

# Factors Predicting Treatment Outcome of Neonatal Sepsis In Hawassa University Comprehensive Specialized Hospital, Southern Ethiopia: A Retrospective Cohort Study

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## ABSTRACT

**Background:** Neonatal sepsis is a systemic infection that affects newborns within the first 28 days of life. It has a significant effect on newborn mortality Worldwide. It could be responsible for as much as one-third of all neonatal deaths globally each year. The associated factors as well as clinical outcomes of neonatal sepsis are not well quantified. The aim of this study was to assess the treatment outcome and associated factors of Neonatal Sepsis in Hawassa University Comprehensive Specialized Hospital.

**Methods:** A retrospective Cohort study was conducted. All neonates admitted to neonatal intensive care unit from July 28, 2014 to July 28, 2019 were included. The source of data was registration book and patients' card. After being double checked for accuracy, data was entered into EpiData 3.1 and analyzed using SPSS version 22. Testing for statistical association between the variables was done using bivariate and multivariate logistic regressions. Poor treatment outcome includes refuse to take the treatment, development of complications, being referred to other health facilities and neonatal death.

**Results:** All charts met enrollment criteria. More than three fourth of the infants who treated were improved or recovered. Among the study participants, More than half were male and about half of them were younger than 3 days on admission. Majority of the mothers were found in the age group of 18 to 25 years. The poor treatment outcome for neonatal sepsis was high (16%). The predictors for poor treatment outcome of neonatal sepsis were being referred from other health facility (AOR=0.29, 95% CI: 0.24-0.89) and longer duration of treatment (AOR=0.36, 95% CI: 0.14-0.90).

**Conclusion:** The poor outcome of neonatal sepsis was a significant health problem in the study area. Strengthening referral system and focusing on quality of care will improve poor outcome of neonatal sepsis.

**Keywords:** Neonatal sepsis, Treatment outcome, Sidama, Southern Ethiopia

## Introduction

Globally, infections are the leading cause of neonatal deaths (1-3). Neonatal sepsis is a systemic infection occurring in infants at less than 28 days of life and responsible for causing morbidity and mortality of newborns(4). Neonatal sepsis is characterized by a positive blood culture within the first 28 days of life and is defined as a systemic inflammatory response syndrome in the presence of or as a result of a suspected or

confirmed infection with or without associated bacteremia.(5, 6). It can occur within or after the first 72 hours birth of life (7, 8). The infection within the first week after birth is called early onset whereas that occurs between the 8<sup>th</sup> and the 89<sup>th</sup> day after birth is late-onset sepsis (3, 9). The possible causes of early onset sepsis are organisms prevalent in the maternal genital tract, delivery room or operating theatre while

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nosocomial or community-acquired infection is usually responsible for late onset sepsis (7).

Sepsis related neonatal morbidity and mortality remain a significant global public health challenge (10). The WHO estimates that every year, four million newborn children die in the first four weeks of life. In developing nations, sepsis is the commonest cause and is probably responsible for 30-50% of the total neonatal deaths each year (11). Sepsis causes 28% of neonatal deaths in Africa, placing a burden on the continent's public health system with significant economic consequences (2). In Nigeria, 56.5% of the neonates were discharged in good condition after treatment while death occurred in 31.8% of them with the case-fatality rate of 26% (12).

In Ethiopia, the magnitude of the problem is significant (10). It is one of the leading causes of newborn mortality, responsible for about one-third (33%) of neonatal deaths and 5% of perinatal mortality. According to the study conducted in Tikur Anbessa and Felegehiwot Teaching Hospitals; 83.2% and 84% of the neonates with neonatal sepsis had improved at discharge while 12.5% and 14% were discharged in dead condition respectively (13, 14). The proportion of overall poor outcomes including death was 26% in Bishoftu (15). Bacterial virulence factors, timing of intervention and choice of antimicrobial therapy have a significant impact on treatment outcome of neonatal sepsis (16).

Despite of these facts and several efforts; there is little information on the status of neonatal sepsis treatment outcome in Ethiopia and virtually none in the study area. Therefore, the aim of this study was to assess the treatment outcome of neonatal sepsis. The results of this study will be a significant contribution to efforts to improve newborn health. It can also serve as the baseline for further studies.

## Methods

### Study Design, participants and setting

Retrospective Cohort study design was employed in Hawassa University Comprehensive Specialized Hospital. The hospital had more than 350 beds and expected to serve more than 12 million people of Sidama, Southern and Oromia Regions. It is found in Hawassa City, 275 km from the capital of Ethiopia, Addis Ababa. The neonatal department of the hospital had an average annual admission of more than 1,000 neonates. The study participants were all neonates admitted to neonatal department of Hawassa University Comprehensive Specialized Hospital.

### Inclusion and Exclusion Criteria

#### Inclusion Criteria

All neonates admitted to the neonatal departments of Hawassa University Comprehensive Specialized Hospital from July 28, 2014 to July 28, 2019 were included in the study

#### Exclusion Criteria

All incomplete records and lost charts of admitted neonates, during the study period, were excluded from the study

#### Sample Size

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

n= Where n is the sample size

Z  $\alpha/2$ = is the standard normal deviate (for 95% confidence level), 1.96

d= is the marginal error (taken as 0.05)

p= is the proportion

Therefore, based on the above single population proportion formula the sample size was calculated as:

$$n = \frac{(1.96)^2 * 0.26(1-0.26)}{0.05^2} = 296$$

Therefore, 296 neonates were considered for this specific study.

### Data Collection tool, techniques and period

After reviewing various literatures, data collection tool was adopted from study conducted in Mekele, Ethiopia(17). Pretesting was done on 30 charts or 10% of the total sample size. Data collection was conducted by trained data collectors from April to June, 2020.

Medical record numbers of the neonates were obtained from Neonatal Intensive Care Registration book. Integrated individual medical records were obtained by the selected record number and required data was collected by using data collection tool. Discharge summary was used to retrieve the outcome of neonatal sepsis.

Principal investigator checked for clarity and completeness of the collected data on daily bases. Consent was received from all stakeholders before reaching source document.

### Measurement of the outcome

Dependent variable for this study was the treatment outcome of neonatal sepsis. It was assessed by collecting recorded secondary data of four subsequent years' from 2014 to 2019. Each factor was dichotomized and coded. Then, 0 was

given to the group hypothesized as having poor outcome and 1 was given to the group hypothesized as having better outcome. Sex, gender, employment/qualification, age, educational status and other variables were included as the independent variables.

### Statistical Analysis and Quality Control

Adopted and standardized data collection tool, trained data collectors and daily supervision were among the efforts undertaken to assure data quality. Data was entered into epidata 3.1 and exported to and analyzed by SPSS version 22. It was edited, cleaned and coded before undertaking any analysis. Descriptive exploratory analysis was made to check for outliers and missing values. Then, simple frequencies were undertaken to describe characteristics for treatment outcome of neonatal sepsis.

To simplify the analyses, dichotomization was done. Both bivariate and multivariate logistic regression models were undertaken. To determine whether an association is exist or not, Odds ratios with 95% confidence interval (CI) and p-value of less than 0.05 were utilized. Those variables with  $p \leq 0.25$  during bivariate logistic regression were considered for final model of multivariate logistic regression.

### Operational definitions

Early onset of neonatal sepsis- is the onset of sepsis from birth to 3 days of life as it has been recorded on the chart. Late onset of neonatal sepsis- is the onset of sepsis developed within 4 to 28 days of life as it has been recorded on the chart. Preterm: - delivery of an infant before completion of 37 weeks of gestation. Good outcome: If neonate is improved after completing the treatment without any complications like: seizure, meningitis, shock, deafness and blindness. Poor outcome: If neonate is refused the treatment, develop complication, referred to other health institutions and died.

### Ethical approval

Ethical approval was obtained from the Institutional Review Board (IRB) of the Hawassa University College of Medicine and Health Sciences (Ethical Approval number: HUCMHS/IRB/125/14). Permission letter was written to concerned bodies of Hawassa University Comprehensive Specialized Hospital. Data was collected retrospectively from the records of the patients. All eligible records were accessed after getting consent/permission from concerned bodies. Informed consent was not required from

study participants since the data were collected from patient charts after their discharge.

## Results

### Socio demographic Characteristics

A total of 296 newborns were included in the study; with an overall response rate of 100%. More than three fourth (83.8%) of neonates with neonatal sepsis who received treatment were improved/recovered. Nearly half (47.6%) of the study participants were under three days old at the time of admission, and more than half (59.1%) of them were male. Majorities (55.4%) of the mothers were found in the age group of 18 to 25 years (Table 1).

### Neonatal health related factors

Most of the newborns (52.4%) were admitted with late onset neonatal sepsis. Sixty five (22%) of them had low birth weight and over two thirds (68.9%) had referred from other health facilities. Nearly all (93.6%) neonates participated in this study were term and meningitis accounts for 20.6% of the sepsis admission. Few (3.7%) had a history of birth asphyxia, and some (10.1%) were resuscitated. Less than 7 Apgar score accounts for 115 (38.9%) and 113(38.2%) at 1<sup>st</sup> and 5<sup>th</sup> minute respectively and blood culture was done only for 22(7.4%) neonates. The majority of the neonates (60.8%) were hospitalized for less than 7 days.. About 61.1% of mothers delivered their newborn in hospital and 31.4% of them delivered by caesarean section. 95.6% of them received ANC follow up during pregnancy of the index neonate. 4.7% mothers had history of febrile attack during pregnancy, 13.5% had history of PROM, 8.8% had history of obstructed labor and 40.2% stayed on labor for more than 12 hours duration (Table 2).

### Antibiotics Used for Treatment

Ampicillin and gentamycin were given for

**Table 1.** Socio-demographic characteristics of mothers and neonates admitted with sepsis in HUCSH, Southern Ethiopia, (n=296)

Variable		Frequency	Percent
Mother's age	18-25 years	164	55.4
	26-35 years	123	41.6
	36-45 years	9	3
Residence	SNNPR	174	58.8
	Oromia	122	41.2
Neonate's age	Birth to 3 days	141	47.6
	4-28 days	155	52.4
Neonate's sex	Male	175	59.1
	Female	121	40.9

**Table 2.** Neonatal health related factors among neonatal sepsis admitted to HUCSH, (n=296)

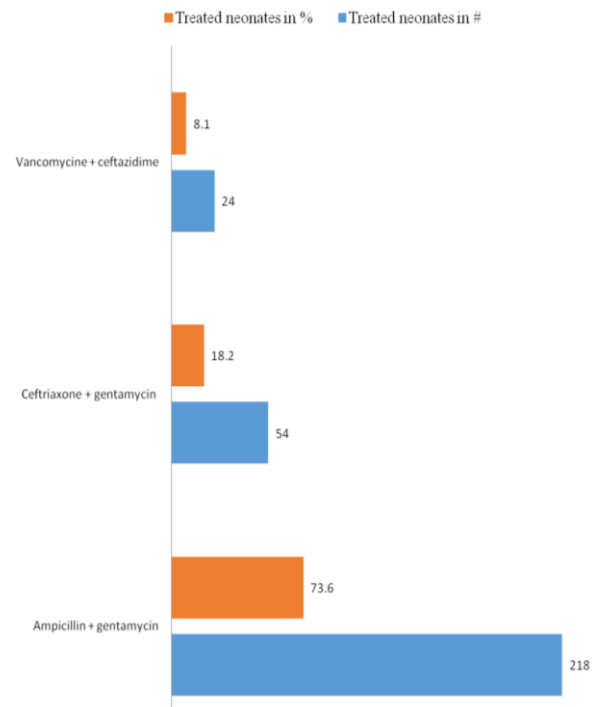
Category	Variable	Frequency	Percent
APGAR score at 1 <sup>st</sup> min.	<7	115	38.9
	≥7	181	61.1
APGAR score at 5 <sup>th</sup> min	<7	113	38.2
	≥7	183	61.8
Birth Weight at birth	<2500 grams	65	22
	2500-4000 grams	209	70.6
	>4000 grams	22	7.4
Duration of treatment	Less than 7 days	180	60.8
	8-14 days	87	29.4
	≥15 days	29	9.8
Treatment outcome on discharge	Improved/healed	248	83.8
	Death	48	16.2
ANC Visit	Yes	283	95.6
	No	13	4.4
Place of Delivery	Hospital	181	61.1
	Others	115	38.9

73.6% of the treatment in this study, followed by Ceftriaxone + gentamycin (18.2%). Ceftriaxone was used with precaution instead of cefotaxime despite the fact that it is not a drug of choice due to market availability issues. 8.1% of the neonates in this study received treatment with Vancomicine and ceftazidime. (Figure 1).

**Factors predicting treatment outcome of neonatal sepsis**

In final model of multivariate analysis, the referral case and prolonged therapy remained statistically significant. Accordingly, neonates who

were not referred from another health facility were 71% less likely to experience poor outcome (AOR=0.29, 95%CI: 0.24-0.89) than neonates who were referred from other health facility Besides this, duration of treatment lasting less than 14 days had 64% lower chance of having poor outcome than a treatment lasting more than 14 days (AOR=0.36, 95% CI: 0.14-0.90) (Table 3).



**Figure 1.** Types of antibiotics used in neonatal sepsis admitted to HUCSH, Southern Ethiopia

**Table 3.** Factors predicting treatment outcome of neonatal sepsis in HUCSH, (n=296)

Variable	Category	Poor treatment outcome		COR (95% CI)	AOR (95% CI)
		Yes	No		
sex	Male	23	152	1.72(0.92-3.20)	0.54 (0.27-1.08)
	Female	25	96	1	1
ANC	Yes	44	239	2.41(0.12-1.40)	0.61(0.08-4.34)
	No	4	9	1	1
Referral	Yes	43	161	0.22(0.08-0.56)**	0.29(0.24-0.89)*
	No	5	87	1	1
Type of delivery	SVD	35	161	0.22(0.15-0.31)*	0.84(0.35-1.21)
	Instrumental delivery	2	5	1.84(0.34-9.87)	4.82(0.51-45.57)
	Caesarean section	11	82	1	1
Antibiotic given for treatment	Ampicillin+gentamycin	29	189	0.15(0.10-0.23)*	0.54(0.19-1.55)
	Ceftriaxone+gentamycin	12	42	0.29(0.15-0.54)*	0.24(0.21-1.43)
	Vancomycine+ceftazidine	7	17	1	1
Treatment Duration	≤14 days	39	228	2.63(0.12-0.24)**	0.36(0.14-0.90)*
	>14 days	9	20	1	1

NB

√\*P<0.05, \*\*p<0.01, \*\*\*p<0.001

√ Relatively safe population from scientific point of view were taken as reference category

√ COR is Crude Odds Ratio; AOR is Adjusted Odds Ratio

√ ANC is Antenatal Care, SVD is Spontaneous Vaginal Delivery

## Discussion

The result of poor treatment outcome (16.2%) in this study was comparable with a study done in Bahir dar Felege Hiwot (14%) and Tikur Anbessa Specialized Hospitals (12.5%) (14). Besides this, the result is also comparable with report from Democratic Republic of Congo (18.7%) (18). However, it was lower than death report in Federal Medical Centre of Nigeria (31.8%) (12). The difference in study years could account for discrepancy since this study might be used a better treatment strategy than the one used in the year that the Nigerian report was published. The finding was relatively higher than that of Cameroon, Southeastern Mexico and India (19). This variation might be due to the difference in the study area as the previous studies might have relatively better medical facilities than the current study setting and also the difference in study approach as the current study considered death and long duration of treatment without good prognosis to be poor treatment outcome. As only death was considered as the poor treatment outcome in the three studies, this may increase the proportion of poor treatment outcome.

Significant statistical association existed between referral from other healthcare facilities and poor treatment outcome of neonatal sepsis. Findings from Tanzania provided evidences in favor of this (20). The possibility of case getting complicated on the travel before arriving to the healthcare facility since Ethiopian referral system might not have life supporting care like oxygen on the travel. Poor medical facility at primary health facilities from where the neonates are referred might be another reason. This could make the situation worse before the referral.

Neonates who have been treated for long duration of more than two weeks. In this study, neonates who received care for a duration of more than two weeks, had a more chance of experiencing poor treatment outcomes than those who were treated for shorter period of time. On the other hand, the drug adverse response could be the reason as it is evidenced in prolonged treatment. Neonates may contract various nosocomial infections after admission to NICU that can complicate the case of neonatal sepsis on arrival and this may support the association (21, 22). For instance, gentamycin, which was evidenced to be frequently used in this study, has renal toxicity effect that may end up with poor outcome over a long period of time. Additionally, neonates who received prolonged care may be referred from other health facilities after certain number of days

of treatment and this study found that referral was a predictor of a poor treatment outcome.

### **Strength and validity of the results**

Well trained and experienced data collectors, high response rate and absence or minimized selection bias are among the strengths. We can therefore conclude that our results are likely to reflect the real scenario of treatment outcome for neonates with neonatal sepsis. Still, some associated factors and the magnitude of the problem identified in this study can likely to reflect the situation in other hospitals with similar status. We were able to collect information on several factors and assess their relative contribution to the treatment outcome by adjusting for other factors.

### **Limitation of the study**

This study had several limitations. As it was a retrospective in nature; we might have overlooked some important service and social related factors. Given that the data were collected from secondary source; there is a high chance of missing crucial variables. Due to the fact that this conclusion was based on the secondary data from a single institution, it is impossible to generalize the findings to other local institutions.

## Conclusion

Neonatal sepsis had a poor treatment outcome (16.2%). Neonatal sepsis treatment duration of greater than 2 weeks and referrals from other health facilities were the risk factors for poor treatment outcomes. In all level of healthcare in Ethiopia, it is crucial to strengthen the referral system. Early detection followed by quality services are important to minimize the duration of neonatal stay. In addition, it is also preferable to strengthen Neonatal Intensive Care Unit at primary health facilities.

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## Conflicts of interest

The authors declare that they have no conflicts of interest.

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