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Research Article

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

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ABSTRACT

Background: The incidence of neonatal sepsis (NS) varies from 6 to 9 cases per 1000 live births, but is higher among low-birth-weight neonates. Therefore, the purpose of this study was to examine the risk factors, antimicrobial use pattern and clinical outcomes of NS at Bishoftu General Hospital, neonatal intensive care unit, Debrezeit-Ethiopia.
Methods: A prospective cross-sectional study was conducted using pretested and validated checklists.
Results: Among the total 306 neonates (0-28 days of age) recruited, 249 (81.4%) were age ≤7 days, 169 (55.23%) were male, 251 (82%) were attended antenatal care, 136 (44.44%) were low in birth weight (≤2.5 kg) and 155 (50.7%) had total of white blood cell count ≥12000/mm^3. 221 (72.2%) of the neonates diagnosed as sepsis received antibiotics while 74 (24.2%) received antibiotics for other diagnosis. 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%). A significant number of neonates ($p = 0.000$) with 95% confidence interval of (1.934-8.967) were born in health center and developed sepsis. This value is 4.2 times higher when compared with the neonates born in the 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 the natural way. A significant number of neonates born from mothers' with urinary tract infections (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.
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 NS.

Keywords: Neonatal sepsis, Neonatal antimicrobial use pattern, Neonatal sepsis risk factors

INTRODUCTION

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

The incidence of NS varies from 6 to 9 cases per 1000 live births, but is higher among low-birth-weight (LBW) 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 is mainly empirical due to the 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 central nervous system 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 BGH 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 16 beds, 5 staff members and 2 cleaners. Among staff members, two of them were physicians and three of them were nurses. More than 1000 of neonates admitted at NICUs annually to get medical services.

Study period

The study period was from October 15, 2014 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

- Neonates with early discharge
- Neonates with incomplete patient chart information, and
- Neonates expired without taking any treatment on arrival.

Study variable

The main study variables include age, sex, birth weight (BW), gestational age (GA), mode of delivery (MOD), mother condition (fever, urinary tract infections [UTI]), and duration of labor.

Data organization, presentation and analysis

Data were coded and entered into the Statistical Package for Social Science version 19 for Windows. Figures and Tables were used to present the findings. Chi-square and binary logistic analysis were used to investigate any associations further. The 95% confidence interval (CI) and $p < 0.05$ was considered as 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 were 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 (0-28 days of age) recruited, 249 (81.4%) were age less than or equal to 7 days, 169 (55.23%) were male, 251 (82%) were attended antenatal care, 136 (44.44%) were LBW (≤2.5 kg) and 155 (50.7%) had total of white blood cell count ≥12,000/mm^3. 124 of the neonates (40.52%) were born within 12-24 h of labor 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).

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

Variables	Frequency	Percentage
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	82.0
No	55	18.0
DOL		
<6 h	33	10.8
6-12 h	108	35.3
12-24 h	124	40.5
> 24 h	41	13.4
GA		
Preterm <37 weeks	64	20.9
Term 37-42 weeks	228	74.5
Postterm >42 weeks	14	4.6
MOD		
Vaginal	249	81.4
Caesarian section	38	12.4
Instrumental	19	6.2
TWBC		
<5000/mm^3	13	4.2
5000-12,000/mm^3	138	45.1
>12000/mm^3	155	50.7

ANC: Antenatal care, DOL: Duration of labour, GA: Gestational age, MOD: Mode of delivery, TWBC: Total white blood cells, BGH: Bishoftu General Hospital, NICU: Neonatal intensive care unit

Pattern of antimicrobial use and treatment outcomes

221 (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).

Determinants of NS

In this study, we have identified that significant number of neonates (p = 0.000) with 95% CI of (1.934-8.967) were born in health center and developed sepsis. This value is 4.2 times higher when compared with 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 the 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

NS 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

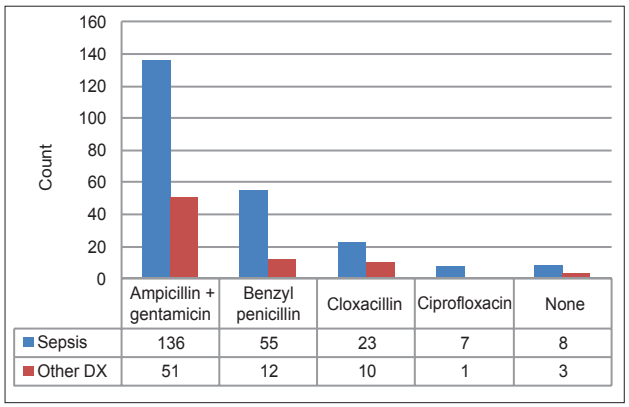

Figure 1: Types of antibiotics used in neonates admitted to Bishoftu General Hospital, neonatal intensive care unit, Debrezeit-Ethiopia; 2014 (*n* = 306).

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

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			
<6 h	90 (29.4)	42 (13.7)	132 (43.1)
6-12 h	139 (45.4)	35 (11.4)	174 (56.8)
MOD			
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)

MOD: Mode of delivery, BGH: Bishoftu general hospital, NICU: Neonatal intensive care unit

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 to 2008 reported that overall EONS incidence was 0.77 cases/1000 live births, and among those born at ≥37 weeks it was found to become ~0.5 cases/1000, compared with ~3.0 cases/1000 live births occurring at <37 weeks gestation.[15,16] Different studies also showed that 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 found any significant figures in this regard. However, as 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]

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 LBW.[19] Similarly, different studies came up with the conclusion that LBW infants are a high risk of developing sepsis compared with 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 LBW (VLBW, or BW <1500 g), 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% CI of (1.934-8.967) were born in health center and developed sepsis. This value was 4.2 times higher when compared with the neonates born in home by traditional birth attendants. The possible reason for this could be prolonged labor before visiting health facilities that could complicates 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. This figure could possibly give us a proxy clue of fetus suffocation, early rapture of membrane and environmental contamination with nosocomial infections during delivery rather than pointing only to the risks gained by using instrumental procedures.

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	Sepsis	Other diagnosis	Significance	AOR	95.0% CI for AOR	
					Lower	Upper
Sex						
M	131	38	0.445	0.8	0.442	1.431
Age						
0-7 days	191	58	0.126	0.6	0.265	1.178
TWBC						
>12,000/mm^3	118	37	0.940			
5000-12,000/mm^3	102	36	0.910	1.1	0.253	4.688
<5000/mm^3	9	4	0.809	1.2	0.276	5.199
Labour duration						
>24 h	30	11	0.733			
12-24 h	92	32	0.831	0.9	0.269	2.874
6-12 h	82	26	0.440	0.7	0.245	1.842
<6 h	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	0.000*	4.2	1.934	8.967
Hospital	124	19	0.015	2.6	1.197	5.443
MOD						
Vaginal	187	62	0.081			
C/S	26	12	0.046	4.3	1.025	17.924
Instrumental	16	3	0.026*	6.3	1.252	31.768
GA						
Pre-term <37 weeks	39	25	0.194			
Term 37-42 weeks	178	50	0.214	4.7	0.408	54.441
Post-term >42 weeks	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	0.080	10.921
Overweight >4 kg	11	2	0.830	0.8	0.068	8.643
UTI						
Yes	38	32	0.002*	2.9	1.489	5.527
Fever						
Yes	90	42	0.284	1.4	0.755	2.609

*Significance, GA: Gestational age, AOR: Adjusted odds ratio, BW: Birth weight, UTI: Urinary tract infections, TWBC: Total white blood cell, ANC: Antenatal care, LBW: Low birth weight, NBW: Normal body weight, BGH: Bishoftu general hospital, NICU: Neonatal intensive care unit

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, whereas 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

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).

Variables	Recovery	Death	Unknown	Pearson Chi-square Asymptotic significant (two-sided)
Ampicillin+gentamicin	136	27	24	0.797
Benzyl penicillin	55	5	7	
Cloxacillin	23	5	5	
Ciprofloxacin	7	1	0	
Sepsis	229	0	0	0.000
Other diagnosis	0	40	37	

BGH: Bishoftu general hospital, NICU: Neonatal intensive care unit

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]

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, MOD and mother with UTI during delivery were the most common risk factors for the incidence of NS. 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.

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Abbreviations

BGH: Bishoftu General Hospital
EONS: Early onset NS
LONS: Late onset NS
NICU: Neonatal intensive care unit
NS: Neonatal sepsis
ROM: Rupture of membranes.

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