

# Assessment of the Incidence of Neonatal Sepsis, its Risk Factors, Antimicrobials Use and Clinical Outcomes in Bishoftu General Hospital, Neonatal Intensive Care Unit, Debrezeit-Ethiopia

Minyahil Alebachew Woldu<sup>1\*</sup>, Molla Belay Guta<sup>2</sup>, Jimma Likisa Lenjisa<sup>2</sup>, Gobezie Temesgen Tegegne<sup>2</sup>, Gurmu Tesafye<sup>2</sup> and Hunduma Dinsa<sup>2</sup>

<sup>1</sup>Department of pharmacology and clinical pharmacy, Addis Ababa University, Ethiopia

<sup>2</sup>Department of pharmacy, Ambo University, Ethiopia

\*Corresponding author: Minyahil Alebachew Woldu, Department of pharmacology and clinical pharmacy, College of health sciences, School of pharmacy, Addis Ababa University, P.O. Box 9086, Ethiopia, Tel: +251-91-2648527; E-mail: [minwoldu@gmail.com](mailto:minwoldu@gmail.com)

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## Abstract

**Background:** The incidence of neonatal sepsis (NS) varies from 6 to 9 cases per 1,000 live births, but is higher among low-birth-weight neonates. The purpose of the present study was to examine the risk factors, antimicrobial use pattern and clinical outcomes of NS.

**Methods:** A prospective cross-sectional study was conducted using pretested and validated checklists.

**Results:** Among the total 306 neonates 249(81.4%) were age less than or equal to 7days, and 169(55.23%) were male, while 251(82%) were attended antenatal care, 136 (44.44%) were low in birth weight (<2.5Kg) and 155(50.7%) had total of white blood cell count >12000/mm<sup>3</sup>. Two hundred twenty one (72.2%) of the neonates were receive antibiotics for management of sepsis while 74 (24.2%) were receive antibiotics for other managements. The most frequently prescribed antibiotic was the combination of 'ampicillin + gentamicin' with 67(21.9%) followed by single antibiotic prescriptions of benzyl penicillin 33(10.8%) and cloxacillin 8(2.6%). A significant number of neonates ( $p=0.000$ ) with 95% C.I of (1.934-8.967) were born in health center and developed sepsis. This value is 4.2 times higher when compared to the neonates born in home. A significant number of neonates born with the aid of instrument in hospitals were also developed sepsis ( $p=0.26$ ). The risk of acquiring sepsis in neonates born with the aid of instruments was 6.2 times higher than children born vaginally in natural way. A significant number of neonates born from mothers' with urinary tract infection (UTI) developed sepsis ( $p=0.02$ ) and this figure was 2.9 times higher than neonates born from mothers' with no UTI.

**Conclusions:** In the present study, the most common risk factors for the incidence of neonatal sepsis were place of delivery, mode of delivery and mothers with UTI.

**Keywords:** Neonatal sepsis; Neonatal antimicrobial use pattern; Neonatal sepsis risk factors

## Background

According to the international pediatric consensus conference of 2001, neonatal sepsis (NS) is defined as systemic inflammatory response syndrome in the presence of or as a result of suspected or proven infection in a neonate [1]. The normal fetus is sterile until shortly before birth as the placenta and amniotic sac are highly effective barriers to infections. At birth, the newborn loses the protection afforded to it in the uterus and gets exposed to the microbial world [2]. Bacterial organisms causing NS may differ among countries, however, in most developing countries, gram-negative bacteria remain the major source of infection [3]. In addition, bacterial organisms causing NS have developed increased drug resistance to commonly used antibiotics, making its management a challenge for both the public and private health sectors [4].

Early onset neonatal sepsis (sepsis that presents during the first 5–7 days of life) usually is caused by organisms acquired from the maternal genital tract. The most common pathogens found in early-onset

neonatal sepsis are group B streptococcus (50%) and *E. coli* (20%). Other primary pathogens include *Listeria monocytogenes*, *Enterococcus*, and other Gram-negative bacilli (e.g., *H. influenzae*, *Klebsiella pneumoniae*) [5,6]. In developed countries, bacterial infections in neonates are commonly due to *Escherichia coli*, other enterobacteriaceae, *Listeria monocytogenes*, and coagulase negative staphylococci and group B *Streptococcus* [7]. Late-onset sepsis (sepsis presenting after 5–7 days postnatal age) usually is caused by these primary organisms or by nosocomial pathogens, such as coagulase-negative staphylococci (CONS), particularly *S.epidermidis*, *S.aureus*, *Pseudomonas* species, anaerobes, and *Candida* species [5].

The incidence of NS varies from 6 to 9 cases per 1,000 live births, but is higher among low-birth-weight neonates [5]. Bacterial sepsis is considered to be an important cause of neonatal mortality [8]. The World Health Organization estimated that there are approximately five million neonatal deaths per year of which 98% occur in developing countries [9]. The number of children dying from sepsis in the world has almost doubled in the past 20 years [10]. This may be due to the fact that antimicrobial therapy in most developing countries are mainly empirical due to a relative lack of appropriate laboratory facilities for culture and sensitivity of bacteria in several health

facilities [11]. Furthermore, surviving infants can have significant neurological sequelae as a consequence of CNS involvement, septic shock or hypoxemia secondary to severe parenchymal lung disease [12]. Therefore, the purpose of the present study was to examine the risk factors, antimicrobial use pattern and clinical outcomes of NS at Bishoftu general hospital (BGH), neonatal intensive care unit (NICU), Debrezeit-Ethiopia.

## Methods

### Study area

The study was conducted at Bishoftu general hospital which is located in Oromiya regional state, Bishoftu (Debrezeit) town, Ethiopia. It is 47 km away from Addis Ababa towards east. The hospital provides services for approximately 130,000 population of the town and surrounding population. The NICUs of BGH contain sixteen beds, five staff members and two cleaners. Among staff members, two of them were physicians and three of them were nurses. More than one thousands of neonates admitted at NICUs annually to get medical services.

### Study period

The study period was from Oct. 15/2013 to April-15/ 2014.

### Study design

A prospective cross-sectional study was conducted using pretested and validated checklists.

### Sample size and sampling techniques

A total of 306 patients were recruited using a systematic random sampling technique, considering the number of sick neonates admitted to BGH, NICU per day.

### Source population

All pediatric population enrolled to BGH, NICU during the study period.

### Study population

All neonates admitted to BGH, NICU during the study period.

### Inclusion criteria

All neonates admitted to BGH, NICU during the study period.

### Exclusion criteria

1. Neonates with early discharge.
2. Neonates with incomplete patient chart information.
3. Neonates expired without taking any treatment on arrival.

### Study variable

The main study variables include age, sex, birth weight, gestational age, mode of delivery, mother condition (fever, Urinary Tract infection (UTI)), and duration of labor.

## Data organization, presentation and analysis

Data was coded and entered into the Statistical Package for Social Science (SPSS) version 19 for Windows. Figures and tables were used to present the findings. Chi-square and binary logistic analysis were used to further investigate any associations. A 95% CI and p-value of < 0.05 was considered to be statistically significant.

### Data quality assurance

A 5% sample pretest was performed on randomly selected patients before the beginning of the study. A pretested and validated check list was used. All steps in data collection and recording were closely monitored by the principal investigator and daily collected data was, recorded and compiled for the next day study.

### Ethical considerations

Ethical clearance was obtained from the Ambo University ethical review committee and official letter of co-operations was provided to BGH prior to data collection. Patient consent was obtained prior to data collection and no personal identity was disclosed. The raw data was not made available to anyone, and was not used as the determinant of any identity or subjects.

## Results

### Socio-demographic, risk factors and clinical data

Among the total 306 neonates (age in between 0-28 days) recruited for this study, 249(81.4%) were age less than or equal to 7days (Early onset neonatal sepsis (EONS)), 169(55.23%) were male, 251(82%) were attended Antenatal Care/Clinic (ANC), 136 (44.44%) were low in birth weight (<2.5Kg) and 155(50.7%) had total of WBC count >12000/mm<sup>3</sup>. One hundred twenty four of the neonates (40.52%) were born within 12-24 hours of labour duration, and 249(81.4%) were full term (Table 1). Among 306 mothers, 38 (22.8%) had UTI during delivery, and 249 (81.4%) delivered per vaginal (Table 2).

### Pattern of antimicrobial use and treatment outcomes

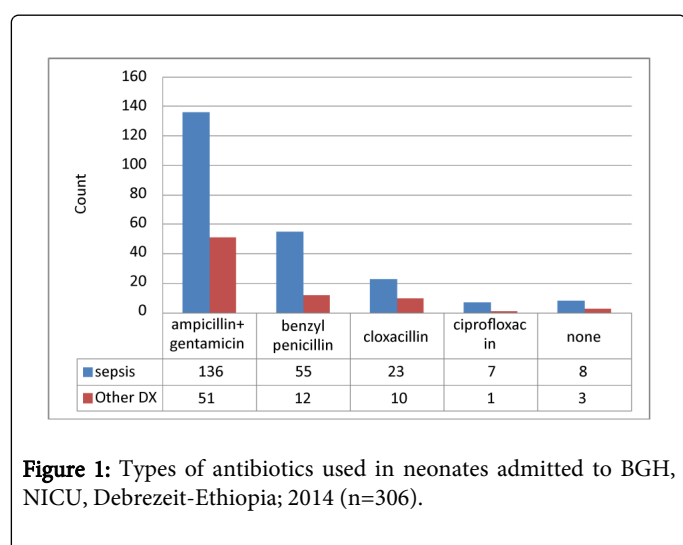
Two hundred twenty one (72.2%) of the neonates diagnosed as sepsis received antibiotics while 74 (24.2%) received antibiotics for other diagnosis (Table 2). The most frequently prescribed antibiotic was the combination of 'ampicillin + gentamicin' prescription 67 (21.9%) followed by the single antibiotic prescriptions of benzyl penicillin 33 (10.8%) and cloxacillin 8 (2.6%) (Figure 1).

Forty (13.1%) of the neonates were expired after admission and in all the cases the cause of death was other diagnosis rather than sepsis itself. In 37(12.09) of the neonates the status of their clinical outcome was unknown because they were referred for further investigation and management (Table 2).

Variables		Frequency	Percent
Sex	Male	169	55.2
	Female	137	44.8
Age	0-7 days	249	81.4
	8-28 days	57	18.6
ANC	yes	251	82
	No	55	18
DOL	< 6hrs	33	10.8
	6-12 hrs	108	35.3
	12-24 hrs	124	40.5
	> 24 hrs	41	13.4
GA	preterm < 37 wks	64	20.9
	term 37-42 wks	228	74.5
	post term > 42 wks	14	4.6
MOD	vaginal	249	81.4
	caesarian section	38	12.4
	instrumental	19	6.2
TWBC	< 5000/mm <sup>3</sup>	13	4.2
	5000-12000/mm <sup>3</sup>	138	45.1
	>12000/mm <sup>3</sup>	155	50.7

ANC=Antenatal Care, DOL= Duration of labour, GA= gestational age, MOD= Mode of delivery, TWBC=Total White blood cells

**Table 1:** Socio-demographic and clinical data distribution of neonates admitted to BGH, NICU, Debrezeit-Ethiopia 2014 (n=306).



**Figure 1:** Types of antibiotics used in neonates admitted to BGH, NICU, Debrezeit-Ethiopia; 2014 (n=306).

### Determinants of neonatal sepsis

In this study we have identified that significant number of neonates ( $p=0.000$ ) with 95% C.I of (1.934-8.967) were born in health center and developed sepsis. This value is 4.2 times higher when compared to the neonates born in home. A significant number of neonates using instrument in hospitals were also developed sepsis ( $p=0.26$ ). The risk of acquiring sepsis in neonates born using instrument was almost 6.2 times more common than children born vaginal in natural way. A significant number of neonates born from mothers' with UTI developed sepsis ( $p=0.02$ ) and this figure was almost 2.9 times higher compared to neonates born from mothers' with no UTI diagnosis (Table 3). The association between clinical outcomes, sepsis and antibiotic use was investigated and significant numbers of neonates (Pearson Chi-Square,  $p=0.000$ ) were recovered once they diagnosed as sepsis using antibiotics (Table 4).

### Discussion

Neonatal sepsis is an important cause of neonatal morbidity and mortality [13]. Among the 306 neonates recruited in our study, 81.0 % were diagnosed as EONS and 19% were presented as LONS. The study showed that there were more EONS admissions than LONS. This finding was in agreement with the study conducted Tikur Ambessa

hospital, Addis Ababa, Ethiopia [14]. But, active surveillance from 2005-08 reported that overall EONS incidence was 0.77 cases/1000 live births, and among those born at  $\geq 37$  weeks it was found to become  $\sim 0.5$  cases/1000, compared to  $\sim 3.0$  cases/1000 live births occurring at  $<37$  weeks gestation [15,16]. Different studies also showed that gestational age (GA) as an important predictor of EONS risks [16]

although it was established as a risk factor for EONS risks in different studies, our investigation could not find any significant figures in this regard. However, with regard to the association of sepsis with sex, still our finding did not bring significant values, but male gender was predominantly affected in our study too as it was common in other findings [13,17,18].

Variables		Sepsis (%)	Other (%)	Total (%)
Mother with UTI during delivery	Yes	38(12.4)	32(10.5)	70(22.9)
	No	191(62.4)	45(14.7)	236(77.1)
Mother with fever during delivery	< 6hrs	90(29.4)	42(13.7)	132(43.1)
	6-12 hrs	139(45.4)	35(11.4)	174(56.8)
Mode of delivery	vaginal	187(61.1)	62(20.2)	249(81.3)
	caesarean section	26(8.4)	12(3.9)	38(12.3)
	instrumental	16(5.2)	3(0.98)	19(6.18)
Place of delivery	home	15(4.9)	12(3.9)	27(8.8)
	Clinic	38(12.4)	27(8.8)	65(21.2)
	health center	52(16.9)	19(6.2)	71(23.1)
	hospital	124(40.5)	19(6.2)	143(46.7)
Antibiotic Use	antibiotics	221(72.2)	74(24.2)	295(96.4)
	No antibiotics	8(2.61)	3(0.98)	11(3.59)
Clinical outcomes	recovery	229(74.84)	0	229(74.84)
	death	0	40(13.07)	40(13.07)
	unknown	0	37(12.09)	37(12.09)

**Table 2:** Sepsis distribution among the different variables in neonates admitted to BGH, NICU, Debrezeit-Ethiopia 2014 (n=306).

Newborn infants are especially vulnerable to nosocomial infections because of their intrinsic susceptibility to infection as well as the invasive procedures to which they are subjected. This is particularly high for those born prematurely or of low birth weight [19]. Similarly, different studies came up with the conclusion that low birth weight (LBW) infants are a high risk of developing sepsis compared to full-term infants [13,20]. Again our study did not bring significant value but this could be due to the fact in our case there were no infants with very low birth weight (VLBW, or birth weight  $<1500$  grams), because much morbidity and mortality risks remain substantial among infants who are VLBW [16].

Our study identified that 228(74.5%) of the neonates born were full term. This result was similar to other study conducted in resource limited settings [17]. Our study also revealed that significant number of neonates ( $p=0.000$ ) with 95% C.I of (1.934-8.967) were born in health center and developed sepsis. This value was 4.2 times higher when compared to the neonates born in home by traditional birth attendants (TBAs). The possible reason for this could be prolonged labor before visiting health facilities that could complicate the conditions. In other study comparing hospital and home delivery the proportion of hospital birth were higher and therefore it was in line with our study [18].

Our study further demonstrated that, a significant number of neonates born by instrumental procedures in hospitals were associated with incidence of sepsis ( $p=0.26$ ). The risk of acquiring sepsis in neonates born using instrument in our study was almost 6.2 times more common than children born vaginally in natural way. In fact the instruments used were appropriately sterilized. However the reason for the discrepancies in the result could be fetus suffocation, early rupture of membrane (ROM) and environmental contamination with nosocomial infections during delivery rather than pinpointing to the risks gained by using instrumental procedures. And this finding was also similar to the study conducted in Nigeria [17].

A significant number of neonates born from mothers' with UTI developed sepsis ( $p=0.02$ ) and this figure was almost 2.9 fold higher than the neonates born from mothers' with no UTI diagnosis (Table 3). This is because, the most common pathogens found in EONS are found across the vaginal wall and possibly increases the risk while the child was born and pass through the vaginal wall [5,6].

With regard to antibiotic use, 72.2% of the neonates diagnosed as sepsis were received antibiotics. Such haphazard way of antibiotics use was observed due to the fact that empiric management was commonly practiced in the study area. High percentage of neonates were treated by the combination of 'Ampicillin +gentamicin' and this result was in

line with a number studies as it was most common in empiric sepsis management [13].

The association between clinical outcomes, sepsis and antibiotic use was investigated and significant numbers of neonates (Pearson Chi-

Square,  $p=0.000$ ) were recovered once they diagnosed as sepsis using antibiotics. This result indicated the susceptibility pattern of microbials to the antibiotics currently being used at the study place and also in line with the study from other area [13].

Variables		Sepsis	Other diagnosis	Sig.	AOR	95.0% C.I. for AOR	
						Lower	Upper
Sex	M	131	38	0.445	0.8	0.442	1.431
Age	0-7days	191	58	0.126	0.6	0.265	1.178
TWBC	>12000/mm <sup>3</sup>	118	37	0.94			
	5000-12000/mm <sup>3</sup>	102	36	0.91	1.1	0.253	4.688
	< 5000/mm <sup>3</sup>	9	4	0.809	1.2	0.276	5.199
Labour duration	> 24 hrs	30	11	0.733			
	12-24 hrs	92	32	0.831	0.9	0.269	2.874
	6-12 hrs	82	26	0.44	0.7	0.245	1.842
	< 6hrs	25	8	0.338	0.6	0.218	1.689
ANC	No	32	23	0.106	1.8	0.881	3.754
Delivery place	home	15	12	0.002			
	clinic	38	27	0.022	3.3	1.195	9.333
	Health center	52	19	.000*	4.2	1.934	8.967
	hospital	124	19	0.015	2.6	1.197	5.443
Mode of delivery	Vaginal	187	62	0.081			
	C/S	26	12	0.046	4.3	1.025	17.924
	instrumental	16	3	.026*	6.3	1.252	31.768
GA	preterm < 37 wks	39	25	0.194			
	term 37-42 wks	178	50	0.214	4.7	0.408	54.441
	post term > 42 wks	12	2	0.429	2.6	0.249	26.286
BW	LBW < 2.5 kg	95	41	0.818			
	NBW 2.5-4 kg	123	34	0.959	0.9	0.08	10.921
	Overweight >4 kg	11	2	0.83	0.8	0.068	8.643
UTI	Yes	38	32	.002*	2.9	1.489	5.527
Fever	yes	90	42	0.284	1.4	0.755	2.609

GA=gestational age, aOR=adjusted odds ratio, BW=birth weight, UTI= urinary tract infections, TWBC=total white blood cell, ANC= antenatal care, \*=significance

**Table 3:** Binary Logistic Regressions showing the association between sepsis and the different variables in neonates admitted to BGH, NICU, Debrezeit-Ethiopia 2014 (n=306).

Variables	Recovery	Death	Unknown	Pearson Chi-Square Asymp. Sig. (2-sided)
ampicillin + gentamicin	136	27	24	.797
benzyl penicillin	55	5	7	

cloxacillin	23	5	5	.000
ciprofloxacin	7	1	0	
sepsis	229	0	0	
Other diagnosis	0	40	37	

**Table 4:** Crosstabs showing the association between clinical outcomes, incidence of sepsis and pattern of antibiotic use in neonates admitted to BGH, NICU, Debrezeit-Ethiopia 2014 (n=306).

## Limitations of the Study

All the important information may not be recorded well or available as expected. For some critical cases patients' charts may be unavailable for data collection. In most of patients charts' the complication data and previous drug therapy may not be available.

## Conclusions

In the present study, the most common risk factors were identified and place of delivery, mode of delivery and mother with UTI during delivery were the most common risk factors for the incidence of neonatal sepsis. Empirical antibiotic treatment was by far the mainstay of NS management in the study area and the combination of 'ampicillin +gentamicin' prescription was the dominant one. From single antibiotic prescription, benzyl penicillin and cloxacillin were the front runner considering the frequency of prescription. The overall clinical outcomes of NS were excellent in the study area while too much fatality was reported for the other diagnosis. Based on the finding of the present and the above mentioned conclusion the following recommendations were made:

The prevention of the most common risk factors will reduce the risk of NS. Based on this result we recommend health policy makers to focus on the prevention of risk factors rather than treating the disease after it occurs.

Empirical regimens for NS must be taken into consideration especially considering the risk of resistance, misdiagnosis and mismanagement. Thus, sensitivity testing should be performed.

## Competing Interests

The Authors' declare that there are no competing interests.

## Author's Contributions

MAW has made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data and has been involved in drafting the manuscript or revising it critically for important intellectual content; and has given final approval of the version to be published. MBG has made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data. JLL has been involved in drafting the manuscript or revising it critically for important intellectual content. GTT has been involved in drafting the manuscript or revising it critically for important intellectual content. GT has been involved in revising it critically for important intellectual content. HD has also been involved in revising it critically for important intellectual content.

All Authors read and approved the final manuscript.

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