SCHOOL OF GRADUATE STUDIES

TREATMENT OUTCOME OF MENINGITIS AND ITS ASSOCIATED FACTORS AMONG NEONATES ADMITTED IN PUBLIC HOSPITALS AT HARAR TOWN, EASTERN ETHIOPIA

MSc Thesis

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TREATMENT OUTCOME OF MENINGITIS AND ITS ASSOCIATED FACTORS AMONG NEONATES ADMITTED IN PUBLIC HOSPITALS AT HARAR TOWN, EASTERN ETHIOPIA

A Thesis Submitted to the College of Health and Medical Sciences, School of Graduate Studies, Haramaya University, in Partial Fulfillment of the Requirements for the Degree of Master's in Clinical Pharmacy.

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APPROVAL SHEET

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I hereby certify that I have read and evaluated the thesis entitled "**Treatment Outcome of Meningitis and Its Associated Factors among Neonates Admitted in Public Hospitals at Harar Town, Eastern Ethiopia**" prepared under my guidance by **Getahun Tamiru**. I recommend that it be submitted as fulfilling the thesis requirement.

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LIST OF ABBREVIATIONS AND ACRONYMS

CSF	Cerebrospinal Fluid
E. coli	*Escherichia coli*
GBS	Group B Streptococcus
GBD	Global Burden of Disease
HFCSUH	Hiwot Fana Comprehensive Specialized University Hospital
IHRERC	Institutional Health Research Ethics Review Committee
JGH	Jugal General Hospital
NICUs	Neonate Intensive Care Units
PI	Principal Investigator
S. aureus	*Staphylococcus aureus*
UK	United Kingdom
VIF	Variance Inflation Factor

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ABSTARCT

Background: Meningitis in neonates significantly burdens public health in low- and middle-income countries. However, data on treatment outcomes and factors contributing to poor prognosis are scarce. This study aimed to assess treatment outcomes of meningitis and associated factors among neonates treated at public hospitals in Harar, eastern Ethiopia.

Methods: A facility-based cross-sectional study was conducted involving 506 neonates who received treatment between October 1, 2020, and October 31, 2024, at Hiwot Fana Comprehensive Specialized University Hospital and Jugal General Hospital. Data were obtained from medical records. Treatment outcomes were classified as "good" or "poor." Both binary and multivariate logistic regression analyses were performed to identify factors associated with poor treatment outcomes. A P-value of less than 0.05 and an adjusted odds ratio with a 95% confidence interval were utilized to establish statistical significance.

Results: One hundred sixty-nine (33%) neonates had experienced poor treatment outcomes. Delivered by vacuum (AOR=3.06, 95% CI: 1.03 to 9.05), positive culture of cerebrospinal fluid (AOR=3.53, 95% CI: 1.45 to 8.57), cerebrospinal fluid protein more than 400 mg/dl at admission (AOR=17.9, 95% CI: 7.95 to 40.3), cerebrospinal fluid glucose less than 10 mg/dl at admission (AOR=3.89, 95% CI: 1.55 to 9.77), seizure at admission (AOR=5.6, 95% CI: 2.78 to 11.4), seizures during hospitalization (AOR=14.4, 95% CI: 5.85 to 35.2), presences of early onset neonatal sepsis (AOR=3.5, 95% CI: 1.49 to 8.20), and predisposition to congenital hydrocephalus (AOR=4.73, 95% CI: 1.46 to 15.2) were factors associated with poor outcome of treatment.

Conclusion: The study found that approximately 33% of newborns with meningitis experienced poor treatment outcomes. Epilepsy and hydrocephalus were the most commonly observed neurological sequelae. Several factors were associated with poor outcomes, including congenital hydrocephalus, vacuum-assisted delivery, positive cerebrospinal fluid culture, seizures, elevated cerebrospinal fluid protein with low glucose, and co-occurrence with early-onset neonatal sepsis.

Keywords: associated factors; treatment outcome; meningitis; neonates; eastern Ethiopia

1. INTRODUCTION

1.1. Background

Meningitis is a central nervous system infection that can cause inflammation in the subarachnoid space of the brain and spinal cord (WHO, 2025). It is usually caused by infectious agents, such as bacteria, viruses, fungi, and parasites (Kliegman, 2016; WHO, 2025). Newborns are at a high risk for meningitis due to their immature immune systems (Bedetti *et al.*, 2023; Bundy, 2023). It can be classified as early-onset (≤72 hours) or late-onset (>72 hours) based on the time of infection occurring after birth (Ku *et al.*, 2015; Bundy, 2023).

Pathogens causing neonatal meningitis differ depending on the neonate's gestational age at birth, age at presentation, and geographic location (Bundy, 2023). In early-onset meningitis, Group B Streptococcus (GBS) and *Escherichia coli (E. coli*) are the most prevalent pathogens (Aleem and Greenberg, 2019; Mashau *et al.,* 2022; Bedetti *et al.*, 2023; Zúñiga *et al.*, 2023; Lee *et al.*, 2024). The pathogens of late-onset meningitis vary depending on gestational weeks, birth weight, and setting (Bundy, 2023). GBS and *E. coli* are prevalent pathogens among neonates that develop meningitis in the community (Giannoni *et al.*, 2018; Chauhan, 2020; Wong *et al.*, 2021). Staphylococci, *Staphylococcus aureus (S. aureus),* and Klebsiella are prevalent pathogens among neonates that develop meningitis in the healthcare setting (Wu *et al.*, 2017; Giannoni *et al.*, 2018; Lee *et al.*, 2024).

Globally, the incidence rate and mortality rate of neonatal meningitis were 854·8 (609.2-1183.3) and 137.2 (109.5-177.8) per 100,000 population, respectively, in 2019 (Wunrow *et al.*, 2023). Developed countries have reported lower incidences and mortality rates of neonatal meningitis, 0.3- 0.4 per 1,000 live births and 2%-10%, respectively (Sturgeon *et al.,* 2018; Mashau *et al.,* 2022; Ou-Yang *et al.*, 2023; Zúñiga *et al.*, 2023). However, incidence and mortality rates of neonatal meningitis are higher in developing countries, 0.5-6 per 1,000 live births and 20-37%, respectively (Thaver and Zaidi, 2009; Mwaniki *et al.*, 2011; Kumar *et al.*, 2018; Xu *et al.*, 2019; Guillén-Pinto *et al.*, 2020; Ikumapayi *et al.*, 2022; Mashau *et al.*, 2022).

Incidence and mortality rates of meningitis are high in Sub-Saharan Africa, a region referred to as the “meningitis belt” (Wunrow *et al.,* 2023). For example, the incidence rate of neonatal meningitis in Kenya was 96 per 1000 live births (Mwaniki *et al.,* 2011). The mortality rate is reported as 24% in Angola, 29.4% in Tanzania, and 37% in the Gambia (Pelkonen *et al.,* 2020; Ikumapayi *et al.,* 2022; Pishori *et al.,* 2023). According to a systematic analysis of the Global Burden of Disease, Ethiopia has the third-highest meningitis fatality rate (Joseph e*t al.,* 2018). Studies done at Gondar Comprehensive Specialized Hospital and Tikur Anbessa Specialized Hospital, Ethiopia, show a 1.73% and 4.7% prevalence of neonatal meningitis, respectively (Melese Abate and Tamrat Zeleke, 2016; Sirak Biset *et al.,* 2021).

Globally, among neonates who survive meningitis, 20–50% develop different neurological sequelae, such as hearing loss, blindness, epilepsy, hydrocephalus, subdural empyema, and psychomotor developmental delay (Lin *et al.,* 2012; Rodenburg-Vlot *et al.,* 2016; Gordon *et al.,* 2017; El Tahir *et al.,* 2019; Ou-Yang *et al.,* 2023; Sampe *et al.,* 2024).

The factors predicting a poor prognosis of meningitis among neonates include seizures, high protein levels in the cerebrospinal fluid (CSF), low birth weight or preterm birth, early onset of meningitis, and low CSF glucose levels (Mao *et al.,* 2018; Ou-Yang *et al.,* 2023; Sampe *et al.,* 2024).

1.2. Statement of the problem

Globally, the number of deaths under 5 years has reduced from 112.7 million in 1990 to 52.2 million in 2019, but the mortality of neonates remains high (UNICEF, 2019). A systematic review of the GBD data shows that meningitis mortality around the globe dropped by 21% between 1990 and 2016, from 403,012 to 318,400. However, the incidence rose from 2.5 million in 1990 to 2.82 million in 2016 in low-income countries with still higher mortality and incidence rates (Joseph *et al.,* 2018).

Meningitis is a deadly and debilitating disease; it strikes quickly, causes serious health, economic, and social consequences, and affects people of all ages in every part of the world, particularly neonates (WHO, 2024). Mortality of neonates from meningitis has varied from 10% in high-income countries to 58% in low-income countries (Furyk *et al.,* 2011). Survivors develop neurological and neurocognitive sequelae, such as hearing loss, focal neurological deficits, or memory impairment, which vary by geography from 9.4% in Europe to up to 21% and 25% in

Southeast Asia and Africa, respectively (Trotter *et al.,* 2017). A study done by Ouchenir *et al.* (2017) in Canada indicated a 7% mortality rate and a 74% morbidity rate among neonates diagnosed with meningitis. Similarly, Taiwan reported 10.3% mortality and 77.8% neurological complications (Lee *et al.*, 2024). However, a study done in India reported that neonatal meningitis has a terrible prognosis, with 29.1% of cases of mortality (Barik *et al.*, 2022).

Between 1990 and 2019, Sub-Saharan Africa was the only region in the world that did not reduce newborn death rates, ensuring the Sustainable Development Goal survival target of less than 12 deaths per 1000 live births unlikely to be realized by 2030 (Liu *et al.*, 2012; UNICEF, 2019). Neonatal meningitis affects 0.1–0.4 newborns/1000 live births, but higher incidences have been reported in low-income countries (Gordon *et al.,* 2017). For example, 24% mortality was reported in Angola (Pelkonen *et al.*, 2020), 37% in Gambia (Ikumapayi *et al.,* 2022), and 24.9% in Tanzania (Pishori *et al.,* 2023). In Ethiopia, a sub-Saharan African country, which is approximately 3.7 to 33.6% of children lost their lives due to meningitis (WHO, 2021). However, there is a lack of evidence that shows the mortality and morbidity rates of neonatal meningitis in Ethiopia.

A systematic study shows that the global costs of newborn meningitis range from $222 to $33,635, which have only been estimated based on healthcare expenses (Salman *et al.*, 2020). Similarly, the median cost lost for patients with bacterial meningitis in Ethiopia was 98,812 ETB (Ethiopian Birr) (US$ 3,593.2) (Temesgen Kabeta *et al.*, 2022).

Despite the higher mortality and morbidity of neonatal meningitis in low-income countries, studies reporting the treatment outcomes and factors associated with poor prognosis have been limited, particularly in Ethiopia. Moreover, the predictors of poor prognosis may differ from place to place.

In Ethiopia, researchers have conducted numerous studies on the prevalence, etiology, treatment, and burden of neonatal meningitis (Ayele Gebremariam, 1998; Abenet Tassew, 2015; Melese Abate and Tamrat Zeleke, 2016; Sirak Biset *et al.,* 2021; Musa Mohammed, 2024). In researcher knowledge, there is just one study on the treatment outcomes and factors associated with poor treatment outcomes among newborns with meningitis in Ethiopia, (Habeneyom Tebeja, 2020). However, the study does not represent the broader population of newborn meningitis because of inadequate sample size. Additionally, there is a scarcity of studies on treatment outcomes and factors associated with poor treatment outcomes in the study area. This study is required to bridge this gap. Therefore, this study aimed to assess the treatment outcomes of neonatal meningitis and its associated factors.

1.3. Significance of the study

The findings of this study may help local health bureaus implement effective strategies, raise awareness, and promote best practices to improve treatment outcomes of neonatal meningitis. This study may help HFCSUH and JGH to allocate resources more effectively, ensuring adequate staffing, equipment, and training are available to manage neonatal meningitis. Also, it may assist healthcare providers in the neonate intensive care units (NICU) at Hiwot Fana Comprehensive Specialized University Hospital (HFCSUH) and Jugal General Hospital (JGH) in reducing morbidity and mortality rates among neonates with meningitis. This study identified the factors associated with poor prognosis to improve the lives of neonates affected by meningitis at HFCSUH and JGH. Additionally, it could serve as a baseline for another researcher to investigate the underlying cause of death and disability in newborn meningitis.

1.4. Objectives

1.4.1. General objective

To assess the treatment outcomes of meningitis and its associated factors among neonates admitted between October 1, 2020, and October 31, 2024, at Public Hospitals in Harar Town, Eastern Ethiopia.

1.4.2. Specific objectives

- To assess the treatment outcomes of meningitis among neonates
- To identify factors associated with poor treatment outcomes of meningitis among neonates

2. LITERATURE REVIEW

2.1. Treatment outcome of neonatal meningitis

A retrospective review conducted at Texas Children's Hospital, USA, between 2010 and 2017 reported an overall mortality of 2% (14/547) among neonates with meningitis, with nearly all deaths occurring in patients with bacterial meningitis (13/14, 93%). Specifically, mortality rates were 10% for Group B Streptococcus (GBS) (6/60), 25% for *Staphylococcus aureus* (2/8), and 5% for *Escherichia coli* (2/37) (Erickson *et al.*, 2021). Similarly, a multicenter retrospective study in Hong Kong, China, reported a 2% (4/200) mortality rate for neonatal meningitis in 2020 (Wong *et al.*, 2021). Another retrospective cohort study conducted in China from 2013 to 2018 showed a 4.2% (11/256) mortality rate, with 62.9% of neonates experiencing a poor prognosis. Among these neonates with poor outcomes, 79.4% developed permanent neurological sequelae, including developmental delay (70%), secondary epilepsy (20%), cerebral palsy (7%), and visual and hearing impairments (18.6%) (Li *et al.*, 2022).

A retrospective cohort study conducted in Canada between 2013 and 2014 reported a 7% (8/113) mortality rate among neonates with meningitis. Among survivors, 72.4% developed sequelae, including motor deficits (spasticity or paresis) (17%), seizure disorders (8.8%), developmental delay (8.8%), and hearing loss (4.4%) (Ouchenir *et al.*, 2017). Similarly, a retrospective cohort study conducted in Taiwan from 2003 to 2020 at two medical centers reported a 6.9% mortality rate among 116 neonates with bacterial meningitis. During hospitalization, 77.6% of patients developed neurological complications, including subdural effusion (49%), seizures (44.8%), ventriculomegaly (41.4%), hydrocephalus (20%), and brain infarctions (8.6%), while 41.6% had persistent neurological sequelae at discharge (Ou-Yang *et al.*, 2023). Additionally, prospective surveillance studies conducted in the UK and Ireland between 2010 and 2012 reported an 8% (25/329) mortality rate for proven neonatal bacterial meningitis, with higher fatality for pneumococcal meningitis (19%, 5/26) compared to GBS meningitis (5%, 7/135) (Okike *et al.*, 2014).

A retrospective cohort study conducted in Taiwan between 2003 and 2020 reported a 10.3% mortality rate among neonates with bacterial meningitis, with 77.8% developing neurological complications during hospitalization, including ventriculomegaly (38.1%), seizures (34.9%), subdural effusion (33.3%), hydrocephalus (18.3%), and brain infarction (1.6%) (Lee *et al.*, 2024).

Similarly, a multicenter descriptive study in Medellin, Colombia, in 2020 reported a 9.5% (4/42) mortality rate from confirmed neonatal bacterial meningitis (Zúñiga *et al.,* 2023). In contrast, higher mortality rates have been reported in other settings: a cross-sectional study in Iran demonstrated 36% mortality among 468 neonates admitted to the NICU at Ghaem Hospital, Mashhad (Boskabadi *et al.*, 2020), while a 1-year observational study in India in 2021 reported 29.1% (16/55) mortality (Barik *et al.*, 2022). Another prospective observational study in India in 2017 showed 11.2% (10/89) mortality, with 30.4% (24/79) of survivors developing neurological sequelae at discharge, and 22% (13/59) exhibiting a low developmental quotient at 3-month follow-up (Kumar *et al.*, 2018). Additionally, a multicenter retrospective study in Turkey reported a 23.5% mortality rate among 634 confirmed cases of neonatal meningitis (Oncel *et al.,* 2024).

Several studies from Africa have reported high mortality rates from neonatal meningitis. A retrospective study conducted in Tunisia between 1990 and 2012 among 55 neonates showed a 40% mortality rate, with 16.4% of survivors developing sequelae (Kamoun *et al.,* 2015). Similarly, a surveillance study in The Gambia reported 37% (10/27) mortality among infants less than two months of age (Ikumapayi *et al.* 2022). In Nigeria, a prospective cohort study (1990–1995) demonstrated a 24.6% mortality rate among 69 neonates with bacterial meningitis. Of the 40 survivors, 22.5% (9/40) developed neurological sequelae, including sensorineural hearing loss (3 cases), hydrocephalus (2), subdural effusion (2), hemiparesis (1), and seizures (1), while 33 survivors showed reduced developmental quotients at 24-month follow-up (Airede *et al.,* 2008). In Angola, a prospective observational study in 2017 reported 24% (33/135) mortality (Pelkonen *et al.,* 2020). Similarly, a prospective cross-sectional study in Tanzania in 2015 found a 29.4% (37/126) mortality rate (Pishori *et al.*, 2023). By contrast, a retrospective cohort study conducted in Tunisia between 1996 and 2010 reported a lower mortality rate of 15.9% (7/44), though 21.6% of survivors developed neurological sequelae (Hamouda *et al.*, 2013).

2.2. Factors associated with treatment outcomes

2.2.1. Socio-demographic factors

Several studies have identified neonatal and perinatal factors associated with poor prognosis in neonatal bacterial meningitis. A retrospective cohort study conducted in Tunisia between 1996 and 2010 found that prematurity ($p = 0.01$) and low birth weight ($p = 0.001$) were significantly associated with poor outcomes among 44 neonates with bacterial meningitis (Hamouda *et al.*, 2013). Similarly, a prospective cohort study in Nigeria (1990–1995) identified low birth weight and lack of exposure to antenatal steroids as predictors of poor treatment outcomes among 69 neonates with meningitis (Airede *et al.,* 2008). Systematic reviews from developing countries have consistently highlighted low birth weight and prematurity as major risk factors for adverse outcomes (Furyk *et al.,* 2011). Moreover, a 2018 systematic review confirmed that low birth weight is a significant predictor of poor prognosis in neonatal meningitis (Mao *et al.*, 2018).

2.2.2. Clinical factors

Several clinical and laboratory factors have been identified as predictors of poor prognosis in neonatal bacterial meningitis. A retrospective cohort study in Taiwan (1984–2008) among 143 neonates found that a CSF protein level greater than 500 mg/dL at admission [OR: 171.18, 95% CI: 25.6–1000], congenital heart disease [OR: 48.96, 95% CI: 6.06–395.64], hearing impairment during hospitalization [OR: 23.40, 95% CI: 3.62–151.25], and seizures at admission or during hospitalization [OR: 10.10, 95% CI: 2.11–48.32] were significantly associated with poor outcomes (Lin *et al.*, 2012). Similarly, two retrospective cohort studies in Taiwan (2003–2020) reported that seizures at onset [OR: 2.40–2.45, $p < 0.05$] and early-onset sepsis [OR: 3.35–3.38, $p < 0.05$] were predictors of poor prognosis (Ou-Yang *et al.,* 2023; Lee *et al.,* 2024). Prospective surveillance in the UK and Ireland (2010–2012) also found that pneumococcal meningitis, compared with other pathogens, was significantly associated with higher mortality among 329 confirmed cases (Okike *et al.,* 2014).

Other studies have highlighted additional clinical indicators of poor outcomes. In China, the presence of meconium-stained amniotic fluid was associated with poor prognosis [OR: 2.31, 95% CI: 1.09–5.17; $p < 0.017$] among 256 neonates (Li *et al.,* 2022). In India, a prospective observational study (2017) among 89 neonates identified prolonged shock [OR: 8.28, 95% CI: 2.1–32.54; $p = 0.001$], seizures [OR: 14, 95% CI: 1.3–21.8; $p = 0.012$], coma [OR: 4.3, 95% CI: 1.73–10.71; $p = 0.001$], and abnormal electroencephalography [OR: 9.6, 95% CI: 3.08–29.85; $p = 0.00$] as predictors of poor short-term outcomes (Kumar *et al.,* 2018). Similarly, a Canadian retrospective cohort study (1979–1998) found that seizures, coma, the use of inotropes, and leukopenia were associated with poor outcomes (Klinger *et al.* 2000).

Systematic reviews support these findings, showing that early-onset meningitis, positive CSF culture, seizures, and elevated CSF protein levels significantly predict poor prognosis (Mao *et al.,* 2018). A prospective cohort study (1990-1995) done in Nigeria demonstrates respiratory distress requiring invasive ventilator support, hypotension requiring inotropes, and the presence of concomitant sepsis as a predictor for poor treatment outcomes from sixty-nine cases of neonatal bacterial meningitis (Airede *et al.,* 2008). Similarly, a retrospective study done in Tunisia demonstrated shock (p=0.02), respiratory distress (p=0.001), and pleocytosis (p=0.05) of less than 500 cells/ mm3 as associated factors for a poor prognosis among 44 neonatal bacterial meningitis cases (Hamouda *et al.,* 2013).

2.2.3. Treatment regimen factors

A retrospective cohort study in Canada (1979–1998) among 101 neonates found that the use of inotropes was significantly associated with poor outcomes (Klinger *et al.* 2000). Similarly, a retrospective cohort study in Taiwan (2003–2020) among 112 neonates reported that the requirement for surgical intervention was associated with poor outcomes [OR: 3.34, 95% CI: 1.78–6.86; $p < 0.001$] (Ou-Yang *et al.,* 2023). In India, a prospective observational study in 2017 among 89 neonates found that the use of mechanical ventilation [OR: 18.55, 95% CI: 3.86–89.01; p = 0.00], prolonged orogastric feeding for more than 3 days [OR: 2.78, 95% CI: 1.01–7.59; p = 0.042], and abnormal electroencephalography [OR: 9.6, 95% CI: 3.08–29.85; p = 0.00] were significant predictors of poor short-term outcomes (Kumar *et al.,* 2018).

2.3. Conceptual framework

Multiple factors have been associated with poor treatment outcomes in neonatal bacterial meningitis. These include neonatal characteristics such as low birth weight and gestational age, pre-existing medical conditions (e.g., congenital abnormalities), and maternal health factors (e.g., infections during pregnancy). Clinical factors such as the duration of symptoms before treatment, presentation at diagnosis, severity of illness, and supportive care measures, including nutrition and management of complications, also play a role. Laboratory and diagnostic indicators, including blood tests, cerebrospinal fluid parameters, type of pathogen, and specific isolated organisms, as well as aspects of antimicrobial therapy such as timing of initiation and choice of agents, have been linked to adverse outcomes.

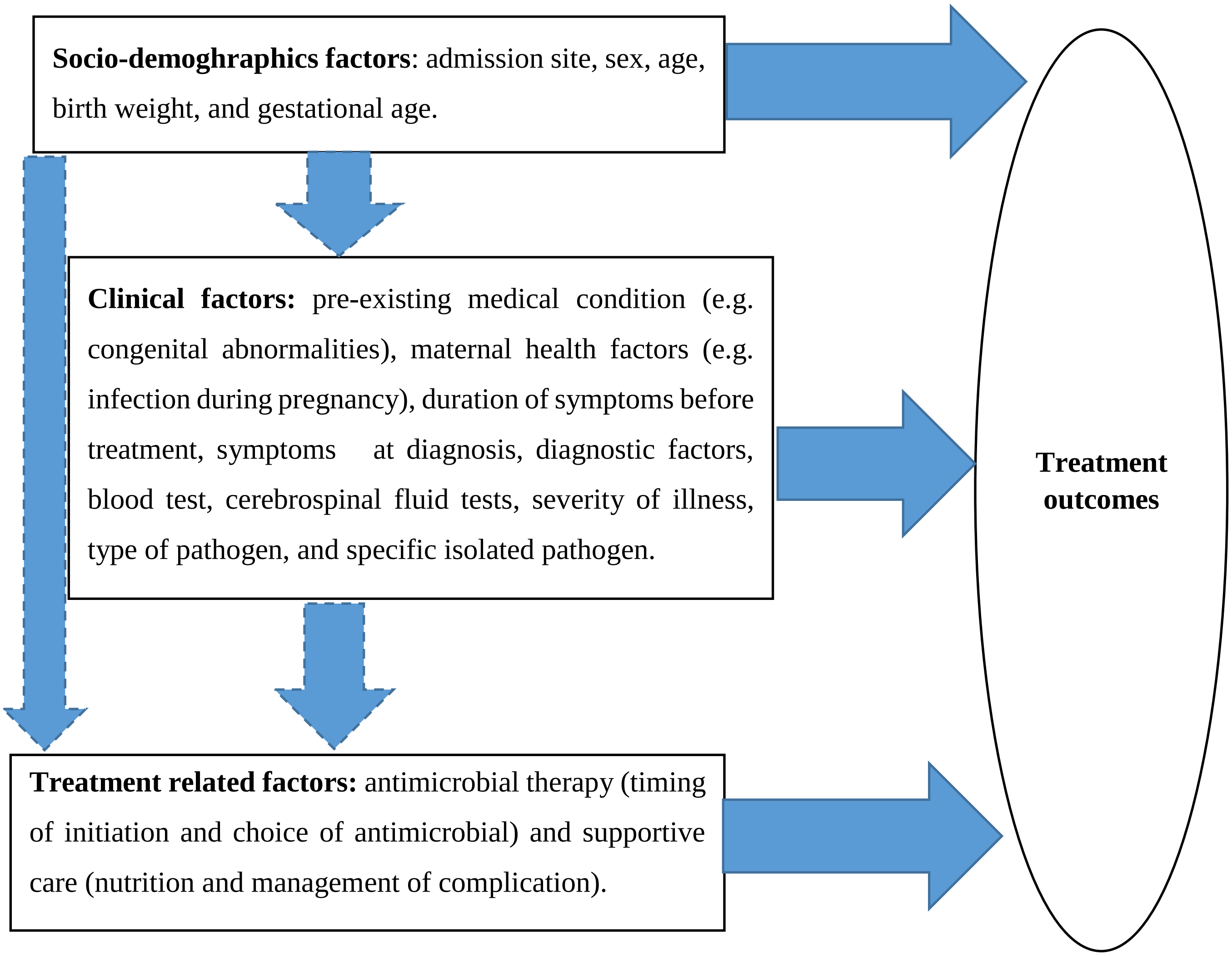

Figure 1: Conceptual framework developed after searching different literature by the principal investigators.

3. METHODS AND MATERIALS

3.1. Study area and period

This study was conducted at two public hospitals in Harar, eastern Ethiopia: Hiwot Fana Comprehensive Specialized University Hospital (HFCSUH) and Jugal General Hospital (JGH). Harar is the capital of the Harari regional state, located approximately 500 kilometers from Addis Ababa, the national capital. The region comprises nine woredas, which include 36 kebeles, 19 urban and 17 rural.

Harar has four hospitals: three governmental (two public and one military) and one private hospital. Additionally, the city has eight public health centers, 32 health posts, 13 non-profit private clinics, and 15 profit-making private clinics. HFCSUH was established in 1948 and became a university-specialized hospital in 2010, while JGH was founded in 1909. Both hospitals have medical, pediatric, surgical, gynecology, and obstetrics wards and provide services including neonatal care, gynecology, ophthalmology, dentistry, adult and pediatric outpatient services, and chronic follow-up care (HMIS of HFCSUH and JGH, 2024). The study was conducted from February 10 to March 20, 2025.

3.2. Study design

A cross-sectional study design was employed in this study.

3.3. Population

3.3.1. Source of population

All medical records of neonates admitted with meningitis in HFCSUH and JGH were the source of the population.

3.3.2. Study of population

All medical records of neonates admitted to the NICUs of HFCSUH and JGH with a diagnosis of meningitis between October 1, 2020, and October 31, 2024, were included.

3.4. Inclusion and exclusion criteria

3.4.1. Inclusion criteria

Neonates under 28 days of age admitted with meningitis from October 1, 2020, to October 31, 2024, were eligible for inclusion.

3.4.2. Exclusion criteria

- Incomplete medical records (i.e., diagnosis, treatment regimen, and discharge summary)
- Neonates discharged against medical advice.
- Neonates discontinued their treatment within 72 hours.
- Neonates referred to another institution.

3.5. Sample size determination

Single- and double-population proportion formulas were applied to determine the sample sizes for the dependent variable and for associated factors, respectively. For the treatment outcome, the sample size was calculated based on the following assumptions: a 95% confidence interval, a 5% margin of error, and a 20.7% proportion, as reported in a study conducted at Tibebegion Comprehensive Specialized Hospital in Bahir Dar, Ethiopia (Habeneyom, 2020).

$$\text{So } n = \frac{(1.96)^2 (1-0.207)*0.207}{(0.05)^2} = \frac{0.630}{0.0025} = 252$$

To calculate the sample size for associated factors, consider these assumptions: a 95% confidence interval, a 5% margin of sampling error tolerated, and an 80% power.

Table 1: Sample size calculation for associated factors of neonatal meningitis in public hospitals at Harar town, Eastern Ethiopia, from February 10 to March 31, 2025.

Factors	**% of unexposed with outcome**	**Odd ratio**	**Z a/2**	**The ratio of unexposed to exposed**	**Sample size**	**References**
Seizure	9.6	10.1	1.96	10.4	110	(Weldegerima *et al.*, 2023)
Preterm	28.9	2.28	1.96	3	254	(Habtamu *et al.*, 2023)
Early-onset sepsis	4.26	4.26	1.96	14.7	482	(Ogundare *et al.*, 2019)
Prolonged shock	40	8.28	1.96	0.3	42	(Kermorvant-Duchemin *et al.*, 2008)
Mechanical ventilation	64.5	18.55	1.96	0.4	40	(Gurubacharya *et al.*, 2011)
Congenital heart disease	22	48.9	1.96	9.4	38	(Sasikumar *et al.*, 2023)

The larger sample size obtained from the single- and double-population proportion calculations was taken as the final value. The sample size for early-onset sepsis was chosen since it provided a larger sample size. After adding 5% to account for possible incomplete records, the final sample size was 506. Finally, 506 medical records of neonates were reviewed.

3.6. Sampling technique and procedure

Representatives from each institution were selected using a simple random sampling technique. First, patient register numbers were obtained from the logbooks. These numbers were then entered into Microsoft Excel, and a lottery method was applied to select the required records. The sample size was proportionally allocated between Hiwot Fana Comprehensive Specialized University Hospital (HFCSUH) and Jugal General Hospital (JGH) based on the number of neonates admitted with meningitis during the study period (HFCSUH = 725; JGH = 321). Accordingly, 351 records were selected from HFCSUH and 155 from JGH.

3.7. Data collection methods

3.7.1. Data collection instruments

A structured data collection tool was prepared in English, based on a review of relevant literature. It comprised closed-ended questions covering socio-demographic characteristics, clinical conditions, and treatment-related factors.

3.7.2. Data collectors and supervisors

Four clinical pharmacists collected the data under the supervision of the principal investigator.

3.7.3. Data collection procedure

Data were collected through a review of patients' medical records. First, the register logbooks of neonates admitted to the wards at HFCSUH and JGH between October 1, 2020, and October 31, 2024, were used to obtain the list of records. The corresponding medical records were then retrieved from the card rooms of both hospitals. After verifying completeness, all relevant information was extracted from the eligible medical records.

3.8. Variables

3.8.1. Dependent variable

- Treatment Outcomes (Good and Poor)

3.8.2. Independent variables

- **Socio-demographic factors**: admission site, sex, age, birth weight, and gestational age.
- **Clinical factors:** pre-existing medical condition (congenital heart defects, down syndrome, congenital hydrocephalus), maternal health factors (complication during deliver (history of PROM, meconium stain in amniotic fluid, chroinammionitcs) and mode of deliver (spontaneous vaginal delivery, C/S, assisted by vacuum), symptoms at diagnosis, blood test, cerebrospinal fluid tests, type of pathogen, and specific isolated pathogen.
- **Treatment-related factors:** antimicrobial therapy (choice of antimicrobial) and supportive care (nutrition and management of complications).

3.9. Operational definitions

- **Confirmed meningitis:** Defined as meningitis in which the causative pathogen is isolated from a primary cerebrospinal fluid (CSF) culture, along with clinical manifestations such as fever, seizures, thermal instability, or poor feeding (MS, 2010; Li *et al.*, 2022).
- **Suspected meningitis:** Defined as meningitis with a negative or absent CSF culture, but in which CSF findings fulfill diagnostic criteria. These include leukocyte counts $>32/mm^3$ in term neonates or $>29/mm^3$ in preterm neonates, glucose levels <34 mg/dl in term neonates or <24 mg/dl in preterm neonates, and protein levels >170 mg/dl in term neonates or >150 mg/dl in preterm neonates (MS, 2010; Li *et al.,* 2022).
- In this study, treatment outcomes were categorized as **good** if neonates recovered or improved and were discharged without complications, and as **poor** if they died during hospitalization, were discharged with complications, or showed no improvement.
- **Neurological complication:** Any condition secondary to meningitis, including seizures, subdural effusion, brain abscess, hearing loss, hydrocephalus, and subdural empyema.

3.10. Data quality control

Before data collection, a counter-check was done on 5% of the sample size at Haramaya General Hospital, and the tool was modified as needed. Appropriate orientation was given to the data collectors on the data abstraction tool and the objective of the data, before starting data collection. Data was checked during collection and before processing to ensure completeness and consistency.

3.11. Methods of data analysis

Data were entered into Epi Info version 7.2.6 to ensure consistency and completeness, then exported to SPSS version 26 for analysis. Descriptive statistics were summarized using frequencies and percentages for categorical variables, and the mean with standard deviation for continuous variables. A binary logistic regression model was employed to examine the independent effect of each variable on treatment outcomes. Variables with a p-value < 0.25 in the bivariate analysis were included in the multivariate logistic regression model to identify independent predictors. A p-value < 0.05 was considered statistically significant. The Hosmer-Lemeshow test was used to assess the goodness-of-fit of the logistic regression model, yielding a P-value of 0.53, which indicated that the model was well-fitted. Multicollinearity among independent variables was evaluated using the variance inflation factor (VIF), which was 1.74, suggesting minimal correlation. Associations between dependent and independent variables were reported using crude odds ratios (COR) and adjusted odds ratios (AOR) with 95% confidence intervals. Data were ultimately presented using tables, graphs, and pie charts.

3.12. Ethical considerations

Ethical clearance was obtained from the Institutional Health Research Ethics Review Committee (IHRERC) of the College of Health and Medical Sciences (Reference No. IHRERC/041/2025). Cooperation letters were submitted to HFCSUH and JGH from the School of Pharmacy and the College, respectively. Data collection commenced only after receiving permission from each institution. Ethical standards were strictly maintained throughout the study. Patient privacy and confidentiality were ensured, and no personal identifiers were recorded.

3.13. Plan for dissemination of the findings

The results of this study will be presented to the School of Pharmacy, College of Health and Medical Sciences, Haramaya University, and copies will be provided to HFCSUH, JGH, and the Harari Health Bureau. Additionally, the findings of this study will be disseminated within the scientific community through publication.

4. RESULT

4.1. Socio-demographic characteristics of patients

This study included 506 neonates with meningitis admitted to the NICUs of HFCSUH (n = 351) and JGH (n = 155). Of these, 278 (54.9%) were male, resulting in a male-to-female ratio of 1.22:1. The majority of patients were early neonates (<7 days old), with a mean age of 8.91 ± 5.92 days (Table 2).

Table 2. Socio-demographic characteristics of neonates admitted with meningitis at public hospitals in Harar town, Eastern Ethiopia, from February 10 to March 20, 2025 (n = 506).

Variable	Category	Frequency	Percent
Site of admission	HFCSUH	351	69.4
	JGH	155	30.6
Sex	Female	228	45.1
	Male	278	54.9
Age (days)	<7	270	53.4
	7-28	236	46.6

HFCSUH: Hiwot Fana Compressive Specialized University Hospital; JGH: Jugal General Hospital

4.2. Neonatal and maternal characteristics of health

In this study, 181 (36.2%) neonates had sepsis at admission. Among these, 116 (22.9%) were diagnosed with early-onset neonatal sepsis, and 65 (12.8%) with late-onset neonatal sepsis. The mean birth weight and gestational age of neonates with meningitis were 3099 ± 393 grams and 36.9 ± 1.13 weeks, respectively. A total of 69 (13.6%) neonates had low birth weight (<2500 g), and 130 (25.7%) were preterm (gestational age <37 weeks). Forty-two (8.3%) neonates presented with pre-existing medical conditions. Most neonates, 314 (62.1%), were delivered via spontaneous vaginal delivery. Pregnancy complications were reported in 119 (23.5%) mothers, including premature rupture of membranes (PROM) in 71 (14%), eclampsia in 31 (6.1%), chorioamnionitis in 11 (2.2%), and meconium-stained amniotic fluid in 6 (1.2%) (Table 3).

Table 3. Neonatal and maternal health characteristics among neonates admitted with meningitis at public hospitals in Harar town, Eastern Ethiopia, from February 10 to March 20, 2025 (N = 506).

Variable	Category	Frequency	Percent
Co-existing Illness	EONS	116	22.9
	LONS	65	12.8
Birth weight of neonate (grams)	<2500	69	13.6
	≥2500	437	86.4
Gestational age of neonate (weeks)	<37	130	25.7
	≥37	376	74.3
Pre-existing medical condition	Yes	42	8.3
Type of pre-existing medical condition	Congenital hydrocephalus	35	6.9
	Down syndrome	4	-
	Congenital heart defects	3	-
Mode of delivery	C/S	153	30.2
	Spontaneous vaginal	314	62.1
	Vacuum	38	7.7
Complications during delivery	Yes	119	23.5
Type of complication	PROM	71	14.0
	Eclampsia	31	6.1
	Chorioamnionitis	11	2.2
	Meconium stain in amniotic fluid	6	1.2

C/S: cesarean section; PROM: premature rupture of membranes

4.3. Laboratory and clinical findings of patients

In this study, the mean cerebrospinal fluid (CSF) white cell count was 1764.3 ± 833.3 cells/µL, with 72 (14.2%) patients having counts above 2500 cells/mm^3. Elevated CSF protein levels (>400 mg/dL) were observed in 118 (23.3%) patients, while 79 (15.6%) had CSF glucose levels below 10 mg/dL, with overall mean protein and glucose levels of 300.2 ± 108.2 mg/dL and 15.4 ± 6.9 mg/dL, respectively. Gram stain was positive in 113 (22.3%) cases, with Gram-positive cocci (63, 12.5%) and Gram-negative rods (40, 7.9%) being the most common organisms identified. CSF cultures were positive in 71 (14%) patients, with GBS (30, 5.9%) and *E. coli* (20, 4%) as the predominant pathogens. Hematological abnormalities included thrombocytopenia (platelet count $<150 \times 10^9$/L) in 35 (6.9%) patients, anemia (hemoglobin <11.5 g/dL) in 199 (39.3%), and leukocytosis (white cell count $>15 \times 10^9$/L) in 134 (26.5%) patients (Table 4).

Table 4. Result of laboratory findings and identified pathogens of meningitis among neonates admitted at public hospitals in Harar town, Ethiopia, from February 10 to March 20, 2025.

Variable	**Category**	**Frequency**	**Percent**
CSF WBC cells/mm^3	<2500	434	85.8
	≥2500	72	14.2
CSF Protein (mg/dl)	<400	388	76.7
	≥400	118	23.3
CSF Glucose (mg/dl)	<10	79	15.6
	≥10	427	84.4
CSF gram stain	Yes	113	22.3
Identified the pathogen from the Gram stain	Gram-positive coccus	63	12.5
	Gram-negative rods	40	7.9
	Gram-positive rods	9	1.8
	Gram-negative coccus	1	0.2
CSF culture	Yes	71	14.0
Isolated micro-organism	GBS	30	5.9
	E.coli	20	4
	Klebsiella	16	3.2
	S. aureus	3	-
	L. monocytogenes	1	-
	Acinetobacter	1	-
WCC (10^9/L)	<15	372	73.5
	≥15	134	26.5
Hgb (g/dl)	<11.5	199	39.3
	≥11.5	307	60.7
Platelet count (10^9/L)	<150	35	6.9
	≥150	471	93.1

CSF: cerebrospinal fluid; EONS: Early Onset Neonatal Sepsis; GBS: Group B streptococcus; Hgb: Hemoglobin; LONS: Late Onset Neonatal Sepsis; WCC: White cell count

The most common clinical manifestations of neonatal meningitis in this study were 475 (93.9%) fever, 419 (82.8%) failure to suck, 302 (59.7%) vomiting, and 298 (58.9%) irritability **(Figure 2).**

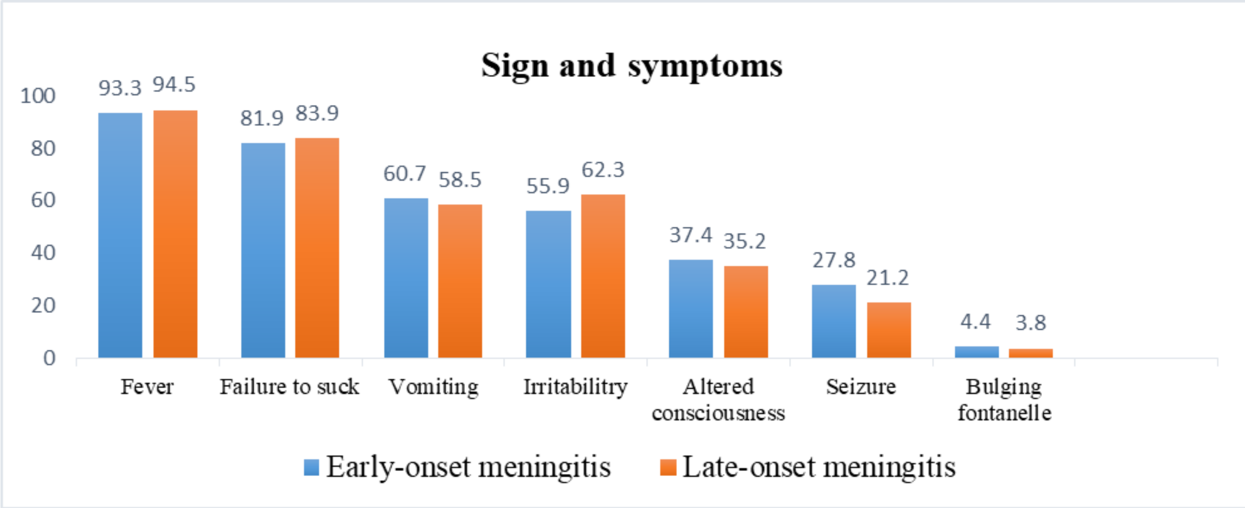

Figure 2. Signs and symptoms of meningitis among neonates admitted at public hospitals in Harar town, Eastern Ethiopia, from February 10 to March 20, 2025.

4.4. Prescribed medication and outcomes of treatment

In this study, most patients (82.2%) were treated with a combination of Ampicillin and Gentamycin, followed by (10.7%) a combination of Ampicillin and Cefotaxime. Among 506 neonates treated for meningitis, 339 (67%) had good treatment outcomes, whereas 167 (33%) had poor treatment outcomes. The death rate for newborn meningitis in this study was 18.8%. In this study, 143 (28.3%) patients experienced complications in a healthcare setting, of which 130 patients developed complications after taking medications for meningitis for at least 72 hours. 411 (81.2%) newborns survived meningitis, and from these 73(14.4%) were discharged with neurological complications, including epilepsy (49, 9.7%), hydrocephalus (11, 2.2%), probable subdural effusion (5, 1.0%), weakness (5, 1.0%), hemiparesis (2, 0.4%), and hearing loss (1, 0.2%) (Table 5).

Table 5. Complications of meningitis and treatment outcomes among neonates admitted at public hospitals in Harar town, Eastern Ethiopia, from February 10 to March 20, 2025.

Variables	Category	Frequency	Percent
Complications developed after 72 hours of treatment	Yes	130	25.7
Complications developed in-hospital	Yes	143	28.3
Complications in the hospital	Seizure	62	12.3
	Renal failure	17	3.4
	Septic shock	16	3.2
	Hydrocephalus	11	2.2
	Subdural effusion	11	2.2
	Respiratory failure	10	2.0
	Brain abscess	9	1.8
	Others*	7	-
Discharged with complications	Yes	73	14.4
Complication at discharge	Epilepsy	49	9.7
	Hydrocephalus	11	2.2
	Subdural effusion	5	1.0
	Weakness	5	1.0
	Others**	3	-
Status of patients at discharge	Improved	248	49
	Recovered	154	30.4
	Dead	95	18.8
	Discharge without improvement	9	1.8
Outcomes of treatment	Poor	167	33
	Good	339	67

Others*…subdural empyema (3, 0.6%); weakness (2, 0.4%); brain infarction (1, 0.2%); ventriculomegaly (1, 0.2%). Others**…. Hemiparesis (2, 0.4%); deafness (1, 0.2%).

4.5. Factors associated with poor treatment outcomes

4.5.1. Bivariate Analysis

Variables such as age (<7 days), low birth weight (<2500 gm), prematurity (<37 weeks), vacuum and cesarean delivery, positive CSF culture, anemia, non-exclusive breastfeeding, seizure upon admission and during hospitalization, EONS, congenital hydrocephalus, and elevated CSF white cell count, protein, and glucose levels had a p-value of less than 0.25. These variables were taken in to multivariable analysis to identify factors associated with the poor treatment outcomes **(Table 6).**

4.5.2. Multivariable Analysis

Multivariate logistic regression analysis identified several independent predictors of poor treatment outcomes among neonates with meningitis. These included delivery by vacuum (AOR = 3.06; 95% CI: 1.03–9.05), positive CSF culture (AOR = 3.53; 95% CI: 1.45–8.57), CSF protein levels >400 mg/dL at admission (AOR = 17.9; 95% CI: 7.95–40.3), CSF glucose levels <10 mg/dL at admission (AOR = 3.89; 95% CI: 1.55–9.77), presence of seizures upon admission (AOR = 5.6; 95% CI: 2.78–11.4), development of seizures during hospitalization (AOR = 14.4; 95% CI: 5.85–35.2), co-existence with early-onset neonatal sepsis (EONS) (AOR = 3.5; 95% CI: 1.49–8.20), and congenital hydrocephalus (AOR = 4.73; 95% CI: 1.46–15.2) (Table 6).

Table 6. Factors associated with poor outcomes among neonates with meningitis treated at public hospitals in Harar town, Eastern Ethiopia, from February 10 to March 20, 2025.

Variables		**Poor treatment outcome**				**P-value**
		No (%)	**Yes (%)**	**COR**	**AOR**	
Age (days)	<7	161(59.6%)	109(40.4%)	2.08(1.42-3.05)	0.72(0.33-1.53)	0.39
	7-28	178(75.4%)	58(24.6%)	1.00	1.00	
Birth weight (grams)	<2500	22(31.9%)	47(68.1%)	5.64(3.26-9.76)	1.95(0.67-5.69)	0.22
	≥2500	317(72.5%)	120(27.5%)	1.00	1.00	
Gestational ages (weeks)	<37	60(42.2%)	70(53.8%)	3.35(2.22-5.08)	1.64(0.68-3.95)	0.27
	≥37	279(74.2%)	97(25.8%)	1.00	1.00	
Mode of delivery	AV	21(53.8%)	18(46.2%)	2.13(1.09-4.19)	3.06(1.03-9.05)[a]	**0.043**
	C/S	94(61.4%)	59(38.6%)	1.56(1.04-2.35)	0.91(0.42-1.96)	0.81
	SV	224(71.3%)	90(28.7%)	1.00	1.00	
CSF culture	Yes	29(40.8%)	42(59.2%)	3.59(2.14-6.02)	3.53(1.45-8.57)[a]	**0.005**
	No	310(71.3%)	125(28.7%)	1.00	1.00	
CSF WBC	≥2500	15(21.4%)	55(78.6%)	10.9(5.85-19.9)	2.67(0.94-7.62)	0.066
	<2500	315(74.6%)	107(25.4%)	1.00	1.00	
CSF protein	≥400	15(12.7%)	103(87.3%)	34.7(18.9-63.6)	17.9(7.95-40.3)[b]	**<0.001**
	<400	324(83.5%)	64(16.5%)	1.00	1.00	
CSF glucose	<10	28(35.4%)	51(64.6%)	4.88(2.93-8.11)	3.89(1.55-9.77)[a]	**0.004**
	≥10	311(72.8%)	116(27.2%)	1.00	1.00	
Hemoglobin	<11.5	103(51.8%)	96(48.2%)	3.09(2.11-4.55)	1.43(0.73-2.79)	0.28
	≥11.5	236(76.9%)	71(23.1%)	1.00	1.00	
Platelet	<150	19(54.3%)	16(45.7%)	1.78(0.89-3.56)	0.42(0.11-1.56)	0.19
	≥150	320(67.9%)	151(32.1%)	1.00	1.00	
Not exclusive breastfeeding	Yes	32(47.8%)	35(52.2%)	2.54(1.51-4.28)	2.07(0.91-4.71)	0.08
	No	307(69.9%)	132(30.1%)	1.00	1.00	
Presence of seizure at admission	Yes	43(34.4%)	82(65.6%)	6.64(4.27-10.3)	5.6(2.78-11.4)[b]	**<0.001**
	No	296(77.7%)	85(22.3%)	1.00	1.00	
Developed a seizure after admission	Yes	16(25.8%)	46(74.2%)	12.3(6.04-24.9)	14.4(5.85-35.2)[b]	**<0.001**
	No	323(72.7%)	121(27.3%)	1.00	1.00	
Presence of EONS	Yes	46(40%)	69(60%)	4.48(2.89-6.95)	3.5(1.49-8.20)[a]	**0.004**
	No	293(74.9%)	98(25.1%)	1.00	1.00	
Congenital hydrocephalus	Yes	10(28.6%)	25(71.4%)	5.15(2.41-10.9)	4.73(1.46-15.2)[a]	**0.009**
	No	329(69.9%)	142(30.1%)	1.00	1.00	

Hosmer-Lemeshow goodness of fit test was fitted with a P-value of 0.53; [a] P >0.05, [b] P<0.001. AOR: adjusted odd ratio; CSF: cerebrospinal fluid; C/S: cesarean section; COR: crude odd ratio; EONS: early onset neonatal sepsis; AV: Assisted with vacuum; SV: Spontaneous vaginal; HFCSUH: Hiwot Fana Compressive Specialized University Hospital; JGH: Jugal General Hospital

5. DISCUSSION

This study assessed the treatment outcomes of neonatal meningitis and the associated factors among 506 newborns admitted to public hospitals in Harar, Eastern Ethiopia.

In this study, 14% of neonates had CSF culture-confirmed bacterial meningitis, which is consistent with findings from Angola (12%) (Pelkonen *et al.,* 2020). However, this prevalence was higher than that reported in North Gondar, Ethiopia (6%) (Wondimu *et al.,* 2023), and Kenya (4.8%) (Laving *et al.,* 2003). These differences may be attributed to variations in the number of CSF samples collected, patient selection criteria, early initiation of antibiotics before sample collection, and laboratory techniques. In the present study, all participants were selected based on having undergone a lumbar puncture and meeting the diagnostic criteria for CSF analysis.

In this study, the most common clinical presentations of neonatal meningitis were fever (93.9%), inability to suck (82.8%), vomiting (59.7%), and irritability (58.9%), while seizures (24.7%) and a bulging fontanelle (4.2%) were less frequently observed. These findings are consistent with previous studies conducted in Gondar, Ethiopia (Wondimu *et al.*, 2023), Angola (Pelkonen *et al.*, 2020), and Taiwan (Lin *et al.*, 2012).

In this study, *Streptococcus agalactiae* (GBS) and *Escherichia coli* were the most commonly isolated microorganisms from positive CSF cultures, consistent with findings from the UK and Ireland (Okike *et al.*, 2014), Taiwan (Lin *et al.,* 2012), and Hong Kong (Wong *et al.*, 2021). In contrast, studies in Kenya (Laving *et al.,* 2003) and Peru (Guillén-Pinto *et al.*, 2020), reported *E. coli* as the predominant organism, followed by GBS. Furthermore, *Klebsiella* species were most frequently observed in studies conducted in Gondar, Ethiopia (Sirak Biset *et al.,* 2021), Angola (Pelkonen *et al.,* 2020), South Africa (Mashau *et al.,* 2022), and Iran (Boskabadi *et al.*, 2020). These variations may be explained by differences in age at presentation (early vs. late onset), gestational age, birth weight, and geographic location.

In this study, 33% of neonates experienced poor treatment outcomes, including hospital death, persistent complications, or lack of improvement, with an in-hospital mortality rate of 18.8%. This mortality rate was lower than those reported in Angola (24%) (Pelkonen *et al.,* 2020), Gambia (37%) (Ikumapayi *et al.,* 2022), Tanzania (29.4%) (Pishori *et al.,* 2023), Tunisia (40%) (Kamoun *et al.,* 2015), and India (29.1%) (Barik *et al.*, 2022). Conversely, it was higher than findings from Taiwan (10.3%) (Lee *et al.*, 2024), Colombia (9.5%) (Zúñiga *et al.*, 2023), and China (4.2%) (Li *et al.,* 2022). These variations may be attributed to differences in early diagnosis, socioeconomic status, sample size, patterns of antibiotic resistance, and access to healthcare services.

In this study, 14.4% of the 411 neonates who survived meningitis developed neurological complications, a finding comparable to that reported in Tunisia (16.4%) (Kamoun *et al.,* 2015). However, this rate was lower than that observed in Canada (72.4%) (Ouchenir *et al.,* 2017), Taiwan (41.6%) (Ou-Yang *et al.,* 2023), India (30.4%) (Kumar *et al.,* 2018), Nigeria (22.5%) (Airede *et al.,* 2008), and another study in Tunisia (21.6%) (Hamouda *et al.,* 2013). Neurological complications were reported in higher numbers in developed countries than in low-income countries. This variation can be explained by differences in diagnostic equipment access, medical expertise, spectrum of pathogens, and incidence of mortality.

This study found that epilepsy and hydrocephalus were among the most common complications of neonatal meningitis, consistent with findings from Taiwan (Lin *et al.,* 2012). Numerous studies have reported secondary epilepsy as the most frequent neurological outcome of neonatal meningitis (Ouchenir *et al.,* 2017; Li *et al.,* 2022; Mashau *et al.,* 2022; Ou-Yang *et al.,* 2023; Zúñiga *et al.,* 2023). Most neonates discharged with neurological complications had developed these conditions during their hospitalization

This study found that neonates delivered by vacuum (AOR = 3.06; 95% CI: 1.03–9.05) were three times more likely to experience death or neurological complications at discharge compared with those born via cesarean section. Previous studies have not specifically examined the association between vacuum-assisted delivery and poor treatment outcomes (Klinger *et al.,* 2000; Airede *et al.,* 2008; Lin *et al.,* 2012; Hamouda *et al.,* 2013; Okike *et al.,* 2014; Kumar *et al.,* 2018; Mao *et al.,* 2018; Li *et al.,* 2022; Zúñiga *et al.,* 2023; Ou-Yang *et al.,* 2023; Lee *et al.,* 2024). This association may be related to exposure to drug-resistant bacteria from contaminated delivery devices. Neonatal meningitis caused by drug-resistant organisms has been strongly linked to increased mortality and morbidity (Airede *et al.,* 2008; Kumar *et al.,* 2018).

This study found that neonates who experienced seizures upon admission (AOR = 5.6; 95% CI: 2.78–11.4) were 5.6 times more likely to have poor treatment outcomes. This finding is consistent with studies conducted in Canada (Klinger *et al.,* 2000), India (AOR = 14; 95% CI: 1.3–21.8) (Kumar *et al.,* 2018), and Taiwan (AOR = 2.40; 95% CI: 1.12–4.14) (Ou-Yang *et al.,* 2023). Similarly, the development of seizures during hospitalization (AOR = 14.4; 95% CI: 5.85–35.2) was strongly associated with poor treatment outcomes, aligning with findings from Taiwan (OR = 10.10; 95% CI: 2.11–48.32) (Lin *et al.*, 2012). Seizures are a well-recognized manifestation and complication of neonatal meningitis, potentially leading to cerebral infarction, hydrocephalus, subdural empyema, or stroke, all of which contribute to adverse outcomes (Volpe J, 2018).

This study revealed that neonates with EONS (AOR = 3.5; 95% CI: 1.49–8.20) were 3.5 times more likely to experience poor treatment outcomes. This finding is consistent with studies conducted in Nigeria (Airede *et al.*, 2008) and Taiwan (OR = 3.38; 95% CI: 1.10–8.04) (Lee *et al.*, 2024). Additionally, neonates with culture-confirmed meningitis (AOR = 3.53; 95% CI: 1.45–8.57) were 3.5 times more likely to have poor treatment outcomes compared with those diagnosed with probable meningitis.

Neonates with CSF protein levels above 400 mg/dL (AOR = 17.9; 95% CI: 7.95–40.3) had a significantly higher risk of poor treatment outcomes compared with those with lower levels. This finding aligns with a study conducted in Taiwan (OR = 171; 95% CI: 25.6–1000) (Lin *et al.*, 2012). Similarly, neonates with CSF glucose levels below 10 mg/dL at admission (AOR = 3.89; 95% CI: 1.55–9.77) were approximately four times more likely to experience poor outcomes, consistent with a study from Southern Taiwan (Chang *et al.*, 2003). CSF protein and glucose are essential markers for diagnosing bacterial meningitis: glucose levels typically decrease due to consumption by bacteria and white blood cells, while protein levels rise due to inflammation and cellular response (Sakushima *et al.*, 2011). High CSF protein and low glucose concentrations indicate greater disease severity and are associated with an increased risk of complications.

6. Limitations and strengths of the study

The study has three primary limitations. First, the data were derived exclusively from retrospective reviews of medical records, which inherently limited the available information. Key maternal variables, such as history of infections during pregnancy, socioeconomic status, underlying maternal illnesses, antenatal care utilization, and substance use during pregnancy, were absent.

These factors are known to influence neonatal outcomes. Second, the assessment of treatment outcomes for neonatal meningitis was confined to the duration of hospitalization. As a result, the study was unable to capture long-term neurodevelopmental consequences, such as cognitive impairment, behavioral challenges, or delays in motor and language development, which often emerge months or years after the acute illness. Furthermore, the impact of neonatal meningitis on school performance and quality of life in later childhood remains unexplored in this study. Third, the study did not differentiate between community-acquired and hospital-acquired (nosocomial) infections. This distinction is clinically significant, as the causative organisms, resistance patterns, and prognoses often differ between the two. The inability to categorize infections by their source may obscure important epidemiological and treatment-related insights that could inform infection control practices and antibiotic stewardship. Despite these limitations, this study used relatively modest samples from two larger public hospitals and only included those who fulfilled standard CSF criteria.

7. Conclusion and Recommendation

7.1. Conclusion

This study found that approximately one-third of neonates with meningitis experienced poor treatment outcomes. The most commonly observed neurological complications were epilepsy and hydrocephalus. Predictors of poor outcomes included congenital hydrocephalus, vacuum-assisted delivery, positive CSF culture, seizures, elevated CSF protein coupled with low glucose, and co-existence with EONS. Additionally, neonates with congenital heart defects were at increased risk of adverse outcomes.

7.2. Recommendation

For Clinicians:

- **Early Detection:** Routinely screen neonates diagnosed with meningitis for co-existing conditions, including early-onset neonatal sepsis (EONS), congenital hydrocephalus, and congenital heart anomalies.
- **Monitoring High-Risk Cases:** Pay special attention to neonates presenting with elevated CSF protein (>400 mg/dL), low CSF glucose (<10 mg/dL), positive CSF cultures, or seizures at admission or during hospitalization, as these indicators are associated with higher risk of adverse outcomes.
- **Prompt Management:** Rapidly address seizures, provide supportive care for cardiac defects, and ensure timely and appropriate antibiotic therapy to reduce mortality and prevent long-term complications.

For HFSCUH and JGH

- **Enhance Diagnostic Services:** Strengthen the capacity to perform accurate CSF analyses and cultures to confirm meningitis and guide treatment decisions.
- **Improve Delivery Practices:** Regularly assess and monitor vacuum-assisted deliveries to minimize infection risks that may negatively impact neonatal outcomes.

For Researchers

- **Examine Delivery-Related Risks:** Conduct targeted studies to explore the potential association between vacuum-assisted deliveries and adverse treatment outcomes in neonates with meningitis.
- **Assess Long-Term Outcomes:** Initiate longitudinal research to track neurological and developmental outcomes among survivors of neonatal meningitis.

For Policy Makers

- **Allocate Adequate Resources:** Ensure neonatal intensive care units (NICUs) have sufficient resources for early identification, monitoring, and management of high-risk neonates.

- **Strengthen Training Programs:** Implement focused training for healthcare providers on early recognition, timely intervention, and comprehensive management of neonatal meningitis and its complications.

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Annex I. Data collection checklist

S. No	Variables	Response	Skip/Remark
Part 1: Socio-demographic factors			
1	Admission site	A. HFCSUH B. JGH	
2	Sex	A. Male B. Female	
3	Age (days)		
4	Birth weight of neonate (grams)		
5	Gestational age of neonate (week)		
Part 2: Clinical factors			
6	Is there any identified pre-existing medical condition?	A. Yes B. No	
7	If yes for Q.8, please identify.	A. Congenital heart defects B. Down syndrome C. Congenital hydrocephalus D. Other (Specify)	
8	Is there any identified co-existing illness?	A. Yes B. No	
9	If yes for Q.8, please identify.	A. Early onset sepsis B. Late onset sepsis C. Aspiration pneumonia D. Other	
10	Mode of delivery	A. Spontaneous vaginal deliver B. C/S C. Assisted by vacuum	
11	Is there any complication during delivery	A. Yes B. No	

12	If yes for Q.11, please identify.	A. History of PROM B. Meconium stain in amniotic fluid C. Chroinammionitcs D. Other	
13	Symptoms at diagnosis (it is possible to select more than one)	A. Fever B. Failure to suck C. Seizure D. Irritability E. Vomiting F. Altered consciousness G. Bulging fontanelle H. If other specify	
14	Lumbar puncture was done?	A. Yes B. No	
15	Has any CSF Gram stain been done?	A. Yes B. No	
16	If yes, please specify the pathogen.		
17	Has any CSF culture been done?	A. Yes B. No	
18	If yes, please specify the pathogen type.	A. Bacteria B. Viral C. Fungi D. Other (specify)	
19	If the pathogen is identified, please specify the specific species.		
20	Blood tests	A. White blood cell count (109/L) ________ B. Neutrophil ratio (%) ___________ C. Hemoglobin (g/dl) __________ D. Platelet count (cells/mm^3) _____________ E. C-reactive protein (mg/L) _______________	
21	Cerebrospinal fluid tests (CSF analysis) result	A. Clear ___________ B. Turbid____________ C. Bloody _____________ D. White blood cell count ________ E. Protein (mg/dl) ________ F. Glucose (mg/dl) ________	

Part 3: Treatment-related factors			
22	Choice of initial antimicrobial therapy (drug name, dosage, frequency, and duration)		
23	If antimicrobial therapy changed, please write (drug name, dosage, frequency, and duration)		
24	Patient taking any nutrition?	A. Yes B. No	
25	Is there any complication?	A. Yes B. No	
26	If yes, please specify the complication and its management.		
Part 4: Outcome of the treatment			
27	Status of the patient at discharge	A. Completely recovered B. Improved C. Dead D. Same	
28	Is there any newly developed complication after 72 hours of treatment?	A. Yes B. No	
29	Patient discharged without any improvement after 72 hours of treatment?	A. Yes B. No	
30	Is there any complication at discharge?	A. Yes B. No	
31	If your answer is yes, please identify (possibly select more than one):	A. Epilepsy B. Hydrocephalus C. Weakness D. Deafness E. Subdural empyema F. Subdural effusion G. Brain abscess H. Respiratory failure I. Septic shock J. Renal failure K. Other Specify ________________	

Annex II. Curriculum vitae

1. Background information

Full name: Getahun Tamiru Yirsaw	**Nationality:** Ethiopian
Age: 29 years	**Date of birth:** December 17/1994
Sex: Male	**Phone No̲:** +251932427927/0717427927
Address: Dader, Oromia, Eastern Ethiopia	
Email: tamirugetahun53@gmail.com	
Working institution: Hiwot Fana Comprehensive Specialized University Hospital	

2. Educational background

S. No̲	Name of school	Place	Grade	Year
1	Dader Elementary school	Dader	1-8	2000-2007
2	Dader Secondary High School	Dader	9-10	2008-2011
3	Dader Preparatory school	Dader	11-12	2012-2006
4	Haramaya University, CHMS	Harar	Degree (B. Pharm)	2015-2019
5	Haramaya University	Harar	MSc student of clinical pharmacy	2023 - …

CHMS: College of Health and Medical Science

3. **Qualification:** B. pharm Degree in pharmacy with CGPA of **3.44,** MSc of clinical pharmacy student (CGPA of **3.86**)

4. Language Skills

S. No̲	Language	Listening	Reading	Speaking	Writing
1	**English**	Excellent	Excellent	Excellent	Excellent
2	**Amharic**	Excellent	Excellent	Excellent	Excellent
3	**Oromic**	Excellent	Excellent	Excellent	Excellent

5. Computer skills

- Very good in Microsoft Word, Microsoft PowerPoint, and Microsoft Excel
- Very good in Statistical Package for Social Science software (SPSS)

6. Working experiences

- I have experience dispensing medications in hospital pharmacy outlets at Haramaya Hospital and HFCSUH.
- I have experience in the service of pharmaceutical care at HFCSUH
- I have worked as a Supervisor of staff at Hiwot Fana Comprehensive Specialized University Hospital for 2 years