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BACTERIAL MENINGITIS TREATMENT OUTCOME AND ASSOCIATED FACTORS AMONG CHILDREN ADMITTED TO THE PEDIATRIC WARD, DILLA UNIVERSITY REFERRAL HOSPITAL, DILLA, ETHIOPIA

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ABSTRACT

Background: Meningitis is inflammation of the meninges which affects all age groups from newborn to elderly. The highest mortality and morbidity of meningitis occur in Sub-Saharan Africa despite the advance in technology. Monitoring the level of treatment outcome has significant value in designing strategies to control meningitis. **Objective:** This study aimed to assess the treatment outcome of bacterial meningitis and associated factors among children in the pediatric ward, Dilla University Referral Hospital (DURH), Southern Ethiopia. **Methods:** A retrospective institutional-based cross-sectional study design was used to assess the treatment outcome and associated factors of bacterial meningitis among children registered from March 2019 to February 2020 in DURH. Then data was entered into Statistical Package for Social Science version 25 software for analysis. Bivariate and multivariate analysis was used to determine predictors of favorable treatment outcomes. The odds ratio and 95% confidence intervals were calculated. P-value less than 0.05 were considered as statistically significant. **Results:** Among 120 patients, 82(68.3%) came from rural areas and 81(67.5%) were males respectively. The overall proportion of favorable treatment outcomes was 92(76.7%) while 28(23.3%) have poor treatment outcomes. In this study, being female [AOR= 0.12(0.03, 0.62)], undernourished children [AOR= 0.18(0.03, 0.77)], exclusive breastfeeding 38.7(6.4, 234.4) and clinical presentation such as seizure [AOR= 49 (5.35, 450.31)] and HGF [AOR= 78.69(3.82, 1619.27)] were found to be statistically associated with favorable treatment outcome of meningitis. **Conclusion:** The overall proportion of favorable treatment outcomes was 76.7%. In this study, being female, exclusive breastfeeding, undernourished children, and children with HGF and seizure were significantly associated with Favourable treatment outcomes. Therefore, early diagnosis, critical follows up and effective management of patients with clinical presentation is needed.

KEYWORDS: Treatment outcome, Bacterial meningitis, Dilla University.

BACKGROUND

Bacterial Meningitis (BM) is the inflammation of membranes covering the brain and spinal cord. Meningitis can be due to both infectious and non-infectious causes.[1-3] Bacterial meningitis is one of the most serious pediatric infections. It is associated with a high rate of acute complications and a risk of long-term morbidity and mortality.[4,5] Meningitis cases occur worldwide. Globally, meningitis deaths decreased by 21·0% from 1990 to 2016 while incident cases increased from 2.5 million to 2.82 million in 2016. The highest mortality rates and incidence rates were found in the African meningitis belt.[6] The case fatality rates for meningitis vary by age group, country, causative organism, and time of onset.[7] Bacterial meningitis is a major cause of death both in the developed and developing world. In developed countries, the case fatality rate is 10%, while in other developing countries the mortality rate was 22-35%.[8-10]

Before the introduction of vaccines, *Haemophilus influenza type b* (HIb), *Streptococcus pneumonia*, and *Neisseria meningitides* were reported to be the commonest causes for bacterial meningitis.[1,11-14] The burden of bacterial meningitis due to these pathogens decreased significantly following the introduction of vaccines in the high-income nation. However, BM continues to be a cause for concern in Low and Middle-Income Countries (LMIC) either due to the absence of immunization vaccines in their national immunization programs.[12,15,16] In resource-poor settings, particularly in areas with high Human Immune Virus (HIV) prevalence such as sub- Saharan Africa, the mortality rate of BM was as high as 50%.[17] Mortality rates

associated with pneumococcal, HIb, and meningococcal meningitis were 45%, 29%, and 8%, respectively. At 0–4 years of age, the estimated incidences of HIb meningitis and all classic HIb diseases were 70 and 100 cases per 100,000 population per year respectively.[18] Bacterial meningitis has remained a serious health concern for Ethiopia for the past few decades.[1] In Ethiopia, bacterial meningitis accounts for approximately 6-8 % of hospital admissions with a case fatality rate of as high as 22-28%.[19] For example, at Jimma University patients managed as cases of Acute Bacterial Meningitis (ABM) suffered from a high rate of poor outcomes (36.7%) with a mortality rate of 22.2%.[20]

Factors that may increase the risk of meningitis were the age of infancy, history of head injury, bottle feeding, recent upper respiratory infection, tuberculosis infection, overcrowded living conditions, low socioeconomic status, and compromised immune system.[21-24]

In most occurrences, if the disease is diagnosed early and adequate treatment started on time, the patient will be improved immediately.[16,25] However, delayed presentation and treatment initiation, limited diagnostic facility, and poor standards of care are some of the major reasons for poor outcomes of meningitis in Africa.[26-28] The survivors of meningitis may suffer from permanent damage including auditory loss, neurologic disability, or physical deformity.[29-32] Variation in serotype causing meningitis among children from place to place, year to year causes the difference in outcome.[33] This influences policymakers as well as health providers for extra evidence on level treatment outcome. Thus, this study aimed to determine the bacterial meningitis treatment outcome and associated factors among children admitted in the pediatric ward in DURH.

METHODS AND MATERIALS

Study Area and setting

This cross-sectional study was conducted at DURH. It is found in Dilla town, Gedeo zone Southern Nations, Nationalities, and Peoples' Region (SNNPR). It was named DURH in 2001, E.C. It is located 360km from Addis Ababa and 90km from Hawassa which is the administrative center of Southern nations. The hospital had departments such as internal medicine, surgery, Gynecology& Obstetrician, pediatric, orthopedic & psychiatric wards. The Department of Pediatric has three wards such as the Neonatal Intensive Care Unit (NICU), the critical ward & the Therapeutic Feeding Unit (TFU) with a total of sixty-one (61) beds. Most of the patients come from the Gedeo Zone, Sidama Region as well as the West Guji Zone.

Study design, period, and population

A retrospective institutional-based cross-sectional study design was conducted from April 2020 to May 2020. All children beyond 1 month to 15 years old admitted to DURH pediatric ward from March 2019 to February 2020 were considered as source populations. Children beyond 1 month to 15 years old admitted with BM cases and had complete documentation were included in the study. Patients who have incomplete information on the register were excluded from the study.

Sample size estimation and sampling techniques

The sample size was determined by using single population proportion formula, $\mathbf{n= (z_1-\alpha/2)^2 x\ p\ (1-p)\ /\ d^2}$ with a margin of precision of 5%, $\mathbf{\alpha/2}$ = 1.96, the desired confidence interval of 95% and proportion of bacterial meningitis taken as 50% since there was no study done on the prevalence of bacterial meningitis. After adding 10% for non-response rate, the total sample size was 422. Since the number of patients seen in the pediatric ward was less than 10,000 we used a correction formula. The final sample size after the correction was found to be 120. Before starting to select a study sample, all cases of under-five children admitted and discharged from the DURH pediatric ward were sorted & listed from the department discharge logbook. After the establishment of the sampling frame, the selection of study samples was done using Simple random sampling techniques by lottery method.

Data collection procedures and quality management

Data were collected by a review of the participant chart and admission registration logbook using a predefined questionnaire. Questionnaires were developed in English. The questionnaire has factors such as sociodemographic data, health-related factors, comorbidity condition, clinical manifestation, treatment outcome, and laboratory results of Cerebro Spinal Fluid (CSF) analysis as well as treatment-related factors. Before data collection, two-day training was given to data collectors and supervisors to have a common understanding of the data collection tool. The pre-test was performed in Yirga Chafe Hospital and based on this result; the questionnaire was modified for some unclear ideas and statements. The collected data were checked for completeness and consistency of response manually. In case of inconsistent and incomplete data, the questionnaires were returned to the data collector for correction.

Study Variables and Operational Definitions

The dependent variable was bacterial meningitis treatment outcome. The final treatment outcome of patients under treatment was cured, referred, left against treatment, and died. The treatment outcome was considered favorable if the children's outcome was improved or discharged with advice after medical treatment. On the other hand, the treatment outcome was considered poor if the children have died, developed extra complications, and transferred to other health facilities for further management. The socio-demographic factors, health-related factors, co-morbidity conditions, clinical manifestation, CSF results, and treatment-related factors were considered as the independent variables.

Data analysis procedure

Data were coded, cleaned, entered, and analyzed using Statistical Package for Social Science (SPSS) software version 25. Variables with a p-value of less than 0.25 in the bivariate logistic regression analysis were considered as the candidate for multivariate logistic regression analysis. Variable with a p-value less than 0.05 in the multivariate logistic regression model was considered to be statistically significant. Finally, the result of the study was presented in text, graph, pie chart, and table.

Ethics approval and consent to participate

Ethical approval was obtained from the Dilla University School of Public Health Institutional Review Board. The permission to collect data from charts of patients was obtained from the DURH administration.

RESULT

Patient's socio-demographic characteristics

Among 120 study participants analyzed, 82(68.3%) came from rural areas and 81(67.5%) were males. The mean age of the respondents was 2.48(Standard deviation (SD) is 1.3 years). About 53(44.2%) of the patients were in the age group 0-1 year were (Table 1).

Table 1:- Socio-demographic characteristics of children with BM admitted to Dilla University Referral Hospital, March 2019 to February 2020.

Variable	Categories	Frequency (%)
Sex	male	81(67.5)
	female	39(32.5)
Age category	0-1year	53(44.2)
	2 -5 year	34(28.3)
	6- 15 years	33(27.5)
Mean age	$2^{1}/_{2}$ years	2.48 ± 1.236
Residence	Rural	82(68.3)
	Urban	38(31.7)

Patients' Health-related characteristics

Out of 120 patients, 27(22.5%) were undernourished while about 96(80%) of children get exclusive breastfeeding. Among study participants, 111(92.5%) of children were vaccinated whereas 9(7.5%) were unvaccinated. Regarding the number of a person living in the house, 79(65.8%) of children were lived together within a greater or equal 6 families (Table 2).

Table 2:- Health-related characteristics of children with BM admitted to Dilla University Referral Hospital, March 2019 to February 2020.

Clinical characteristics	Categories	Frequency (%)
Undernourished	Yes	27(22.5)
	No	93(77.5)
Immunization status	Fully vaccinated	69(57.5)
	Partially vaccinated	42(35)
	Unvaccinated	9(7.5)
Exclusive breastfeeding	Yes	96(80)
	No	24(20)
# of a person living together	less 6	41(34.2)
	greater than or equal 6	79(65.8)
History of a daycare center	yes	0(0)
	No	120(100)

Patients' clinical characteristics

Out of 120 patients diagnosed with bacterial meningitis, 65(54.2%) had a history of URTI. The main sign and symptoms observed 62(51.7) had a seizure, 21(17.5) fever, 19(15.8) coma, and 18(15%) positive meningeal signs respectively. Regarding the time of initiation of treatment, 106(88.3%), 8(6.7%), and 6(5%) of patients had treated less than 1hrs, 1-2 hrs, and greater than 2hrs respectively. On other hand, out of all patients treated for BM 47 (39.2%) have treated with ceftriaxone only and 53(44.2%) with vancomycin meanwhile 20(16.7%) had received Crystalline penicillin plus CAF or Ampicillin (Table 3).

Table 3:- Clinical characteristics of children with BM admitted to Dilla University Referral Hospital, March 2019 to February 2020.

Clinical characteristics	Categories	Frequency (%)
History of URTI	Yes	65(54.2)
	No	55(45.8)
Recent history of head trauma	No	120(10)
Sign and symptom	Coma	19(15.8)
	Seizure	62(51.7)
	HGF	21(17.5)
	Positive meningeal sign	18(15)
CSF result suggestive	Yes	88(73.3)
	No	32(26.7)
Time of initiation of treatment	less than 1hr	106(88.3)
	1-2hrs	8(6.7)
	greater 2hrs	6(5)
Steroid was given	Yes	86(71.7)
	No	34(28.3)
Time Steroid was given	Before antibiotics	84(97.7)
	with antibiotics	2(2.3)
Treatment has taken	Crystalline penicillin+CAF Or Ampicillin	20(16.7)
	Ceftriaxone	47(39.2)
	Ceftriaxone +Vancomycin	53(44.2)

Patient characteristics and treatment outcome

A total of 92 (76.7%) patients had a favorable treatment outcome, whereas 28 (23.3%) had poor treatment outcomes. From a total of 23 (19.2%) deaths occurred, 12(10%) in males and 11(9.2%) in females. Similarly, the highest proportion of death 12(10%) and 6(5%) has occurred among children in the 6-15 years and 2-5 years age group respectively. The death rate was higher for rural residents 19(15.8%), while there were fewer deaths from urban residents 4(3.3%). The proportion of children who improved after treatment was higher in children fully or partially vaccinated 75(62.5%), whereas 4(3.3%) children improved after treatment in the unvaccinated groups (Table 4).

Table 4:- Patient characteristics and treatment outcomes with BM admitted to Dilla University Referral Hospital, March 2019 to February 2020.

Variable	Categories	Treatment outcome			
		Improved	Referred	died	Left against treatment
Sex	Female	23(19.2%)	2(1.7%)	11(9.2%)	3(2.5%)
	Male	56(46.7%)	3(2.5%)	12(10%)	10(8.3%)
Undernourished	Yes	17(14.2%)	0(0%)	4(3.3%)	6(5%)
	No	62(51.7%)	5(4.1%)	19(15.8%)	7(5.8%)
Age category	0-1years	42(35%)	2(1.7%)	5(4.1%)	4(3.3%)
	2-5years	21(17.5%)	1(0.8%)	6(5%)	6(5%)
	6-15years	16(13.3%)	2(1.7%)	12(10%)	3(2.5%)
Immunization	fully vaccinated	43(35.8%)	4(3.3%)	15(12.5%)	7(5.8%)
	Partially vaccinated	32(26.7%)	0(0%)	4(3.3%)	6(5%)
	Unvaccinated	4(3.3%)	1(0.8%)	4(3.3%)	0(0.8%)
Exclusive breastfeeding	Yes	73(60.8%)	4(3.3%)	7(5.8%)	12(10%)
	No	6(5%)	1(0.8%)	16(13.3%)	1(0.8%)
Residence	Rural	50(41.7%)	4(3.3%)	19(15.8%)	9(7.5%)
	Urban	29(24.2%)	1(0.8%)	4(3.3%)	4(3.3%)

Patient treatment outcome

Among 120 patients, 79 (65.8%) were improved while 41 (34.2%) of them were either died, left against treatment, or referred with complications to other health facilities (Figure 1).

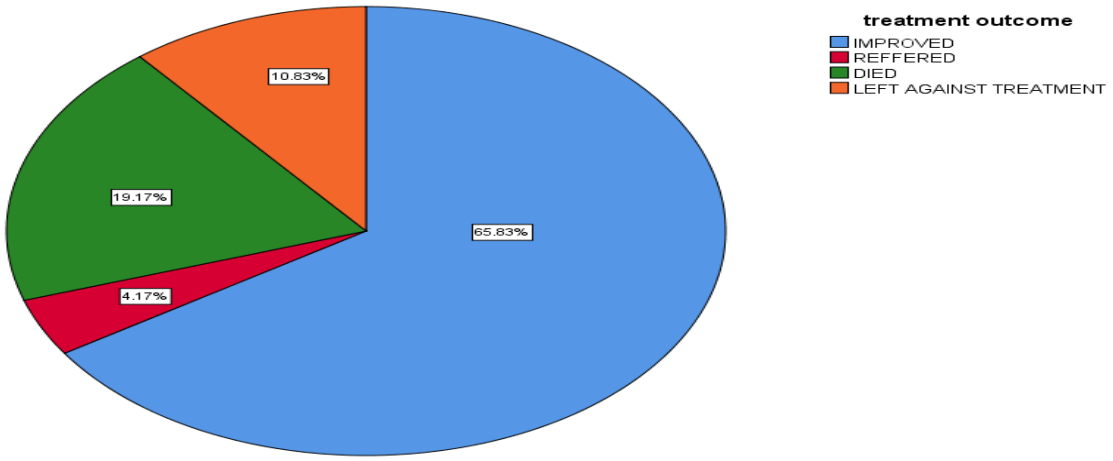

Figure 1:- Treatment outcome of children treated with BM at Dilla University Referral Hospital, March 2019 to February 2020.

Factors associated with Outcome of Acute BM

In bivariate logistic regression variables like age, immunization status, exclusive breastfeeding, overcrowding, clinical presentation, suggestive CSF result, type of antibiotic given were statistically associated with favorable treatment outcome. However, after adjusting for potential confounders in multivariate logistic regression analysis clinical presentation and age have remained statistically significant. Undernourished and female Children were 0.18 and 0.12 times less likely to have favorable treatment outcomes than counterpart [AOR= 0.18(0.03, 0.77)] and [AOR= 0.12(0.03, 0.62)] respectively. On the other hand, children who were exclusively breastfed were 38.7 times more likely to have favorable treatment outcomes than those not feed breast exclusively [AOR= 38.7 (6.4, 234.4)]. Furthermore, children with a seizure on presentation were almost 49 times more likely to have favorable treatment outcomes than those with a coma on presentation [AOR= 49 (5.35, 450.31)]. On the other hand, children with high-grade fever on presentation were 78.69 times more likely to have a good outcome than those with coma on presentation [AOR= 78.69(3.82, 1619.27)] Table 5).

Table 5:- Bivariate and multivariate logistic regression analysis of factors associated with the outcome of bacterial meningitis.

Categories	Outcome at discharge		COR(95%CI)	AOR(95%CI)
	Favorable (%)	Poor (%)		
Age				
0-1 year	46(38.3)	7(5.8)	1	1
2-5 year	27 (22.5)	7 (5.8)	4.8(1.69,13.88)	4.3(0.87,11.33)
6- 15 year	19 (15.8)	14(11.7)	2.84(0.97,8.38)	5.47(0.92,22.77)
Sex				
Male	66(55)	15(12.5)	1	1
Female	26(21.7)	13(10.8)	0.46(0.19,1.09)	0.12(0.03,0.62)*
Residence				
Rural	59(49.2)	23(19.2)	1	1
Urban	33(27.5)	5(4.1)	2.57(0.89,7.40)	1.17(0.17,8.14)
Undernourished				
Yes	23(19.2)	4(3.3)	0.5 (0.16, 1.60)	0.18(0.03,0.77)*
No	69(57.5)	24(20)	1	1
Immunization				
Full vaccinated	50(41.7)	19(15.9)	1	1
Partially vaccinated	38(31.7)	4(3.3)	3.61(1.13, 11.49)	1.21(0.41,3.63)
unvaccinated	4(3.3)	5(4.1)	0.31(0.08,1.26)	0.63(0.12,3.39)
Exclusive breastfeed				
Yes	85(70.8)	11(9.2)	18.78(6.37, 55.33)	38.7(6.4,234.4)
No	7(5.8)	17(14.2)	1	1
History of URTI				
Yes	51(42.5)	14(11.7)	0.81(0.35, 1.88)	
No	41(34.2)	14(11.7)	1	
# of the person in the house				

<6	35(29.2)	6(5)	1	1
6 & more	57(47.5)	22(18.3)	0.45(0.17,1.20)	0.54(0.19,3.38)
Sign & symptoms				
coma	8(6.7)	11(9.2)	1	1
seizure	58(48.3)	4(3.3)	19.93(5.11, 77.86)	49(5.35, 450.31)
HGF	16(13.3)	5(4.1)	4.4(1.13, 17.08)	78.69(3.82,1619.27)
Positive Meningeal sign	10(8.3)	8(6.7)	1.72(0.47,6.32)	3.52(0.51,24.45)
Suggestive CSF result				
Yes	69(57.5)	19(15.8)	1	
No	23(19.2)	9(7.5)	1.42(0.56, 3.58)	
Treatment (Antibiotic)				
C.pencilline+ CAF / Ampicillin	16(13.3)	4(3.3)	1	1
Ceftriaxone	39(32.5)	8(6.7)	1.06(0.28,3.94)	1.67(0.32,26.3)
Ceftriaxone+Vancomycin	18(15)	35(29.2)	0.38(0.11,1.30)	2.93(0.13,6.27)
Time of Antibiotic				
<1 hour	83(69.2)	23(19.2)	2.1(0.62, 6.57)	4.52(0.52,19.39)
>= 1 hour	9(7.5)	5(4.1)	1	1

DISCUSSION

Bacterial meningitis is one of the most serious pediatric infections, as it is associated with a high rate of acute complications and a risk of long-term morbidity and mortality. The overall, proportion of patients with favorable treatment outcomes was 76.7%. This proportion was low compared to previous findings from India (89%)[34] and high compared to report from Jimma(63.3%).[20] However, it is similar to the finding from Bahirdar Ethiopia was 76%[35] and Eastern, Ethiopia(77%).[28] The possible reason for the observed difference between this and the previous studies might be explained by a late arrival to the health facility as most of the patients are from rural areas.

In this study, among 120 children 79(65.8%) were improved, 5(4.2%) were referred, 23(19.2%) died, and 13(10.8%) were left against treatment. The proportion of death in this study was lower than a study from Nepal which was 33.3%[36] and higher than findings from Kosovo (5%)[37] and Bahirdar(3.4%).[35] This is maybe due to complications during the presentation to the health facility and delays in antibiotic therapy treatment initiation.

This finding indicated that well-nourished children have good improvement after getting treated. A high favorable treatment outcome was observed in children who have good nutrition. This is in agreement with previous studies from Bangladesh[38], Sub-Saharan African[39] and Jimma University[40] that reported undernourishment can increase the risk of poor treatment outcomes. This may be related to those children who have malnutrition is believed to be immunosuppression and this can aggravate and complicated infection during treatment.

In this study, children with seizures were 49 times more likely to have favorable treatment outcomes compared to children having a coma. This was consistent with previous studies from Turkey[41] and Jimma University[42] that found a similar degree of risk of poor treatment outcome among children in critical conditions. Moreover, children with HGF were 78 times more likely to have favorable treatment outcomes compared to children having a coma. This was consistent with a finding from Jimma University[20] that found children having HGF have good outcomes compared to children with coma. This may be due to children in a coma were more complicated than patients presented with fever and seizure and difficult to assess other health-related diseases. Even though our study comes up with little scientific shreds of evidence, it has some drawbacks. First, the study was based on documented data (chart review), which may not display all factors that were not documented in patients' files. Moreover, the cross-sectional nature of the study design doesn't infer the temporal relationship between the factors.

CONCLUSION

The overall proportion of favorable treatment outcomes was 76.7%. In this study, being female, exclusive breastfeeding, undernourished children, and children with HGF and seizure were significantly associated with Favourable treatment outcomes. Therefore, early diagnosis, close monitoring, and effective management of children with clinical presentation are needed to improve treatment outcomes. Moreover, strictly follow and immediate consultation with the senior pediatrician is needed for children with coma.

AUTHORS' CONTRIBUTIONS

SE, AK, and YG designed and worked on the study protocol. SE, AK, and YG prepared a data collection tool and provided training to data collectors. SE entered data to SPPS. SE, AK, and YG analyzed the data, interpreted the result, and wrote the draft and final version of the manuscript. All authors read and approved the final manuscript.

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Competing interests: The authors declare that they have no competing interests.

ABBREVIATIONS
ABM: Acute Bacterial Meningitis; AOR: Adjusted Odd Ratio; BM: Bacterial Meningitis, CI: Confidence Interval; CNS: Central Nervous System; COR: Crude Odd Ratio; CSF: Cerebro Spinal Fluid; DURH: Dilla University Referral Hospital; EPI: Expanded Program of Immunization; HGF: High-Grade Fever; HIb: Haemophilus influenza type b; HIV: Human Immune Virus; LMIC: Low and Medium-Income Countries; IPD: Inpatient Department; ICU: Intensive Care Unit; NICU: Neonatal Intensive Care Unit; NGO: Non-Governmental Organization; OPD: Outpatient Department; OR: Odd Ratio; SNNPR: Southern Nations, Nationalities, and Peoples' Region; SPSS: Statistical Package of Social Science Operating; TFU Therapeutic Feeding Unit; UHC: WHO: World Health Organization.

Availability of data and material: The datasets used or analyzed during this study were available from the corresponding author on reasonable request.

Consent for publication: Not applicable.

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