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Original Research Article

Mortality profile of neonatal deaths and deaths due to neonatal sepsis in a tertiary care center in southern India: a retrospective study

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ABSTRACT

Background: The Neonatal mortality rate is an important indicator for newborn care and directly reflects prenatal, intranatal, and postnatal care. Objective: Primary objective was to analyse the neonatal mortality profile, incidence of neonatal sepsis among neonatal deaths and the pattern of antimicrobial resistance.
Methods: This was a retrospective descriptive study done in a tertiary care regional center. All neonatal deaths from January 2017 to December 2017 were reviewed and primary causes of deaths, incidence of sepsis among neonatal deaths and pattern of antimicrobial resistance were analyzed.
Results: Common causes of neonatal deaths were respiratory distress syndrome (27.4%), asphyxia (23.3%), sepsis (20.1%), congenital malformations, extreme preterm, meconium aspiration syndrome. Case fatality rate was high in extreme preterm neonates (96.8%), followed by respiratory distress syndrome (35.9%), asphyxia (33%), meconium aspiration syndrome (29.4%), congenital malformations (28.8%), and sepsis (22.6%). In present study incidence of neonatal sepsis among total neonatal deaths was about 20.1%. Coagulase negative staphylococcus(CONS) (38.6%) and Klebsiella pneumoniae (32.7%) were the predominant organisms isolated. Highest case fatality rate was associated with Pseudomonas sepsis (80%), *K. pneumoniae* sepsis (64.8%), followed by *Escherichia coli* sepsis (57%) and non fermenting Gram negative bacilli (55.6%).
Conclusions: Sepsis still remains one of the leading cause of death in developing countries. Coagulase negative staphylococcus (CONS) and *Klebsiella pneumoniae* were the most common organism. 15 % enterococci and 9.7 % of CONS were resistant to vancomycin. 24 % of *K. pneumoniae* and 16.6% non fermenting Gram negative bacilli were resistant to amikacin. Multidrug resistance is an emerging problem.

Keywords: Antimicrobial resistance, Multidrug resistance, Neonatal sepsis

INTRODUCTION

About 7.6 lakh newborns die every year in India, the highest for any country in the world.

The Neonatal mortality rate has declined from 44 per 1000 live births in 2000 to 29 per 1000 live births in 2012, but the rate of decline has been slow and lags behind that of infant mortality rate.[1] 70% of infant deaths occur in neonatal period.[1]

The NMR is an important indicator for neonatal care and directly reflects prenatal, intranatal, and postnatal care. The Neonatal mortality rate in India is 28/1000 live births and in Tamil Nadu is 15/1000 live births. Current in 2016 the early neonatal mortality rate in India is 22/1000 live births and in Tamil Nadu is 11/1000 live births.[2]

Sepsis is one of the common preventable causes of neonatal death globally. The most sepsis-related deaths occur in low-income and middle-income countries, where

the epidemiology of neonatal sepsis remains poorly understood.[3] This study was conducted to illustrate the neonatal mortality profile. Secondary objectives were to assess the incidence of sepsis and its contribution to neonatal mortality.

The common bacterial agents associated with neonatal sepsis and their antibiotic susceptibility pattern was also analyzed. This will pave the way for initiation of quality improvement measures to reduce the deaths due to neonatal sepsis in the unit.

METHODS

This was a retrospective study conducted at a tertiary care regional neonatal unit in Southern India. Hospital records of all neonatal deaths (term and preterm) during the period from January 2017 to December 2017 were scrutinized and admission details of all neonates were obtained. The primary cause of mortality, incidence of deaths due to sepsis and pattern of antimicrobial resistance were analyzed. Neonatal deaths were classified based on WHO, ICD10 version: 2010 criteria as neonatal sepsis, birth asphyxia, prematurity, respiratory distress syndrome (RDS), neonatal jaundice, meconium aspiration syndrome (MAS), congenital malformations, congenital heart disease, and any other diagnosis.

Neonatal deaths were then stratified into birth weight and gestational age categories to study birth weight and gestational age specific mortality. Both culture positive and culture negative sepsis were included. Blood culture was collected before starting antibiotics and repeat cultures were done whenever there was a clinical deterioration. The isolates were identified based on standard bacteriological techniques in Microbiology department.

Statistical analysis

Data were analyzed using Statistical Package for Social Science Program Version 20.0. Descriptive statistics measures such as mean, standard deviation, rate and proportions were calculated. Chi-square test was used for analysis of categorical variables. Other statistical tests used were percentages and proportions. Hospital Ethical approval was obtained.

RESULTS

There were 1020 (20.2%) neonatal deaths among 5047 admissions during the period. Mean birth weight was 2013±742 grams and mean gestational age was 33±3.9 weeks. Boys were 57%. 99.2% of the neonates received intravenous fluids and 97% required invasive mechanical ventilation. 7.9% had prolonged rupture of membranes for more than 24 hrs and 9% were born through meconium stained amniotic fluid (MSAF). 41.6% were delivered by cesarean section (Table 1).

Table 1: Baseline characteristics of study subjects.

Variables	Number (%) of neonates (n=1020)
Neonatal variables	
Birth weight gms *	2013 (742)
Gestational weeks *	33 (3.9)
Sex	
Boys	580 (57)
Girls	440 (43)
Intravenous fluids	1012 (99.2)
Mechanical ventilation	990 (97)
Maternal variables	
Prolonged rupture of membranes	81 (7.9)
Meconium stained Amniotic fluid	92 (9)
Caesarean delivery	425 (41.6)

*Values are represented as mean (± Standard deviation)

Common causes of neonatal deaths were respiratory distress syndrome (27.4%), asphyxia (23.3%) and sepsis (20.1%). Other causes of mortality were congenital malformation, extreme preterm, MAS and Intraventricular haemorrhage.

Table 2: Neonatal mortality profile.

Cause of mortality	Admitted N (%)	Case fatality N (%)	p value	ODDS ratio (confidence interval)
Sepsis	908 (18)	205 (22.6)	<0.05	1.19 (1-1.42)
Respiratory distress syndrome	776 (15.4)	279 (35.9)	<0.001	2.67 (2.26-3.16)
Asphyxia	721 (14.3)	238 (33)	<0.001	2.23 (1.88-2.66)
Congenital malformations	371 (7.4)	107 (28.8)	<0.001	1.67 (1.32-2.12)
Meconium aspiration syndrome	252 (5)	74 (29.4)	<0.001	1.69 (1.27-2.39)
Extreme preterm	94 (1.9)	91 (96.8)	<0.001	131.39 (41.51-415.92)
Others	1925 (38.1)	26 (1.4)	<0.001	
Total	5047	1020 (20.2)		

Chi square Test

Case fatality rate was high in extreme preterm neonates (96.8%), followed by RDS (35.9%), asphyxia (33%), Meconium aspiration syndrome (29.4%), congenital malformations (28.8%) and sepsis (22.6%). According to ICD-10 criteria, among 1020 neonatal deaths, proportion of deaths due to RDS was 27.4%, asphyxia (23.3%), sepsis (20.1%), congenital malformations (10.5%), extreme preterm (8.9%) and MAS (7.3%). The cause of mortality is significantly associated with case fatality proportion among the neonates, with a highly significant (p<0.001). Highest case fatality rate was among extreme preterm neonates (Table 2).

Table 3: Mortality profile based on birth weight and gestational age.

	Total admissions	Neonatal deaths	Neonatal deaths (%)
Body weight* (gms)			
<1000	145	139	95.9
1000-1499	333	201	60.4
1500-2499	1687	341	20.2
≥2500	2882	339	11.8
Gestational age # (weeks)			
<28	94	91	96.8
28-31	310	207	66.8
32-33	326	109	33.4
34-36	863	170	19.7
≥37	3454	443	12.8

*p<0.001 (Chi square Test), # p<0.001(Chi square Test)

Analyzing the deaths based on birth weight and gestational age showed about 95% of the neonates <1000g and <28 w of gestation expired (Table 3).

Table 4: Profile of bacterial isolates and their case fatality rates.

Organisms	Number of Isolates (n=505) (%)	Number of Deaths(n=178) Case fatality rates (%)
Gram negative		
Klebsiella	165 (32.7)	107 (64.8)
Non fermenting Gram negative bacilli	36 (7.1)	20 (55.6)
E. coli	14 (2.8)	8 (57)
Citrobacter	6 (1.2)	3 (50)
Pseudomonas	5 (1)	4 (80)
Coliforms	4 (0.8)	2 (50)
Gram Positive		
Coagulase negative staphylococcus	195 (38.6)	18 (9.2)
Staphylococcus aures	42 (8.3)	8 (19)
Enterococcus	38 (7.5)	8 (21)

In present study, the incidence of neonatal sepsis among total neonatal deaths was about 20.1 %. Common organisms isolated in present study were Coagulase negative staphylococcus(CONS) (38.6%), Klebsiella pneumoniae (32.7%), Staphylococcus aureus (8.3%), Enterococcus (7.5%). Non fermenting Gram negative bacilli (7.1%), *Escherichia coli* (2.8%), Citrobacter (1.2%), Pseudomonas (1%) and Coliforms (0.8%). Highest case fatality rate of about 80% with Pseudomonas sepsis, 64.8% with Klebsiella sepsis, *E. coli* (57%) and non fermenting Gram negative bacilli (55.6%) were observed (Table 4).

Table 5: Antimicrobial resistance pattern.

Organisms	Number of resistance isolates n (%)
Gram negative	
Klebsiella	
Amikacin	40/165 (24)
Cefataxime	28/165 (16.9)
Non fermenting gram negative bacilli	
Amikacin	6/36 (16.6)
Cefataxime	0/36 (0)
E. coli	
Amikacin	0/14 (0)
Cefataxime	0/14 (0)
Gram positive	
Coagulase negative Staphylococus (CONS)	
Amoxycillin	74/195 (38)
Vancomicin	19/195 (9.7)
Staphylococcus aureus	
Amoxycillin	17/42 (40)
Vancomicin	0/42 (0)
Enterococcus	
Amoxycillin	19/38 (50)
Vancomicin	6/38 (15)

Among gram-negative organisms, 24% of Klebsiella, and 16.6% of non fermenting gram negative bacilli were resistant to amikacin. 16.9 % of Klebsiella were resistant to third generation cephalosporins. Among Gram-positive organisms, 15% Enterococci and 9.7% of CONS were resistant to vancomycin. All S. aureus isolated were sensitive to vancomycin (Table 5).

DISCUSSION

In present study, sepsis was one of the most common cause of neonatal death and others were RDS and asphyxia. Overall mortality rate during the study period was 20.2%. Liu L et al showed preterm birth complications (14.1%), intrapartum related complications (9.4%), and sepsis or meningitis (5.2%) as the leading cause of neonatal deaths.[4] Mmbaga et al had shown an overall mortality of 10.7% over a period of 10 years and leading causes of death were birth asphyxia (n=245, 45.7%), prematurity (n=188, 35.1%), congenital malformations (n=49, 9.1%), and infections (n=46, 8.6%).[5] Million deaths study collaborators showed that three common causes of neonatal mortality were prematurity and low birth weight (0.33 million), neonatal

infections (0.27 million), and birth asphyxia (0.19 million).[6] In a study by Saminathan et al, common causes of neonatal mortality were perinatal asphyxia, followed by prematurity and RDS.[7] According to NNPD report 2002-2003, among the extramural admissions, the common causes of death were asphyxia (48.7%), sepsis (25.2%) and extreme prematurity (13.4%) and in intramural admissions the common causes of death were asphyxia (54.9%), extreme preterm (28.6%), and sepsis (4.1%).According to UNICEF, globally, the main causes of neonatal deaths were preterm birth complications (35%), intrapartum-related complications (24%), and sepsis (15%).[8,9] Similar observations were seen in present study. Still sepsis is one of the leading cause of death in developing countries, whereas extreme prematurity is the leading cause of death in developed countries.

Respiratory distress syndrome (27.4%) was the leading cause of death in present study, and the case fatality rate was 35.9%. Mmbaga et al in their study, reported RDS as a common cause of death contributing to about 10% of total deaths with case fatality rate of about 52%.[5] Specific and simple measures have been identified which could be implemented to reduce deaths related to low birth weight and preterm in low-income countries.[9] In all high-risk pregnancies to be delivered in a tertiary care center, prophylactic use of steroid during premature labor, early initiation of CPAP in labor room and early referral of these preterm neonates for surfactant therapy should be encouraged.

Case fatality rate among neonates with birth weight <1000 gm was very high (95.9 %) while it was 60.4% among neonates 1000 to 1499 g, 20.2% in 1500 to 2499 g, and 11.8 % in neonates >2500 g. In present study, neonates with birth weight <2500 g constituted about 42.9% of total admissions and 66.8% of total deaths. According to Mmbaga et al., neonates with birth weight below 2500 g constituted 29% of all admissions and 52.1% of all deaths.[5] Survival was strongly related to birth weight, with risks for mortality or major morbidity on an average doubling for each 20-25% decrease in birth weight.[10]

In present study, common organisms isolated were Coagulase negative staphylococcus (CONS) (38.6%), and *Klebsiella pneumoniae* (32.7%), *Staphylococcus aureus* (8.3%), Enterococcus (7.5%), Non fermenting Gram negative bacilli (7.1%), *Escherichia coli* (2.8%), Citrobacter (1.2%), Pseudomonas (1%) and coliforms (0.8%). Among culture positive cases, predominant organisms causing mortality were Pseudomonas sepsis (80%), Klebsiella sepsis (64.8%), *E. coli* (57%) and non fermenting Gram negative bacilli (55.6%). *K. pneumoniae* and other Gram-negative organisms were the common causes of sepsis in a study by Zakaria et al, however, in the developed countries, Group B Streptococcus and coagulase-negative staphylococci were the predominant causes of sepsis.[11] According to DeNIS study, the common pathogens implicated in sepsis include E. coli, group B streptococci, listeria monocytogenes, and *Enterococcus spp*.[3] An antibiogram is an overall profile of antimicrobial susceptibility testing results of a specific microorganism to a battery of antimicrobial drugs.[12]

Among gram-negative organisms, 24% of Klebsiella, and 16.6% of non fermenting gram negative bacilli were resistant to amikacin and 16.9% of Klebsiella were resistant to third generation cephalosporins. In DeNIS study,they had observed high rates of multidrug resistance in *Klebsiella spp.* (54%), and *E. coli* (38%) isolates.[3] This high degree of antimicrobial resistance among the Gram-negative organisms in present study is similar to that found in the DeNIS study.[3] Among Gram-positive organisms, 15% enterococci and 9.7% of CONS were resistant to vancomycin. All S. aureus isolated were sensitive to vancomycin. Multidrug resistance is an emerging problem. Limitations of present study were that this was a retrospective study and predominantly, neonatal deaths were analyzed.

CONCLUSION

In present study, sepsis was one of the most common cause of neonatal mortality. Coagulase negative staphylococcus (CONS) and *Klebsiella pneumoniae* were the predominant organisms. *K. pneumoniae* had a high case fatality rate. Gram-positive organisms have developed vancomycin resistance. Multidrug resistance is an emerging problem.

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