Descriptive cross –sectional study on neonatal sepsis in the Neonatal intensive care unit of Tekur Anbessa Hospital, Addis Ababa , Ethiopia

Adib Yusuf . MD*, Bogale Worku MD*

Abstract

Background*: Neonatal infection accounts for nearly 1.75 million deaths worldwide and the developing countries are responsible for about 1.6 million of these deaths. Not only is there a burden of higher infection rates, but increasing resistance to commonly used antibiotics has become an additional and important problem in these resource poor setups. There are only a few published studies done on neonatal sepsis in Ethiopia, and more than a decade has elapsed since the last one. It is prudent to see if there is any change since then.*

Objective*: The general objective of this paper is to study about the demography, symptomatology, etiology and sensitivity patterns of Neonatal Sepsis in the NICU of Tekur Anbessa Hospital.*

Methodology*: This study is a cross-sectional retrospective study which included a population of Neonates with Sepsis clinically suspected and definitive diagnosis made by blood culture within a one year period between Sept.1, 2007 and Aug.31, 2008. Information like Gestational Age, sex, birth weight, the type of infection, their duration of stay, their final outcome, the etiologic bacteria and their sensitivity patterns were recorded. Using the computer program SPSS v16 the study variables were analysed and important associations were evaluated.*

Results*: There were a total of 578 neonates (280 males and 298 females) suspected of sepsis. Culture positivity rate found was 28.7% from the suspected cases.. Early onset sepsis accounted for 36.7% of confirmed sepsis, 45.8% had Late onset sepsis and the rest 17.5% had Hospital acquired sepsis The risk of infection is found to be higher in premature neonates; OR = 2.92 (1.97 <OR<4.31) at 95% CI and the p value is = 0.00; The RR = 2.08. From suspected 578 neonates, 369(63.8%) were ≥2.5 Kg and the rest 209(36.2%) were <2.5 Kg The commonest isolated bacteria are CONS accounting for 41.5% , followed by Staphylococcus aurous (21.6%). Both of these are gram positive bacteria and together they account for the majority (63.1%) of neonatal sepsis. From the gram negatives, Klebsiella spp. has the highest frequency(9.4%), followed by Acinetobacter spp (5.8%), Salmonella spp. (5.3%), Pseudomonas spp(4%) and E. coli(3.5%). The highest number of deaths occurred in neonates with CONS bacteria isolated from their blood culture. An average of 83% of etiologic bacteria are resistant to Ampicillin, 52% are resistant to CAF and 63% to Gentamycin. Average of 62.6% of the Staphylococci are found resistant to Cloxacillin*

Conclusion*: In Ethiopia, sepsis is still an important cause of morbidity and mortality in neonates. Prematurity and low birth weight newborns were noticed to be considerably affected by sepsis with higher chance to acquire sepsis and higher mortality rates as compared to term and normal birth weight newborns. The alarmingly higher percentages of multi-drug resistant isolates urge us to take Infection Prevention measures, like frequent hand washing in the delivery room and NICU, aiming to prevent any transmission of infection in general and to stop the escalating multi-drug resistant strains. It is clearly revealed the importance in doing further studies, such as case-control studies, in order to clearly identify the empirical choice of treatment and possibly avoid some of the pitfalls noticed in this study.*

- *Department of pediatrics and Child health, AAU Faculty of medicine.*

Introduction

Neonatal infections happen to be the most common causes of morbidity and mortality in children, and especially neonates of developing countries.
Based on a multicentre study WHO estimated that there were 126million live births worldwide in 2007. In that year 8 million infants below 1 yr. of age died and of which 5 million of them were neonates below 28 days of age. Form the neonatal deaths, the most common cause was found to be INFECTION (34% i.e. it accounted for nearly 1.7 million deaths), followed by birth asphyxia and trauma (27%) and prematurity (23%) 1

Moreover, neonates are unable to localize infections because of immaturity of their immune system, which will subsequently lead them to develop SEPSIS. 2

Neonatal sepsis is a clinical syndrome of systemic illness accompanied by bacteremia occurring in the first month of life.

We have three types of sepsis in neonatal period; EONS, LONS and HAS.
Early onset Neonatal Sepsis (EONS) is mainly due to vertical transmission during labor and delivery. This type of infection commonly presents with symptoms and sign of sepsis in the first 3 days after delivery.
The Late onset Neonatal Sepsis (LONS) can be due to vertical or horizontal transmission from the community and the neonates clinically present 3 days (72 hrs) after delivery.
Hospital Acquired Infection (HAS) occurs if neonate contracted infection after 72hrs of stay in a hospital or within 7 days after discharge.

Many centers have studied the common causative agents of neonatal sepsis with their sensitivity patterns, so as to decide the Initial/Empiric Antibiotics to start with.

Surprisingly, different findings were found in different settings. 3, 4, 5, 6, 7, 8, 9, 10

To my knowledge there are only few studies done in our setting. 9, 10

Hopefully, this cross-sectional, retrospective study will contribute to the knowledge of the Etiology, Demography, Symptomatology and Initial/Empiric Treatment of choice of neonatal sepsis in the NICU of TAH.

Objective

General objective

The general objective of this paper is to study about the demography, symptomatology, etiology and sensitivity patterns of Neonatal Sepsis in the NICU of Tekur Anbessa Hospital (TAH), a Tertiary and Teaching Hospital in Ethiopia, Addis Ababa.

Methodology

This is a cross-sectional retrospective study which included the entire population of Neonates with sufficient evidence of sepsis in a one year period between Sept.1, 2007 and Aug. 31, 2008, diagnosed and admitted to the NICU of Tekur Anbessa General Specialized Hospital, the teaching hospital under the Medical Faculty of Addis Ababa University, Ethiopia.

The Inclusion criterion was all neonates in NICU of TAH, suspected to have

sepsis and the diagnosis was proven by blood culture. Even though it is not 100% specific or sensitive, the gold standard to diagnose sepsis in a clinically symptomatic patient is the growth of the offending organism in blood culture**.**

The Exclusion criteria are the following:-

Neonates with other confirmed diagnosis like Meningitis, Neural tube defects and other congenital anomalies. The reason is these definite alternate diagnoses will cause statistical error in the assessment of clinical features and case fatality rate of Neonatal Sepsis.

Neonates with important clinical or microbiological data missing are also excluded from the study.

The Data was analyzed by SPSS Windows Version 16 software. Comparisons were made using Chi-square test with Fisher exact test. The values indicating significant statistical difference is considered if $p < 0.05$ and power $(1 - \beta) = 80\%$

Ethical Consideration: - This research is cleared by the Department of Pediatrics and Child Health of Tekur Anbessa Hospital. The study is based on collecting a secondary data retrospectively. It doesn't involve an additional procedure or treatment. This will eliminate the possibility of additional risk of harm to the neonates and also no risk of withholding beneficial treatment.

Confidentiality will not be breached by the study, because the data to be collected will not include names or other personal information. The data is collected from a routine data recording system, and informed consent from the parents of the neonates was not needed.

RESULTS

During the study period of one year 4144 neonates were evaluated in the Neonatal Ward of TAH. From among these 2372 neonates were admitted to NICU and 912 Neonates were suspected of developing Neonatal Sepsis and blood sample was taken for Culture from 578. Only 166 culture samples grew bacteria. See the summary of the enrollment process in Fig. 1.

The culture positivity rate and empirical antibiotic administration rate

The culture positivity rate was 166/578 = 28.7% Almost all (97.6%) of the neonates were started on empirical antibiotics, once they were clinically diagnosed to have sepsis before blood sample was taken for Culture and Sensitivity. The admitting physicians are obliged to start empirical antibiotics, to avoid any delay of life saving treatment.

Frequency of the two Genders with their relative risks for infection

There were a total of 280 males and 298 females suspected of sepsis. From these there were 166 neonates whose blood culture grew bacteria; 92(55.4%) were males and 74 (44.6%) were females. And based on the statistical calculations, the p = 0.033, the Odds Ratio of 1.48 (1.01 – 2.17) for a CI of 95% and Relative Risk of 1.32 (1.02 – 1.71) for males was found. This means that male neonates are found to be 1.32 times more prone to acquire culture proven sepsis as compared to female neonates and the difference in the development of sepsis between male and female neonates is actually statistically significant.

Significance of gender for the final outcome

But there was no statistically significant difference between males and females in their final outcomes. 19 from 74 (25.7%) of culture confirmed septic female neonates died and 22 from 92 (23.9%) of confirmed septic male neonates died. The OR= 1.10 (0.51-2.37) RR=1.07 (0.63-1.83) for 95% CI, and the P value=0.79

Frequency of the Types of sepsis

4144 neonatal seen in the neonatal ward of Tikur Anbessa Hospital and 57.2% of theses were admitted to the NICU. 1711(72.1%) of the admitted neonates were suspected to have infection

61(36.7%) of the neonates were diagnosed with Sepsis at the age of <72hrs (Dx=EONS), and the rest 104(62.7%) of the neonates were diagnosed with sepsis at the age of >72hrs. Most of them76/166 (45.8%) had LONS and 29/166 (17.5%) had HAS.

Significance of Gestational Age for development of NS

Fetuses expelled before 28 completed weeks of gestational age were considered abortuses. There were 36 (21.7%) neonates between 28 to 33 weeks inclusive of GA. And there were 50 (30.1%) neonates between 34-36 weeks of GA. There were 80 (48.2%) neonates who were ≥37 weeks of GA of which 75 (45.2%) were between 37 and 42 weeks and 5(3%) were >42 weeks of Gestational age.

When we consider the risk of development of sepsis in Premature (<37 weeks) neonates as compared to mature ones (≥37 weeks) from suspected 578 neonates, 381(65.9%) were ≥37 weeks and the rest 197(34.1%) were preterms (<37 Wks). From these suspected cases, 80 mature neonates (21 % of the neonates suspected of Sepsis whose GA ≥37 weeks) were confirmed by blood culture and 86 premature neonates (43.7% of neonates suspected of Sepsis with GA <37 Wks) were confirmed to have sepsis by blood culture. The Odds Ratio was 2.92 (1.97 <OR<4.31) at 95% Confidence Interval and the p value is = 0.00; The Relative Risk (RR) = 2.08. This suggests that the chance to develop sepsis in the Preterms as compared to Terms is 2.08 times more and based on these calculations, the difference in the findings between the preterm neonates and the term neonates is statistically significant, and not merely by chance.

Significance of Birth Weight for development of NS

When we see their Birth Weight, only one neonate (0.6%) who weight <1 Kg was confirmed to have sepsis. There were 24 (14.5%) neonates who weight between 1 and 1.49 Kg. The neonates who weight between 1.5 and 2.5 Kg were 50(30.1%). There were 91(54.8%) neonates who weight > 2.5 Kg.

When we evaluate the risk of development of sepsis in Birth Weights (BW) <2.5 Kg as compared to BW ≥2.5 Kg from suspected 578 neonates, 369(63.8%) were ≥2.5 Kg and the rest 209(36.2%) were <2.5 Kg. From these suspected cases, 91 neonates with BW≥ 2.5 Kg (24.7% of BW ≥2.5 Kg neonates suspected of Sepsis) were confirmed by blood culture and 75 neonates whose BW <2.5 Kg (35.9% of <2.5 Kg neonates suspected of Sepsis) were confirmed to have sepsis by blood culture. The Odds Ratio was 2.27 (1.1.55<OR<3.32) at 95% Confidence Interval and the p value is = 0.00; the Relative Risk (RR) is 1.81. This means the chance to develop sepsis in the BW<2.5 Kg Neonates as compared to BW ≥2.5 Kg Neonates is 1.81 times more. Based on these calculations, the difference in the findings between the low birth weight neonates and the normal BW neonates is statistically significant, and not merely by chance.

Frequencies of sites of delivery

When we see the sites of delivery of the neonates with sepsis, 52 (31.3%) neonates were from the same hospital TAH, making it the commonest area of referral to NICU, followed by Other Hospitals such as Gandhi Memorial hospital, Saint Paul Hospital and other governmental or private or NGO Hospitals comprising of 49 neonates (29.5%), those NB delivered from Health Centers were 46 (27.7%). The number of NBs delivered at home was 12 (7.2%). There were a total of 7 neonates delivered in conditions considered as Miscellaneous (either on the streets; in a taxi or while on any mode of transportation on the way to Health Facilities; or when the sites of delivery was not known) they comprise of 4.2% of admitted and confirmed cases of Neonatal Sepsis.

Frequencies of Demographic and Clinical Features

The most common clinical feature was Temperature deregulations (especially hypothermia, but some had hyperthermia), followed by depressed mental status (lethargic or coma). The 3rd most common presentation was respiratory finding (either respiratory distress or apnea).

The demography, clinical features, the modes of delivery, the duration of stay and the outcome frequencies war summarized in Table 1 and Table 2 below.

Table 1. . **Clinical Features of neonatal sepsis in NICU of TAH.**

Table-1 Clinical Features			
Type of Infection	Frequency	Percent	% of abnormal clinical finding
Early onset neonatal sepsis-EONS	62	37.3	
Hospital acquired sepsis-HAS	29	17.5	
Late onset Neonatal sepsis-LONS	75	45.2	
Temperature			
High; >38 Co	53	31.9	96.4%
Low; <36 Co	107	64.5	
Normal	6	3.6	
Respiratory Distress			
No Respiratory Distress	48	28.9	
Had Respiratory Distress	106	63.9	71.1%
Had Apnea	12	7.2	
Jaundice			
No Jaundice	116	69.9	69.9%
Jaundiced	50	30.1	
Mental Status			
Coma	25	15.1	74.7%
Lethargic	99	59.6	
Conscious	42	25.3	
Neonatal Reflexes			
Intact Neonatal Reflexes	38	22.9	
Depressed Neonatal Reflex(es)	104	62.7	62.7%
Appropriate Reflex for Preterms	24	14.5	

Table-2 **showing Patient Demography in neonates at NICU of TAH**

Age at Diagnosis	Frequency	Percent
0-3	62	37.3
4-7	83	50
8-30	21	12.7
Total	166	100
Gender		
Female	74	44.6
Male	92	55.4
Total	166	100
Gestational Age		
28-33	36	21.7
34-36	50	30.1
37-42	75	45.2
>42	5	3
Total	166	100
Birth Weight		
<1Kg	1	0.6
1.0 – 1.49Kg	24	14.5
1.5 -2.49Kg	50	30.1
≥2.5Kg	91	54.8
Total	166	100
Site of Delivery		
TAH-A6	52	31.3
Health Center	46	27.7
HOME	12	7.2
Others (eg. In a taxi, streets, etc)	7	4.2
Other Hospitals	49	29.5
Total	166	100
Mode of Delivery		
Cesarean Section	20	12
Instrumental	24	14.5
Spontaneous Vaginal	122	73.5
Total	166	100
Duration of Stay		
<1 week	52	31.3
≥1&<2week	64	38.6
≥2&<3week	31	18.7
≥3week	19	11.4
Total	166	100
Outcome		
EXPIRED	41	24.7
Discharged Improved	125	75.3
Total	166	100

The Final Outcome of Neonates with sepsis

There were 502 deaths in NICU in one year. The total mortality rate of the NICU admissions in one year is 502/2372 = 21.2%. We can't estimate the actual case fatality rate for the neonatal sepsis, but for those cases with adequate clinical and microbiologic data we can calculate the Case Fatality Rate to be 41/166 = 24.7%.
Neonates with prolonged hospital stay (≥ 2 weeks) were 50 (31.1% of diagnosed neonates)

Frequencies of isolated Bacteria

The commonest isolate is CONS accounting for 41.5% of all blood cultures. Its significance as infectious agent is discussed. The second most common isolate was Staphylococcus aurous. Both of these are gram positive and together they account for the majority (63.1%) of neonatal sepsis. No Group B Streptococcus (GBS) was isolated.

From the gram negatives, Klebsiella Pneumonia has the highest frequency, followed by Acinetobacter spp, Salmonella spp., Pseudomonas spp, E. coli, and other Klebsiella spp. When we group all the Klebsiella species together, they account for 22 isolates from 171 cultures, making it responsible for about 13% of all infections.

Fatality risk of the etiologic bacteria
When we see the correlations between the Etiologic bacteria and the Mortality Rate, the commonest etiologic bacteria, CONS has the highest number of deaths, which is 18 (accounting for 43.9% of all deaths due to sepsis). And when we see the fatality rate of all the neonates infected with CONS, the proportion is 18 deaths from 71 culture proven CONS infections (25.4%).
The second highest number of death was brought about by S. aurous, the fatality cases were 5 (12.2% of all deaths due to sepsis). Following S. aurous, the two next common causes of death were Klebsiella pneumoniae and Acinetobacter, each accounting for 4 deaths (9.8% of all deaths, each.)

Antibiotic Sensitivity and Resistance Pattern
The antibiotic resistance patterns of important etiologic bacteria for Neonatal Sepsis, in the descending order of their frequency are summarized in Table 3.

Table 3 :-Summary of the resistance pattern of the commonest bacteria isolated at the NICU of Tikur Anbessa Hospital (TAH)

Antibiotics / Bacteria	Ampicillin	CAF	Erythomycin	Gentamycin	Cloxacillin	Methicillin	PenicillinG	Cotrimox	Ceftriaxon	Clindamycin	Vancomycin	Norfloxacin	Ciprofloxacin
Gram Positives (The numbers here are the % of resistant strains to the corresponding antibiotic)													
CONS	84.1	44.8	63.9	71.2	68.1	66.7	85.5	76.1	47.7	5.9*	15.7	30.2	23.5
S. aurous	66.7	27.8	63.3	58.1	52.2	41.7	69.7	44.4	41.2	20*	17.2	30.6	25.8
Gram Negatives (The numbers here are the % of resistant strains to the corresponding antibiotic)													
Klebsiella pneumoniae	100	93.8	nd	93.8	nd	nd	nd	60	87.5	nd	mnd	20	13.3
Acinetobacter	100	100	nd	77.8	nd	nd	nd	60.7	55.6	mnd	20	60	.0
Salmonella spp.	100	100	nd	100	nd	nd	nd	100	100	nd	66.7	.0	.0
Pseudomonas spp.	85.7	83.3	mnd	33.3	nd	nd	mnd	71.4	14.3	mnd	mnd	14.3	14.3
E. Coli	83.3	50.0	mnd	40	nd	nd	nd	16.7	33.3	mnd	mnd	33.3	33.3

mnd Majority Not Done
I.e. For a bacterium, if more than 50% of the sensitivity test was not done, then it would be Hasty Generalization to consider the sensitivity result.

nd Not Done or Not Appropriate for the specific antibiotic sensitivity test for the bacteria

* Majority was not done, but since this drug is important for the treatment of the bacteria, the results were included.

DISCUSSION

Almost all (97.6%) of the neonates were started on empirical antibiotics, once they were clinically diagnosed to have sepsis before blood sample was taken for Culture and Sensitivity. The reason for the delay of sample for Blood Culture was (1) The Bacteriology Unit closes after the Off Duty hours and weekends (2)sometimes the attendants don't pay for the Investigation soon enough. Apparently the admitting physicians are obliged to start empirical antibiotics, to avoid any delay of life saving treatment.

The culture positivity rate

Culture positivity rate in this study was 28.7% in the NICU of TAH, Addis Ababa, Ethiopia. This low percentage is probably because of administration of antibiotics before sample was taken for culture. This low positivity rate was also found in other studies. In an Indian study [11] it was 25.2%. Even in TAH, Ethiopia there was a study in adult patients [12] which got only 21.4% of positivity rate.

Frequency of the genders with their relative risks for infection and mortality risks

This indicates, despite the higher incidence of NS in male neonates, there was no statistical significance in the case fatality rates between the two sexes.

There were a total of 280 males and 298 females suspected of sepsis. From these there were 166 neonates whose blood culture grew bacteria; 92(55.4%) were males and 74 (44.6%) were females. And based on the statistical calculations, the p = 0.033, the Odds Ratio of 1.48 (1.01 – 2.17) for a CI of 95% and Relative Risk of 1.32 (1.02 – 1.71) for males was found.

This goes well with our scientific knowledge that males are affected by infection more than female neonates. It has been postulated that it is probably because of a sex linked genetic basis for susceptibility. In addition variations in immune function between the sexes might also play a role 13-15.
In the study 19 from 74 (25.7%) of culture confirmed septic female neonates died and 22 from 92 (23.9%) of confirmed septic male neonates died. But there was no statistically significant difference if we try to see between males and females in their final outcomes; the OR= 1.10 (0.51-2.37) RR=1.07 (0.63-1.83) for 95% CI, and the P value=0.79

Significance of prematurity and low birth weight as a risk for development of NS and poor outcome

As mentioned earlier chance to develop sepsis in the Preterms as compared to Term NBs is 2.08 times more, and the difference in the findings between the preterm neonates and the term neonates is statistically significant, and not merely by chance.

As summarized in Table 3, from among those with confirmed sepsis, comparing the **Preterms** to those with **Term NBs** according to their stay for ≥2 wks, it is found that NBs with the GA<37wks are **2.65 times** likely to stay≥2 wks as compared to those with GA≥37 wks and it is statistically significant, even though it can be explained by their prolonged stay because of other concomitant problems such as VLBW, which warrants a longer stay in the Kangaroo Mother care, until they are discharged with gain of adequate weight.

The difference in infection development between the BW<2.5 and BW≥2.5 Kg newborns was seen. It is found that the chance to develop sepsis in the BW<2.5 Kg Neonates as compared to BW ≥2.5 Kg

Neonates is 1.81 times more and it is statistically significant.
Regarding the comparison between the final **outcome** of **Prematures** to those with **Term NB** with confirmed neonatal sepsis, the OR=2.49 (1.11 – 5.62), the RR=2.00 (1.12 – 3.59) and the P-value = 0.015. It is concluded that the GA<37 is **twice** likely to die as compared to those with GA≥37 wks and it is statistically significant.

The Case Fatality Rate
This study showed that the Case Fatality Rate due to confirmed NS to be 24.7%.
Even though the high number of neonatal death because of sepsis is alarming, similar findings are noticed in other developing countries. In Nigerian study 30.1%, in Saudi Arabian study 22.5%, in Zimbabwe 29%, in Turkey 22.75%, in Indian studies 15.2 – 32% and in Jordan 40% of septic neonates died [16- 23]

Further on WHO estimated that under 5 year mortality during neonatal period to reach 22%, making it the highest period of mortality in children less than 5 years old. together, these organisms are claimed to account for approximately 65-70% of infections, a proportion that has been stable for the last three decades.[3, 4]

In a multicentre study done in San Francisco and Atlanta, Group B Strept. and E. coli are found to be commonest and are followed by organisms like Staphylococci(S. aurous and CONS), S. Viridians, Enterococci, L. monocytogens, Klebsella and Pseudomonas.[5, 6]

From the developing countries, one Indian study showed, Gram-negative organisms were isolated in 60% cases, with Klebsiella 33.8%, Enterobacter 7.5%, Alcaligenes faecalis 4.9%, and Escherichia coli 4.6% being the common microbes. Staphylococcus aureus 24.4%, followed

From among causes of neonatal deaths, the commonest cause was due to infection (34%) 1.

The Commonly isolated Bacteria
As clearly demonstrated in **Table-3**, the commonest bacteria isolated from blood cultures in clinically suspected Neonatal Sepsis are Coagulase Negative Staphylococci (CONS), followed by Staph. aurous, both of which are gram positive and these organisms alone account for 63% of Neonatal Sepsis. These pathogens are followed by Klebsiella pneumoniae, Acinetobacter spp., Salmonella spp., Pseudomonas spp. and E. coli (in descending frequency) which are all gram negative enteric bacteria, and together accounting for about 28%. There are a few other gram positive and gram negative bacteria which make up for the remaining 9%.

Most literatures from developed countries such as USA and Great Briton cite the common causative organisms to be GBS and enteric bacilli, especially Escherichia coli;Take
by coagulase-negative staphylococci 7.9%, were the major Gram-positive isolates [7].

In Pakistan, Khyber Teaching Hospital, Peshawar city, a study showed a different pattern. Escherichia coli was the most common organism found (36.6%), followed by Staphylococcus aureus (29.5%), Pseudomonas (22.4%), Klebsiella (7.6%), and Proteus (3.8%). No group B streptococcus was grown [8]

In African countries like, Senegal, South Africa, Gambia, Nigeria, Kenya, Uganda and Zimbabwe the commonest cause to be S. aurous. But in the developing countries of the Middle East, Latin America, South Asia and Asia Pacific countries the commonest etiologic agent of Neonatal Sepsis is Klebsiella pneumoniae. These

studies excluded CONS as a contaminant [11-13].

There are also other studies with completely different findings [9, 10,]

There seem to be difference in the isolated organisms from different countries and even same site but different time. The above findings clearly show us about the importance of local / Institution based survey of blood culture for assessment of common organisms.

Antibiotic Resistance Patterns

From the gram positives, CONS has higher resistance percentage than S. aurous except for Floroquinolones, Vancomycin and Clindamycin. Even though the additive effect of Ampicillin and Gentamycin dual therapy was not evaluated in study, both organisms showed significantly high resistance to both antibiotics. Majority of CONS isolated are resistant to both Methicillin and Cloxacillin. In comparison, majority of S. aurous isolated from the blood cultures are sensitive to Methicillin, but about half of the isolated S. aurous bacteria are resistant to Cloxacillin. Both CONS and S. aurous are most sensitive to Vancomycin and Clindamycin. But unfortunately, these drugs are very expensive and there are even times when these drugs are not available in the pharmacies. These bacteria are also sensitive for Floroquinolones and to a lesser extent to Chloramphenicol. From the relatively affordable drugs to the majority of Ethiopian community, Chloramphenicol would have been applicable had it not been for the fear of Gray Baby syndrome and potential hematologic side-effects such as agranulocytosis, thrombocytopenia and aplastic anemia, which made this drug less used in the neonates.

The Floroquinolones and especially Ciprofloxacin, is found to be associated with lesser resistance pattern for these gram positive bacteria. The fear in the use of this drug was the possibility that it could cause arthropathy with erosions of the cartilage in weight bearing joints, as it was seen in immature animals. But recent studies failed to demonstrate any causative associations of floroquinolones in development of any pediatric arthropathy [24-25]

From the gram negatives isolated in this study, the commonest isolates are Klebsiella pneumoniae, Acinetobacter, Salmonella, Pseudomonas spp. and E. coli. All five of these gram negative isolated bacteria have high percentage of resistance to Ampicillin and the commonest three gram negative isolated bacteria are also mostly resistant to Gentamycin, Cotrimoxazol, Chloramphenicol and to Ceftriaxon. Pseudomonas and E. coli have relatively lower percentage of resistance to Gentamycin and to Ceftriaxon.

All gram negative isolated bacteria in this study are found to be highly sensitive to Ciprofloxacin.

Comparing these results with those in the developed countries, there are findings some that are similar and others different. In general the resistance pattern of the six common isolated organisms is alarming, because majorities are having multi-drug resistance. The isolation of bacteria with multi-drug resistant pattern might be partly explained by the prior use of empirical Ampicillin and Gentamycin therapy before sample for culture was taken in almost all neonates (97.6%), allowing for selective growth of the multi-resistant strains. On the other hand the high mortality rates found in neonates with sepsis would also indicate the importance of these multi-drug resistant bacteria.

Conclusions & Recommendations

Based on the findings of the study, we can conclude that sepsis is still an important cause of morbidity and mortality in the Neonatal period. Males seem to be affected more than female neonates, even though there was no significant difference in the mortality rates between the sexes.
It is clearly shown in this study and so many other studies in developed and developing countries, the significantly high morbidities and mortalities associated with infections in premature babies. This warrants the urging of the Obstetrics side for their additional effort to avoid premature deliveries.

The antibiotic resistance pattern is alarming for a developing country like Ethiopia, because the empirical treatment in our setup is Ampicillin and Gentamycin, while 83% of etiologic bacteria are resistant to Ampicillin and about 63% to Gentamycin. More over an average of 62.6% of the Staphylococci are resistant to Cloxacillin (another drug available in our setup).

There seem to be difference in the isolated organisms from different countries and even same site but different time. This finding clearly shows us about the importance of local / Institution based survey of blood culture for assessment of common organisms.
It is always better to prevent a disease from occurring than curing it. Frequent and strict hand washing and all the rest points of Infection Prevention protocol should be observed by the NICU and delivery room staff, aiming to prevent any transmission of infection in general, and to stop the escalating multi-drug resistant strains.

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