Yes 2, No
16	Viral Load (copies/mm ³)?	1.yes 2.no If yes specify which steroid
17	treatment given?	
18	History of cough?	1, Yes 2, No
19	History of Chronic Liver Disease?	1, Yes 2, No

20	History of heart failure?	1, Yes 2, No
21	History of Diabetes Mellitus?	1, Yes 2, No
22	Use of steroid	1.yes 2.no
23	If yes to q19 specify which steroid was used	

Part III. Behavioral factors

Number	Variable	Answer
1	Cigarette smoking history?	1.yes 2.no
2	If yes to Q1 quantify the amount?	
3	Any Drug use?	
4	Alcohol Use History?	1.Yes 2.no
5	If yes to Q4 specify the amount	

Part IV. Prognosis and outcome at discharge

Number	Variables	Answer
1	What was the Length of hospital stay in days?	_____
2	What was the Outcome after diagnosed with CNS TB?	1, Discharged with improvement 2, Left against medical advice 3, Died 4,others(disappeared, transferred)
3.	If died what was cause of death	_____

4	What was Treatment given?	1, Anti TB drugs 2, Additional drugs_____
5	what complications were there?	1.Stroke 2.hydrocephalus 3.seizure 4.vision impairment 4.others_____
6	Functional status at discharge (mRS score)	1.0-2 2.3-5 3.6

ANNEX 2: DECLARATIONS

DECLARATION INVESTIGATOR

I undersigned resident, declare that this thesis is my original work, has never been conducted in the study area, and that all the resources and materials used for the research have been duly acknowledged.

Investigator: _____

Signature _____

Date _____

DECLARATION ADVISORS

We the undersigned Advisors declare that this research is our original work in partial fulfillment of the requirement for a specialty certificate in internal medicine for the above resident to our best knowledge. We confirmed that this thesis is ready for defense with our approval as the university advisors.

Name of primary advisor

Dr. Sebona Girma (M.D, Assistant professor of internal medicine)

Date _____ Signatures _____

Name of secondary Advisor

Dr. Abay Burusie ((PHD, Assistant Professor Public Health)

Date _____ Signatures _____

Department Head

Dr. Wubshet Abraham (M.D, Assistant professor of internal medicine)

Date _____ Signatures _____