

Time to Death and Its Predictors among Children with Bacterial Meningitis in Southwest Ethiopia, 2022. A Retrospective follow-up study

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Abstract

Background

Bacterial Meningitis (BM) is an infectious disease characterized by infection and inflammation of the meninges covering the brain and spinal cord. Globally, it is a major cause of morbidity and mortality, affecting 2.81 million children each year.

Objective

The aim of the study was to assess the time to death and its predictors among children with bacterial meningitis in Southwest, Ethiopia.

Methods

Institutional-based retrospective follow-up study design was conducted among 372 paediatric patients with bacterial meningitis. Systematic random sampling was used to select eligible medical records from February 15 to March 15, 2022. Kaplan-Meier survival curve and log-rank were computed to estimate and compare failure time. Bivariate and multivariable Cox-regression models were fitted to identify predictors of time to death. A hazard ratio (HR) and adjusted hazard ratio (AHR) with a p-value < 0.05 were considered statistically significant.

Result

The overall median time of death was 16 (95% CI, 11.4-17.5) days. Impaired consciousness (AHR=3.88; 95%CI 1.9- 7.9), seizure (AHR=2.2; 95%CI 1.06- 4.45), and steroid drug use (AHR=4.8; 95%CI 2.03-11.3) were predictors significantly associated with time to death.

Conclusion

The proportion of deaths was high compared to those of the previous studies. Impaired consciousness, seizure and use of steroid were associated with time to death.

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Keywords: Time to death, Paediatrics, Bacterial Meningitis, Southwest Ethiopia

Introduction

Bacterial Meningitis (BM) is an infectious disease characterized by infection and inflammation of the meninges covering the brain and spinal cord and results in significant worldwide morbidity and mortality.[1] It is a major cause of morbidity and mortality, which affects 2.81 million children every year globally. The World Health Organization estimates global mortality from bacterial meningitis to be approximately 290,000 annually. A large number of these deaths occur in the African region.[2]

Global Burden of Disease (GBD) 2016 reported that, mortality from meningitis has declined by 21% from 1990 to 2016, while incident cases increased from 2.5 to 2.82 million in 2016, but significant differences in geographic distribution and age groups persist. In 2016, among all age groups, 0.6% of deaths and almost 3% of all deaths in children under 5 years of age were due to meningitis. Most (84.6%) of the deaths occurred in low and low-to-middle-income countries, with the highest mortality rate shown in the African meningeal belt.[3] According to a systematic analysis of the global burden of diseases in 2017, bacterial meningitis is responsible for about 288,000 annual deaths of children, of which more than half (53%) are children aged under five years.[4]

The African continent has the highest rates of bacterial meningitis in the world. A region in sub-Saharan Africa that stretches from Ethiopia in the east to the Gambia in the west and comprises 26 countries with over 400 million people is known as the meningitis belt because of its high endemics and prevalence.[5] Epidemics remain an ongoing threat in the meningitis belt countries of sub-Saharan Africa and six of the ten countries with the highest rates of meningitis mortality are in this region. The World Health Organization African Region report showed that the case-fatality rate among laboratory-confirmed

bacterial meningitis cases was 17.7%, out of which 20.9%, 12.8%, and 12.2% of deaths were due to *Streptococcus pneumoniae* (Pneumococcus), *Neisseria meningitidis* (Meningococcus), and *Haemophilus influenzae* type B, respectively.[6] In another report from 5 countries in the meningitis belt region, the average annual incidence of suspected meningitis reveals 31.3 cases per 100,000 population, with about 39% of the cases being under 5-year-old children. The overall case fatality rate was reported to be 8%.[5]

Ethiopia is one of the countries in the African meningial belt region. It is recorded that the largest outbreak of 1600 cases was in 1989. However, there have been frequent small-scale outbreaks throughout Ethiopia up to this time.[7] The surveillance of bacterial meningitis in Ethiopia within the 2012–2013 report showed that the BM mortality rate from meningococcal cases was 11.1%, whereas the rate of pneumococcal cases was 16.7%. About 62.6% of incident cases were children under 19 years old.[8] According to the GBD report in 2016, Ethiopia is the 3rd country with the top meningitis incidence (192,617 cases) and deaths (17,313 cases), next to India and Nigeria.[3] From 2001 to 2010 in Ethiopia, a median of about 1,056 suspected cases of meningitis yearly were reported to the WHO.

In response to that, conjugate vaccines against HiB and pneumococcal conjugate vaccines were introduced in 2007 and 2011, respectively.[9] In addition, as part of WHO's three pillars of strategy, the federal Ministry of Health has introduced the Men-A conjugate vaccine initiative for *Neisseria meningitidis* (Meningococcus) in Ethiopia. [8] However, the problem continues to be of great concern and remains a major global and national health problem, which needs action to attain the Sustainable Development Goal and the “Defeating Meningitis by 2030 Global Road Map.”[7,10]

The purpose of this study was to assess time to death and determine predictors of mortality among children with bacterial

meningitis in Southwest Ethiopia. There is a gap on detailed and general evidence on survival time, basis for monitoring, screening, and identifying bacterial meningitis in the study area. In terms of the extent of how long children with bacterial meningitis survive after their diagnosis in Ethiopia was not studied. The factors determining the death of children with bacterial meningitis in Ethiopia are not well established.

Method

Study design, Area, and Period

An institution-based retrospective follow-up study was conducted among children with Bacterial meningitis at Jimma University Medical Center. Jimma University Medical Center is one of the oldest public hospitals in the country, which was established in 1930, and currently serves as a teaching hospital in south-west Ethiopia with a catchment population of over 15 million. It is located in the city of Jimma, 352 km southwest of the capital, Addis Ababa. The center has 800 beds providing service for 160,000 outpatients and 45,000 inpatients to a diverse population from four surrounding regional states. Data were collected from February 15, 2022, to March 15, 2022.

Source and Study Population

The source populations were all children with bacterial meningitis above one month and under 15 years admitted to the paediatric ward of Jimma University Medical Center. The source of data were records of children with bacterial meningitis aged above one month and under 15 years admitted to paediatric ward from January 01, 2019 to December 31, 2021. Records of study participants that were lost or incomplete information on important study variables (date of admission, discharge and outcome status) were also excluded.

Sample size determination

The sample size was calculated by the following single population proportion formula.

$$n = \frac{(Z\alpha/2)^2 \times P(1-P)}{(d)^2}$$

Where: n= sample size; p= proportion of death; 32.65%=0.3265; a= confidence interval (95%); d= is the margin of sampling error tolerated (5%) = 0.05.

The proportion of deaths (32.65%) was taken from another study.[15]

Therefore

$$n = \frac{(1.96)^2 \times 0.3265(1-0.3265)}{(0.05)^2} = 338$$

By considering 10% for incomplete medical charts, which is 34, the total sample size was 372.

Sampling procedures

The sampling frame was the records of all children aged from one month to 15 years with bacterial meningitis admitted to Jimma university medical center from January 1, 2019 to December 31, 2021. A systematic sampling technique was utilised to choose the required number of samples (chart of patients). The sample size was proportionally allocated for each year by the formula $n_i = n \times N_i / N$. Where n_i =sample from the i th year, n =final sample size, N_i = total study population of the i th year and N = total study population. Which is (102 from a total 170 in 2019), (120 from 200 in 2020) and (150 from 250 in 2021) and the first record to start with was number two (second record) which was selected randomly.

The interval $(K) = N/n = 620/372 = 1.7$ which is approximated to 2. Thus, every second chart was selected by using a systematic random sampling technique until the required number for the sample was obtained. Where K = interval N =total population at paediatrics ward by bacterial meningitis from 01st January 2019, to 31st December 2021, n = final sample size of the study.

Data Collection Tool and Procedure

The data extraction format was adapted in English to extract the relevant variables

from the patient chart to meet the study objectives.[15] The tool has five parts containing socio-demographic, health-related, clinical, laboratory and treatment-related factors. Data were collected through a record review. Records were collected by using the children's medical record numbers, which are found in the health management information system registration book. The records of all study subjects were selected according to the eligibility criteria. Death and other outcomes were confirmed by the discharge note from the patient chart and registration book. Six graduate (BSc) nurses were recruited from outside Jimma University Medical Center; two to serve as supervisors and four as data collectors. Supervisors checked the collected data daily for completeness. Data collection was done on working days, and 25 to 30 minutes were taken to complete one questionnaire. The starting point for this retrospective follow-up was the time of admission with a diagnosis of bacterial meningitis, and the end was the date of death, date of loss to follow-up, date of transfer out, or date of self-discharge.

One day training was given for supervisors and data collectors on what information they should collect and how, from targeted data sources. To ensure completeness and agreement with the objective of the study, data extraction tool was pretested with 5% (19) of medical charts in another hospital, which was not included in the study. Consistency was checked through a random selection of charts and the principal investigator crosschecked their similarity. Experts examined the content of the tool to ensure that it accurately measured the intended variables and aligned with the study objectives. Their evaluation helped identify potential biases, ambiguities, and gaps, ensuring the tool's clarity, consistency, and effectiveness in capturing reliable data. Data validity and reliability were checked. [15]

Data Analysis and Processing

Before data entry, each data collection tool was checked for completeness.

Data were cleaned, coded, and entered into Epi Data version 4.6, and then exported to SPSS version 27 and STATA software for analysis. The outcome of each subject was dichotomized into death and censored. The Kaplan-Meier failure curve was used to estimate and compare failure time. Comparison of the two failure curves was done using the log-rank test. The proportional hazard assumption of the Cox regression model was checked using the Schoenfeld residual test. Collinearity was detected by calculating the variance inflation factor. A bivariate Cox regression model was fitted for each explanatory variable, and the variables having a p-value <0.25 were included in the multivariable Cox model to identify independent predictors of mortality among children with bacterial meningitis. Hazard Ratio with its 95% confidence interval (CI) was used to estimate the strength of association, and p-value < 0.05 was considered statistically significant.

Ethical considerations

The study was approved by the Research Ethical Committee of Addis Ababa University College of Health Sciences and the School of Nursing and Midwifery (Ref: MN 10/2022/ Protocol number 08/22/SNM). Since the study was conducted with the records of the patients, direct informed consent from patients was not taken. Instead, approval to review patient records was obtained from Jimma University Medical Center. A supporting letter was received, and the aim of the study was shared with the patients' record office. Patient identification numbers as well as their names were excluded, and the data were used only for the study to maintain confidentiality. The study was performed in accordance with the Declaration of Helsinki.[16]

Results

Sociodemographic characteristics of study participants

Among 372 records of children with bacterial meningitis admitted to Jimma University Medical Center, 359 (96.5%) records

of children fulfilling the criteria were enrolled in the study. About 13 (3.3%) records were removed due to lost and incomplete data. Among 359 children, more than half, 212 (59.1%), were males, and nearly half, 189 (52.6%) of participants were from urban residences. The age of the children ranges from one month to 156 months. The mean age was 18.45 months, and the median age was 6 months. More than three-fourths, 284 (79.1%), of the children were under the age of two years at admission. About two-thirds, 242 (67.4%) of the children had the number of siblings greater than or equal to three, and more than half, 202 (56.3%), of the children were living in crowded houses (Table 1).

Table 1. Socio-demographic characteristics of children with bacterial meningitis in Jimma University Medical Center Southwest Ethiopia 2022 (N=359)

Socio-demographic Variable	Category	Frequency (%)
Sex	Male	212 (59.1)
	Female	147 (40.9)
Age category	< 2 year	284 (79.1)
	2-5 year	44 (12.3)
	≥5 year	31 (8.6)
Residence	Urban	170 (47.4)
	Rural	189 (52.6)
No of sibling	≥3	242 (67.4)
	<3	117 (32.6)
No of Persons in house	≥5	202 (56.3)
	<5	157 (43.7)

Health-Related and Clinical Characteristics of Children

Among the 359 selected study participants, about half, 175 (48.7%), of the children were undernourished, and the majority, 281 (78.3%), were vaccinated. Remarkably, a significant majority, 299 (83.3%), were exclusively breastfed. Of all the study participants, 76 (21.2%) had upper respiratory tract infections (25 (7.0%)), had history of head trauma, and 227 (63.2%) of the children had comorbidity. Moreover,

more than half 200 (55.7%), of participants had a duration of illness greater than or equal to three days. Of the total study subjects, more than two-thirds, 256 (71.3%), had high-grade fever, and 202 (56.3%) had vomiting/nausea, whereas about half of the subjects had fast breathing 168 (46.8%) and seizure, 175 (48.7%). In this study, about one-third of the study subjects had impaired consciousness 112 (31.2%). Moreover, about 42 (11.7%) had neck stiffness, 41 (11.4%) had high-pitched cry, and 15 (4.2%) had positive sign (kerning /brudzinski sign) (Table 2).

Table 2. Health-related and clinical characteristics of children with bacterial meningitis in Jimma University Medical Center southwest Ethiopia 2022 (N=359)

Health-related and clinical characteristics	Category	Frequency (%)
Under nutrition	Yes	175 (48.7)
	No	184(51.3)
Immunization status	Complete	281(78.3)
	Incomplete	78(21.7)
Exclusive breastfeeding	Yes	299 (83.3)
	No	60 (16.7)
Upper respiratory tract infection	Yes	76 (21.2)
	No	283 (78.8)
History of head trauma	Yes	25 (7.0)
	No	334 (93.0)
Comorbidity	Yes	227 (63.2)
	No	132 (36.8)
Duration before admission	≥3 days	200 (55.7)
	<3 days	159 (44.3)
High-grade fever	Yes	256 (71.3)
	No	103 (28.7)
Fast breathing	Yes	168 (46.8)
	No	191 (53.2)
Impaired consciousness	Yes	112 (31.2)
	No	247 (68.8)
Seizure	Yes	175 (48.7)
	No	184 (51.3)
Neck stiffness	Yes	42 (11.7)
	No	317 (88.3)
Vomiting or nausea	Yes	157 (43.7)
	No	202 (56.3)
High-pitched cry	Yes	41 (11.4)
	No	318 (88.6)
Kerning / brudzinski sign	Yes	15 (4.2)
	No	344 (95.8)

Laboratory and treatment related characteristics

Out of 359 study participants, lumbar puncture was done for about 225 (62.7%) subjects. From this 33 (14.6%) of subjects had turbid gross appearance of cerebrospinal fluid (CSF) and more than one-third 81 (35.8%) of subjects had CSF glucose $\leq 45\text{mg/dl}$. Moreover, about one forth 59 (26.1%) study participants had CSF protein >100

and about 31 (13.7%) participants had CSF WBC ≥ 100 at admission. However, about 217 (60.4%) study participants had serum WBC $\geq 11,000$ per μl . Among all study participants around half 170 (47.4%) had taken steroid drug, and about 166 (46.2%) of children were received oxygen. Of all study subjects, majority 290 (80.8%) of children received ceftriaxone, 221 (61.6%) received gentamicin, 86 (24.0%) received ampicillin, and 109 (30.4%) received vancomycin (Table 3).

Table 3. Laboratory and treatment related characteristics of children with bacterial meningitis in Jimma University medical center southwest Ethiopia 2022 (lab related N=225 and treatment related N=359)

Characteristics	Category	Frequency (%)
LP done	Yes	225 (62.7)
	No	134 (37.3)
Gross appearance of CSF	Turbid	33(14.6)
	Crystal clear	193(85.4)
CSF glucose	$\leq 45\text{mg/dl}$	81 (35.8)
	$>45\text{mg/dl}$	145 (64.2)
CSF protein	>100	59 (26.1)
	≤ 100	167 (73.9)
CSF WBC	<100	195 (86.3)
	≥ 100	31 (13.7)
Serum WBC (N=359)	≥ 11000 per μl	217 (60.4)
	<11000 per μl	142 (39.6)
Treatment used		
Steroid	Yes	170 (47.4)
	No	189 (52.6)
Oxygen	Yes	166 (46.2)
	No	193 (53.8)
Ceftriaxone	Yes	290 (80.8)
	No	69 (19.2)
Ampicillin	Yes	86 (24.0)
	No	273 (76.0)
Gentamicin	Yes	221 (61.6)
	No	138 (34.4)
Vancomycin	Yes	109 (30.4)
	No	250 (69.6)
Ceftazidime	Yes	24 (6.7)
	No	335 (93.3)

Proportion of mortality

Three hundred fifty nine children with bacterial meningitis have followed a total of 3407-child day's observation with a minimum of one day to maximum of 30 days. Among study participants, 98 (27.3%) of death was observed through the follow up time.

Two hundred sixty one participants were censored with 232 (64.6%) recovered, 13 (3.6%) transferred and 16 (4.5%) left against medical service. The overall incidence death rate of the cohort was 2.87 (95% CI, 2.35-3.5) per 100 child days.

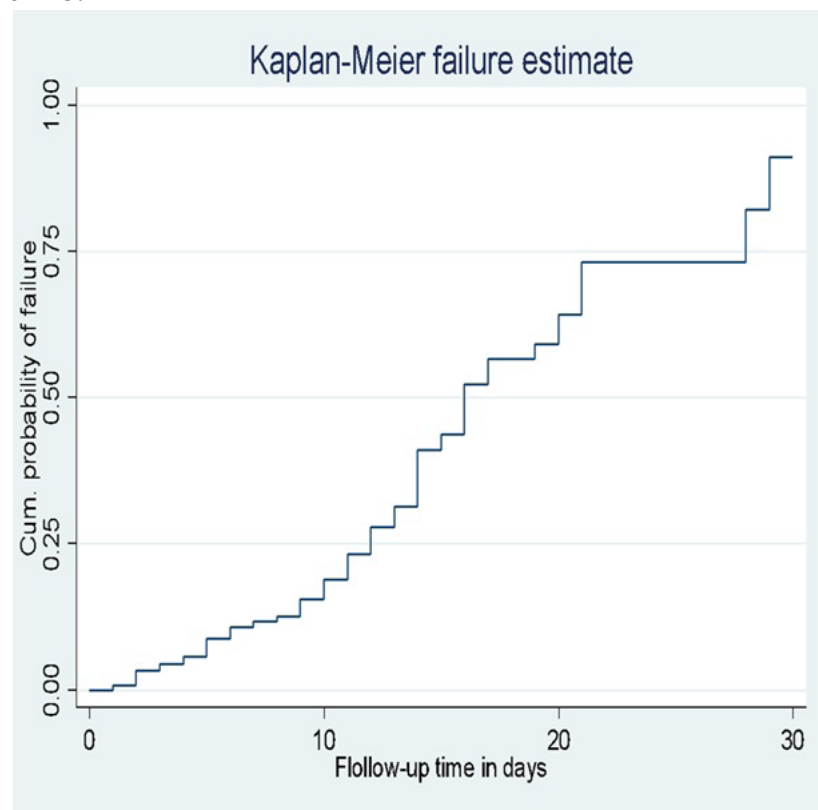


Figure 1. Kaplan-Meier failure curve of children with bacterial meningitis in Jimma University Medical Center Southwest Ethiopia 2022 (N=359).

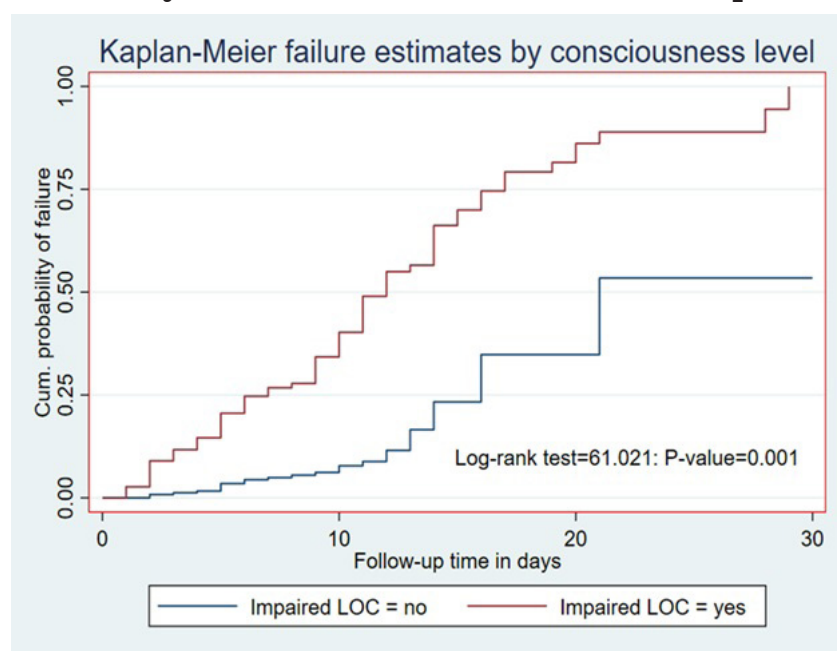


Figure 2. Kaplan-Meier failure curve by Impaired consciousness of children with bacterial meningitis in Jimma University Medical Center Southwest Ethiopia 2022 (N=359).

Time to death of children with bacterial meningitis

The median time to death of the entire cohort was 16 (95% CI, 11.4-17.5) days. The cumulative probability of failure at the end of 7th day was 11%, at 14th day was 28.8%, at 21th day was 59.6%, at 28th day was 73.1% and at the end of follow-up was 91.75%. The study showed that the highest rate of mortality occurs between 1-7 and 8-14 days after admission. As the length of hospital stay increase, the hazard of time to death will increase (Figure 1).

In this retrospective cohort study, children with impaired consciousness had a higher risk of death than normally conscious children.

The median time to death of children who had impaired consciousness was 12 days, which is lower than 21 days for children with normal consciousness level. This difference is statistically significant with p-value=0.001 (Figure 2).

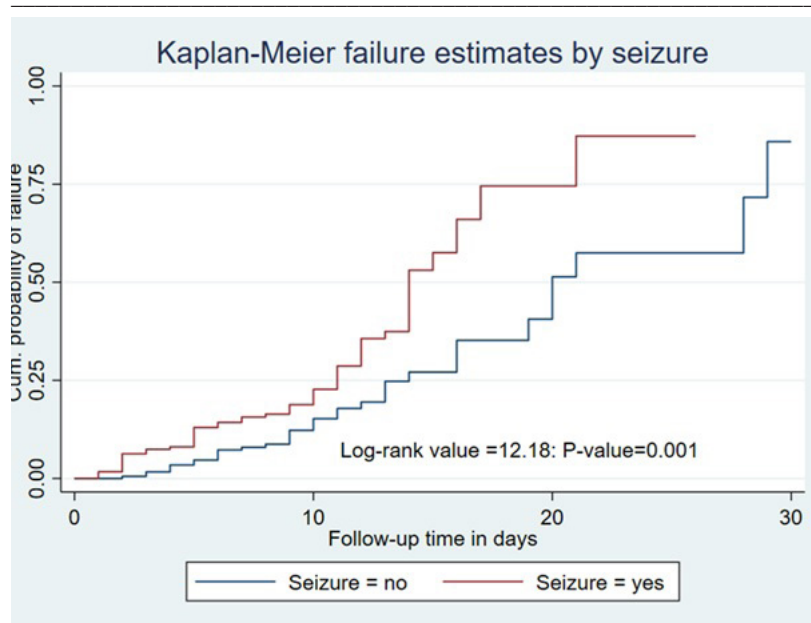


Figure 3. Kaplan-Meier failure curve by seizure of children with bacterial meningitis in Jimma University Medical Center Southwest Ethiopia 2022 (N=359).

The finding revealed that children who were presented with seizure on admission had an increased risk of death than those who had no seizure. The median time to death of children with seizure was 14 days, which is shorter than those children who had no seizure (20 days). This difference is statistically significant with p-value=0.001 (Figure 3).

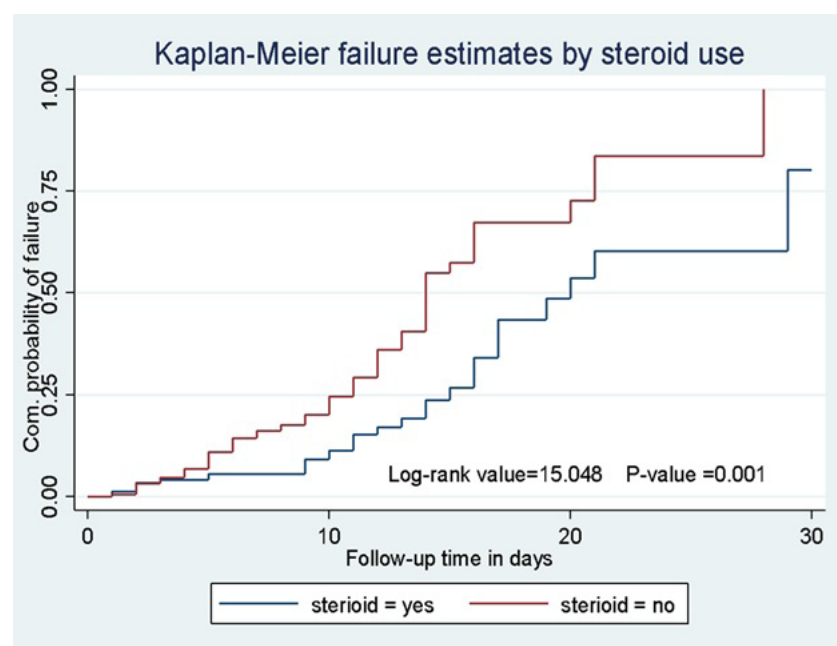


Figure 4. Kaplan-Meier failure curve by steroid drug treatment of children with bacterial meningitis in Jimma University Medical Center Southwest Ethiopia 2022 (N=359)

Predictors of time to death among children with bacterial meningitis

The bivariate Cox proportional hazard regression model indicated that age, under nutrition, exclusive breastfeeding status, comorbidity, duration before admission, impaired consciousness, seizure, positive sign (kerning/brudzinski), CSF glucose, CSF protein, CSF WBC, use of steroid,

oxygen use, ceftriaxone and ampicillin were associated with time to death ($p < 0.25$). Variables having $p < 0.25$ in bivariate analysis were fitted to multivariable cox proportional hazard regression model. In the multivariable Cox proportional hazard model impaired consciousness, seizure and steroid drug use were significantly associated variables with the outcome variable ($p < 0.05$).

The hazard of death among children who had impaired consciousness was 3.88 times higher than in their counterparts (AHR=3.88; 95% CI 1.9- 7.9). The risk of death among children who had seizures was 2.2 times as high as in children who had no seizure (AHR=2.2; 95% CI 1.06- 4.45).

Children who were not treated with a steroid drug had 4.8 times higher risk of death than children who were treated with it (AHR= 4.8; 95% CI 2.03-11.3) (Table 4).

Table 4. Bivariate and multivariable Cox proportional hazard regression analysis of predictors of time to death among children with bacterial meningitis admitted at paediatric ward of Jimma University Medical Center, Southwest Ethiopia, 2022

Variables	Category	Death (%)	Censored (%)	AHR & 95%CI	P-value
Age	Under 2 years	86 (30.3)	198 (69.7)	1.41 (0.3, 6.5)	0.662
	2 to 5 years	10 (22.7)	34(77.3)	0.78 (0.13, 4.6)	0.782
	Above 5 years	2 (6.5)	29 (93.5)	1	
Undernutrition	Yes	64(36.6)	111(63.4)	0.63 (0.3, 1.3)	0.211
	No	34 (18.5)	150 (81.5)	1	
Exclusive breast-feeding	Yes	70 (23.4)	229 (76.6)	1	
	No	28 (46.7)	32 (53.3)	0.97 (0.45, 2.1)	0.949
Comorbidity	Yes	86 (37.9)	141 (62.1)	1.86 (0.73, 4.7)	0.19
	No	12 (9.1)	120 (90.9)	1	
Duration before admission	≥3 days	71(35.5)	129(64.5)	1.03 (0.49, 2.2)	0.923
	<3 days	27(17)	132(83)	1	
Impaired consciousness	Yes	69(61.6)	43(38.4)	3.88 (1.9, 7.9)	0.001***
	No	29(11.7)	218 (88.3)		
Seizure	Yes	69(61.6)	43(38.4)	3.88 (1.9, 7.9)	0.001***
	No	29(11.7)	218(88.3)	1	
Positive sign	Yes	62(35.2)	114(64.8)	2.2 (1.06, 4.4)	0.033*
	No	36(19.7)	147(80.3)	1	
CSG glucose	Yes	11(73.3)	4(26.7)	1.93 (0.73, 5.0)	0.181
	No	87(25.3)	257(74.7)	1	
CSF protein	≤45mg/dl	28 (34.6)	53 (65.4)	0.94 (0.45-2)	0.877
	>45mg/dl	23 (15,9)	122 (84.1)	1	
CSFWBC	>100	22 (37.3)	37 (62.7)	1.26 (0.61-2.6)	0.529
	≤100	29 (17.4)	138 (82.6)	1	
Use of steroid	≥100	11 (35.5)	20 (64.5)	0.88 (0.41-1.9)	0.752
	<100	40 (20.5)	155 (79.5)	1	
Oxygen use	Yes	49(29.5)	117(70.5)	1	
	No	49(25.4)	144(74.6)	1.51 (0.7, 3.24)	0.294
Ceftriaxone	Yes	95(32.8)	195(67.2)	1	
	No	3(4.3)	66(95.7)	0.35 (0.06, 2.08)	0.249
Ampicillin	Yes	11(12.8)	75(87.2)	1.05 (0.37, 2.96)	0.919
	No	87(31.9)	186(68.1)	1	

*Statistically significant at $p<0.05$; ***statistically significant at $p<0.001$

Discussion

The study aimed to assess the time to death and its predictors among children with bacterial meningitis, and the sociodemographic, health-related, clinical, laboratory and treatment-related predictors. The finding showed that by the end of the follow-up period, 261 children were censored, and 98 had died resulting in the death proportion of 27.2%, and an incidence rate of 2.87 per 100-child day. The overall proportion of deaths that occurred in this study was similar to that of the study done in Nigeria, at 27.2%.[19] The possible explanation of this similarity might be due to the same age range of the study participants, of one month to fifteen years, a retrospective study design, covering the African meningeal belt region, and a similar review of three years' records.

The finding, however, was higher than that of the study conducted in North America, 2.8%, Central America, 23.7%, [21] and Pakistan, 10.1%. [20-22] The possible explanation for this difference might be the difference in paediatric ward setup and level of care. Unlike in our case, developed country hospitals have advanced paediatric intensive care units and advanced medical and surgical care for children with bacterial meningitis. The finding was also higher than studies done in Ethiopia: Dilla 19.2%, [11] Debreworkos 4.1%, [13] Bahir Dar 3.4%, [18] Harar 11.1% [4] respectively. This discrepancy might be due to differences in the age of study participants, study design, sample size, and study period during the coronavirus epidemic. Another possible explanation for this difference may be due to the health-seeking and utilization behaviour of the community, and immediate access to a high level of care, since JUMC is the only referral hospital in southwest Ethiopia serving four regions. Our study site is the only referral center in southwest Ethiopia; as a result, children with complicated bacterial meningitis from four regions were referred to the hospital, which may result in high death rate.

However, the finding of this study was lower than the study conducted in Nepal 33.3 %, [23] Malaysia 31.2%, [24] Angola 37% [24] and 32.65% Bedele south west Ethiopia. [15] This might be due to the design, sample size, difference in study population, study period (with coronavirus epidemic), and differences in healthcare infrastructure. Another possible explanation for this difference may be due to the introduction of the conjugate vaccine in Ethiopia.

The median time to death in this study is 16 days, which is in line with the study done in Central America, 14 days. [20] The possible reason might be due to the same characteristics of study subjects with age and the same study design used. The finding of this study is notably different from the prospectively conducted descriptive study done in Angola, 18.5 hours, [25] Nigeria, 6 days, [19] and Madagascar, 4.5 days. [17] The discrepancy might be due to study design, sample size, age difference between study participants, and health care setup practice and policy of the country. The differences in study design, sample size, and age distribution influence survival estimates and risk factor identification.

In this study, impaired level of consciousness was a statistically significant predictor of time to death among children with bacterial mortality. About one-third of study participants had impaired consciousness. Our result showed that children who had an impaired level of consciousness were 3.88 times at risk of death, having short median time of 12 days compared to that of their counterparts, at 21 days. This finding is consistent with previous studies in Malaysia 30.8%, [24] Afghanistan 16.5%, [26] Malawi 28.2%, [27] Angola, [25] Nigeria, [19] and Ethiopia (Harrar, 46%, Gondar, 32.5%, and Jimma, 55.6%). [4,7,12,28] The finding is supported by the clinical evidence that an altered level of consciousness on admission may be present due to untreated bacterial meningitis resulting from late presentation at the hospital. This critical condition causes brain injury and death within a short time.

Moreover, coma during admission may result from cerebral hemorrhage, hypoglycemia, and cerebral edema, which contribute to an increased risk of mortality and immediate death.

The result also showed that seizure was a significant predictor of time to death. Children who had seizures were 2.2 times more likely to die than children who had none. Based on our study, about half of the children had a seizure during admission. Children with BM, who were admitted with seizures, had a shorter survival time (median time to death of 14 days) than those children who had no seizure (20 days). This finding was supported by studies done in Angola 32%, [25] Nigeria, [19] and Ethiopia (Dilla 51.6%, Gondar 40% and Debre Markos 29%). [11-13] The clinical evidence that the immature brain in children deteriorates if the child develops a seizure supports this finding. Seizures may occur due to cerebral irritation caused by the inflammatory process, leading to severe meningitis and an increased risk of early death. Our study revealed that steroid drug use was a significant predictor of time to death from bacterial meningitis. The findings revealed that 52.3% of children were not treated with steroid drugs. Although the use of steroids like dexamethasone in managing bacterial meningitis in children remains controversial, they can help reduce mortality by inhibiting pro-inflammatory mediators. Our result reveals that children who were not treated with the steroid drug had a 4.8 times higher likelihood of dying than those who were treated with the steroid drug. Study participants, who were not treated with a steroid drug, had shorter survival time than those who were treated with a steroid drug. This finding is consistent with the prospective cohort study finding in Afghanistan of 47.4%, [26] and studies done in Ethiopia (Bahir dar 56.4% and Jimma 33.3%). [18,28] It is also supported by the clinical evidence that since bacterial meningitis causes severe inflammation of the meninges, lack of steroid drug administration before any antibiotics causes

neurological damage, including hearing loss, cognitive impairment, seizure, focal neurological deficits and death. However, our finding is not supported by studies done in Taiwan, [29] and a meta-analysis in china. [30] The possible reason for the variation might be due to the difference in age, study design, study setting and other sociodemographic characteristics of study participants.

Strengths and Limitations of the study

The strength of this study is that a large sample comprising more than half the study population covering three years was used to increase representativeness. Likewise, the study population at Jimma University Medical Center represented a large catchment area, thereby increasing the generalizability of the findings. However, the limitation is that the study was retrospective, based on previous patient chart records, which did not necessarily display all the required study factors like religion, ethnicity, and educational status of the family. In addition, incomplete records were removed from the sample, which may have introduced a selection bias and a likely under- or over-estimation of time to deaths. That notwithstanding, the results of this study shed some light on the estimated time to death among children with BM in Jimma University Medical Centre, which can be used for more comprehensive studies on the subject.

Conclusion and Recommendation

The proportion of BM mortality was found to be 27.2% and the overall median time to death was 16 days. Impaired level of consciousness, seizure and non-steroid drug use are predictors associated with death from bacterial meningitis in children. Based on the findings the researchers recommend strengthening health care strategies to provide quality care to children with bacterial meningitis. To prevent complication and death of admitted children, health professionals should provide steroid drug consistently before or during antibiotics administration.

Health care providers should closely monitor and follow up children admitted with bacterial meningitis. Prospective studies should be conducted to determine the effect of a wide range of predictors on time to death from bacterial meningitis.

Authors' Contributions

AWA was participating in the Conceptualization; Data curation; Formal analysis and Funding acquisition; GST and TKT had gone through Investigation; Methodology; Software; Supervision; Validation; Visualization; Roles/Writing - original draft; and Writing - review & editing.

Declaration of competing interest

The authors declared that there is not any conflict of interest to this study.

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Availability of the data

The data are accessible from the corresponding author upon reasonable request.

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References

1. Oordt-Speets A, Bolijn R, van Hoorn R, Bhavsar A, Kyaw M . Global etiology of bacterial meningitis: A systematic review and meta-analysis. *PLoS ONE*.2018; 13(6): e0198772. <https://doi.org/10.1371/journal.pone.0198772>
2. WHO. Defeating meningitis by 2030: baseline situation analysis. 2010 MenAfriVac® vaccine launch Burkina Faso. *who website* . 2019;68. https://terrance.who.int/mediacentre/data/sage/SAGE_Docs_Ppt_April2019/9_session_meningitis/April2019_Session9_defeating_meningitis_baseline_situation_analysis.pdf. Accessed on February 3rd 2024.
3. GBD2016MeningitisCollaborators. Global, regional, and national burden of meningitis, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet. Neurology*.2018;17(12), 1061–1082. [https://doi.org/10.1016/S1474-4422\(18\)30387-9](https://doi.org/10.1016/S1474-4422(18)30387-9)
4. Adem F, Tasew A, Siraj A, & Mohammed M. Treatment Outcomes and Associated Factors among Children Hospitalized with Acute Bacterial Meningitis in Eastern Ethiopia: A Cross-Sectional Study. *Patient related outcome measures*.2020; 11, 241–248. <https://doi.org/10.2147/PROM.S277586>
5. Soeters H, Diallo A, Bicaba W, Kadadé G., Dembélé A, Acyl M, Nikiema C, Sadji Y, Poy A, Lingani C, Tall H, Sakandé S, Tarbangdo F, Aké F, Mbaeyi S, Moïsi J, Paye M, Sanogo, Y Vuong, J Wang X, ... MenAfriNet Consortium . Bacterial Meningitis Epidemiology in Five Countries in the Meningitis Belt of Sub-Saharan Africa, 2015-2017. *The Journal of infectious diseases*.2019; 220(220 Suppl 4), S165–S174. <https://doi.org/10.1093/infdis/jiz358>
6. Mwenda J, Soda E, Weldegebriel G, Katsande R, Biey N, Traore T, de Gouveia, L, du Plessis M, von Gottberg A, Antonio M, Kwambana-Adams B, Worwui A, Gierke R, Schwartz S, van Beneden C, Cohen A, Serhan F, & Lessa F. Paediatric Bacterial Meningitis Surveillance in the World Health Organization African Region Using the Invasive Bacterial Vaccine-Preventable Disease Surveillance Network, 2011-2016. *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America*.2019; 69(Suppl 2), S49–S57. <https://doi.org/10.1093/cid/ciz472>

7. Esayas Kebede Gudina. Assessment of Treatment Strategies in Acute Bacterial Meningitis in Ethiopia. *Ludwig-Maximilians-Universität, Munich*. 2016. https://edoc.ub.uni-muenchen.de/20115/7/Gudina_Esayas.pdf. Accessed 20 Jan 2024
8. The Ethiopian public health institute. Third phase post meningitis campaign vaccination coverage survey, Eastern Ethiopia. *The Ethiopian Public Health Institute*. 2016. http://dataverse.nipn.eph.gov.et/bitstream/handle/123456789/1082/Report_of_3rd_phase_Post_Men_A_coverage_survey%202016.pdf?sequence=1&isAllowed=y. Accessed 20 Jan 2024
9. Mihret W, Lema T, Merid Y, Kassu A, Abebe W, Moges B, Tenna A, Woldegebriel F, Yidnekachew M, Mekonnen , Ahmed A, Yamuah L, Silamsaw M, Petros B, Oksnes J, Rosenqvist E, Ayele S, Aseffa A, Caugant D, & Norheim G. Surveillance of Bacterial Meningitis, Ethiopia, 2012-2013. *Emerging infectious diseases*. 2016; 22(1), 75-78. <https://doi.org/10.3201/eid2201.150432>
10. Pickering L, Jennum P, Ibsen R, & Kjellberg J. Long-term health and socioeconomic consequences of childhood and adolescent onset of meningococcal meningitis. *European journal of pediatrics*. 2018; 177(9), 1309-1315. <https://doi.org/10.1007/s00431-018-3192-0>
11. Sileshi Elias M, Kaso A, Yabibal Gebeyehu MD. Bacterial meningitis treatment outcome and associated factors among children admitted to the pediatric ward, Dilla university referral hospital, Dilla, Ethiopia. *European Journal of Biomedical and Pharmaceutical Sciences*. 2021.
12. Amare A, Kebede T, & Welch H. Epidemiology of bacterial meningitis in children admitted to Gondar University Hospital in the post pneumococcal vaccine era. *The Pan African medical journal*, 2018;. 31, 193. <https://doi.org/10.11604/pamj.2018.31.193.10254>
13. Abiy H, Shiferaw Z, Tafere Y. Clinical Outcome of Meningitis and Its Risk Factors Among Children Admitted in Debre Markos Referral Hospital Pediatric Ward, Northwest Ethiopia, 2019. *Research Square*. 2020; DOI: 10.21203/rs.3.rs-36044/v1.
14. Tadesse T, Foster T, Shibeshi S, & Dangiso T. Empiric Treatment of Acute Meningitis Syndrome in a Resource-Limited Setting: Clinical Outcomes and Predictors of Survival or Death. *Ethiopian journal of health sciences*. 2017; 27(6), 581-588. <https://doi.org/10.4314/ejhs.v27i6.3>
15. Bekele F, Ahmed A, Kedir A, & Sheleme T. Treatment outcome and associated factors of bacterial meningitis at pediatric wards of southwestern Ethiopian hospital: a prospective observational study. *Journal of pharmaceutical health care and sciences*. 2021; 7(1), 41. <https://doi.org/10.1186/s40780-021-00224-9>
16. World Medical Association (WMA) Declaration of Helsinki (as amended by the 64th WMA General Assembly, Fortaleza, Brazil, October 2013. <http://www.wma.net/en/30publications/10policies/b3/index.html>), accessed 20 Jan 2024
17. Mioramalala A, Razafindratovo R, Rakotozanany A, Miarambola R, Weldegebriel G, Mwenda M, Robinson L. Analysis of Death and Survival Factors Associated with Childhood Bacterial Meningitis at a Reference Pediatric Hospital in Antananarivo, Madagascar. *J Immunol Sci*. 2018; S (003): 17-23
18. Tewabe T, Fenta A, Tegen A, Mezgebu M, Fentie T & Zeleke T. Clinical Outcomes and Risk Factors of Meningitis among Children in Referral Hospital, Ethiopia, 2016: A Retrospective Chart Review. *Ethiopian journal of health sciences*. 2018; 28(5), 563-570. <https://doi.org/10.4314/ejhs.v28i5.7>
19. Kuti P, Bello O, Jegede O, Olubosede O. Epidemiological, clinical and prognostic profile of childhood acute bacterial meningitis in a resource poor setting. *J Neurosci Rural Pract*. 2015 Oct-Dec; 6(4):549-57. doi: 10.4103/0976-3147.165424. PMID: 26752902.

20. Adil M, Hodges S, Charalambous L, Kiyani M, Liu B, Lee H, et al. Paediatric bacterial meningitis in the USA: Outcomes and healthcare resource utilization of nosocomial versus community-acquired infection. *J Med Microbiol.* 2020;70(1). <http://dx.doi.org/10.1099/jmm.0.001276>
21. Olson D, Lamb M, Gaensbauer J, Todd K, Halsey N, Asturias E & Guatemala Pediatric Bacterial Surveillance Working Group . Risk Factors for Death and Major Morbidity in Guatemalan Children with Acute Bacterial Meningitis. *The Pediatric infectious disease journal.* 2015; 34(7), 724–728. <https://doi.org/10.1097/INF.0000000000000720>
22. Bari, A., Zeeshan, F., Zafar, A., Ejaz, H., Iftikhar, A., & Rathore, A. W. Childhood Acute Bacterial Meningitis: Clinical Spectrum, Bacteriological Profile and Outcome. *Journal of the College of Physicians and Surgeons--Pakistan : JCPSP.* 2016; 26(10), 822–826.
23. Shrestha G, Tandukar S, Ansari S. et al. Bacterial meningitis in children under 15 years of age in Nepal. *BMC Pediatr.* 2015;15, 94 . <https://doi.org/10.1186/s12887-015-0416-6>
24. Basri R, Zueter A, Mohamed Z, Alam K, Norsadadah B, Hasa A, Hasan H & Ahmad F. Burden of bacterial meningitis: a retrospective review on laboratory parameters and factors associated with death in meningitis, Kelantan Malaysia. *Nagoya journal of medical science.* 2015; 77(1-2), 59–68.
25. Roine I, Pelkonen T, Bernardino L, et al. Factors affecting time to death from start of treatment among children succumbing to bacterial meningitis. *The Pediatric Infectious Disease Journal.* 2014 Aug;33(8):789-792. DOI: 10.1097/inf.0000000000000350.
26. Rahimi B, Ishaq N, Mudaser G, Taylor WR. Outcome of acute bacterial meningitis among children in Kandahar, Afghanistan: A prospective observational cohort study. *PLoS One.* 2022;17(4):e0265487. <http://dx.doi.org/10.1371/journal.pone.0265487>
27. Wall E, Cartwright K, Scarborough M, Ajdukiewicz M, Goodson P, Mwambene J, Zijlstra E, Gordon S, French N, Faragher B, Heyderman R, & Lalloo G. High mortality amongst adolescents and adults with bacterial meningitis in sub-Saharan Africa: an analysis of 715 cases from Malawi. *PloS one.* 2013; 8(7), e69783. <https://doi.org/10.1371/journal.pone.0069783>
28. Gudina K, Tesfaye M, Wieser A, Pfister H & Klein M. Outcome of patients with acute bacterial meningitis in a teaching hospital in Ethiopia: A prospective study. *PloS one.* 2018; 13(7), e0200067. <https://doi.org/10.1371/journal.pone.0200067>
29. Hsieh Y, Lai R, Lien Y, Chang N, Huang C, Cheng C, Kung T, Lu H. Nationwide Population-Based Epidemiological Study for Outcomes of Adjunctive Steroid Therapy in Pediatric Patients with Bacterial Meningitis in Taiwan. *Int J Environ Res Public Health.* 2021 Jun 12;18(12):6386. doi: 10.3390/ijerph18126386.
30. Shao M, Xu P, Liu J, Liu W, Wu X. The role of adjunctive dexamethasone in the treatment of bacterial meningitis: an updated systematic meta-analysis. *Patient Prefer Adherence.* 2016; Jul 14;10:1243-9. doi: 10.2147/PPA.S109720.