

A Study on The Disease Pattern and Outcome in Neonatal Intensive Care Unit, Tertiary Care Hospital of Andhra Pradesh

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ABSTRACT

Background: There was very scanty data available regarding the neonatal morbidity and mortality patterns in NICU. Hence, the current study aimed to document and analyze the disease pattern, and outcome in neonates admitted in NICU of tertiary care center.

Subjects and Method: A prospective observational study was conducted at neonatal intensive care unit (NICU) of SVRRGGH, Tirupati from September 2014 to August 2015. A total of 2287 newborns were admitted who met selection criteria. All neonate's demographics, clinical profile, and outcome were analyzed.

Results: From a total of 2287 newborns, 71.7% were delivered vaginally, 56.05% were male, 38.0% were <2500 g, and 48.02% were preterm babies. The neonatal deaths consisted of 448 (19.58%) newborns; 71.98% of whom pre-term babies, 80.8% of whom birth weight >2.5kg, 23.2% of whom out born, and majority died before 7 days of age. Neonatal sepsis (30.65%) is the most common cause of death followed by birth asphyxia hypoxic ischemic encephalopathy in 29.04%, hyaline membrane disease (11.03%), neonatal jaundice (9.68%), meconium aspiration syndrome (7.69%), hemorrhagic disease of newborn (1.68%), and congenital malformations (2.79%). There was a statistical association observed between neonatal death and gender ($p=0.023$); neonatal death and mode of admission; neonatal death and gestational age ($p<0.001$); neonatal death and birth Weight ($p<0.001$).

Conclusion: current study identified preterm, low birth weight, neonatal sepsis, birth asphyxia, Hyaline membrane disease as major causes of morbidity and Neonatal sepsis, Hyaline Membrane Disease, and HIE as the major contributors to the neonatal mortality. Improving antenatal care, maternal health checkup and timely referral of high risk cases to tertiary care centers may help to improve neonatal outcome.

Keywords: neonatal sepsis, antenatal care, low birth weight, neonatal mortality.

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BACKGROUND

Neonatal period is the first 28 days of life.

It is the most vulnerable period of life due to different diseases which in most cases

are preventable (Lawn et al., 2014). India contributes to 17.5% of World's Population and nearly one-fifth of the total live births. India contributes to 16% of global maternal deaths, 21% of Under 5 deaths and 27% of neonatal mortality (Sankar et al., 2016). According to Sample Registration System, the current neonatal mortality in our country is 29/1000 live births (Tomar et al., 2014). One of the millennium development goals is to reduce the number of deaths in children under 5 years to two thirds by year 2015 and to achieve this goal reduction in neonatal deaths will be required especially in developing countries (Norheim et al., 2015). Neonatal mortality is not uniform across India. While state of Kerala has already attained single digit NMR (7/1000 live births) (Nagesh and Razak 2016). Even within the state neonatal mortality rate differs between institutions. Main causes of mortality and morbidity in developed countries are unpreventable causes like congenital malformations. But in developing countries main causes are preventable like sepsis, prematurity, birth asphyxia (Rakholia et al., 2014). Though there is decreasing trend in Neonatal Mortality rate in recent years, NMR is still high in developing countries (Goudar et al., 2015). In developing countries death in the newborn period, account for 50-70% of infant mortality (Collaborators 2010). Variations in mortality rates are important because they permit inferences about quality of care. Examination of care practices associated with variation in mortality rates can provide insights into how care practices might be changed to improve outcome (Siva Saranappa et al., 2014).

Transferring women at risk of very preterm birth to perinatal centers for delivery decreases neonatal mortality rate considerably (Marlow et al., 2014). Type of

tertiary care facility to which neonates are transferred may influence outcomes (Hirani et al., 2017). Infants born outside (out born infants) are at increased risk of developing many major neonatal complications and long-term neuro developmental disabilities possibly because of poor access to specialist support (Boogaard et al., 2017).

Improvement of neonatal mortality is a challenge in developing countries such as in India due to scanty data. There is very scanty data which is available regarding the neonatal morbidity and mortality patterns in NICU, even if it was there, it is available mainly from tertiary care level-III NICU's in metropolitan cities (Chawla and Suresh 2014).

Risk factors for neonatal mortality such as place of residency, antenatal care (ANC) follow-up, and neonatal illness were indifferently explained by previous authors (Hoseini et al. 2015; Demisse et al., 2017)

Hence, identifying those factors will be important to guide the development of focused and evidence-based health interventions to reduce neonatal mortality. There is no clear evidence found to identify the magnitude of neonatal mortality and associated factors.

To address these, current study conducted to know the disease pattern of Neonatal admissions which will reflect the disease burden in the community, neonatal health care services at various levels including antenatal care, safe delivery practices, institutional deliveries, care of newborn at birth (Hoseini et al., 2015).

The study of outcome of Neonates in different disease pattern will guide us to prioritize our services, planning and strengthening of neonatal units in the form of improving infrastructure, increasing manpower, proper training of health personnel, and updating the existing protocols. Therefore, regular review of the dise-

ase pattern in any setting is important for providing better services to the patients.

SUBJECTS AND METHOD

1. Study Design

A hospital-based prospective observational study was conducted among 2287 randomly selected neonates admitted to NICU of Sri Venkateswara Ramnarain Ruia Government General Hospital, Tirupati during September 2014 to August 2015.

2. Population and Sample

All neonates admitted to NICU of SVRR general Hospital from September 2014 to August 2015 were the study population. Neonates with incomplete medical records, neonates referred to other places, and left against medical advice were excluded from the study.

The sample size was determined by using a single population proportion formula with assumptions of confidence level at 95% = 1.96, a margin of error (d) = 0.03, and a reasonable proportion of neonatal mortality (p= 0.230) from a previous study Salve et al. (2015) and adding 10% non-retrieval rate, the final sample size became 2287. The sampling frame was prepared for those study populations (admitted neonates) using their Medical Registration Number obtained from their medical records. Finally, the study subjects that had been included in the study were identified by using a simple random sampling technique (computer-based) from the sampling frame (N = 2,287).

3. Study Variables

The dependent variable was neonatal outcome pattern from NICU (either discharge or died).

Sociodemographic characteristics: maternal age, family monthly income, educational level, maternal occupation, religion, marital status, ethnicity, and residence.

Maternal medical and obstetric characteristics: gestational age, gravidity, parity, history of previous preterm birth, birth interval

between current and previous last pregnancy, type of delivery, and other medical complication during pregnancy.

Newborn characteristics: mode of admission of newborn, sex of the newborn, gestational age at birth, birth weight, neonate laboratory/ radiological investigations if necessary. cause of admission of neonate: neonatal sepsis, birth asphyxia HIE, hyaline membrane disease, meconium aspiration syndrome, hemorrhagic disease of newborn, neonatal jaundice, and congenital malformations.

4. Operational Definition of Variables

Neonatal mortality was defined as the number of neonates who died at the neonatal intensive care unit throughout the study period.

Cause of neonatal death means that any medical or other causes diagnosed by pediatricians after conducting the laboratory investigation and recorded on the medical chart as a cause of neonatal death.

Low birth weight was a weight of less than 2,500 g (up to and including 2,499 g) irrespective of the gestational age.

Prematurity was described as live born neonates delivered before 37 weeks and using new bellard scoring.

Neonatal Jaundice was diagnosed by clinical examination (Krammer Scale) and by assessing serum bilirubin.

In born means babies born at Govt. Maternity Hospital, Tirupati.

Outborn means babies referred from private and Govt. Hospitals other than Govt. Maternity Hospital, Tirupati.

Inadequate antenatal visit means that having ANC follow-up < 4 times.

Sepsis was record of infection or sepsis diagnosed either clinically or with culture by professionals during admission of the neonate and recorded on the chart.

Birth asphyxia was diagnosed whenever a neonate had an Apgar score < 6 in the fifth minute and/ or if he/ she did not cry imme-

diately after birth; had respiratory distress, floppiness, loss of consciousness, presence of convulsion, and loss of neonatal reflexes.

Gestational age was the duration of time measured from the first day of conception and expressed in completed weeks.

5. Study Instruments

The hospital NICU is a tertiary Care Centre with level-III care having facilities for mechanical ventilation, warmers, central oxygen line, phototherapy Units, Multi-Channel monitors, exchange transfusion facilities which are needed for care of sick Neonates. Babies are admitted in NICU as per admission criteria by FBNC guidelines and triaged into various levels of care they require. Data of all the admitted babies were documented in a preformed proforma on the basis of postnatal age of baby, gender, place of delivery, gestational age, birth weight, indication for admission and babies were treated according to standard protocols (FBNC), then babies were followed up to the discharge/ death and events during admission period like any complications, interventions were documented.

6. Data analysis

Continuous data were presented as mean and standard deviation and range and categorical data were presented as frequency and percentage. Results are analyzed by chi-square goodness of fit test $P \leq 0.05$. The data were analyzed using SPSS version 22.0.

7. Research Ethics

The current study protocol was approved by Institutional Ethics Committee of Sri Venkateswara Ramnarain Ruia Government General Hospital, Tirupati. Informed consent in the local language has been provided, and explained, and Consent was obtained from parents of guardians of the neonate.

RESULTS

1. Sample Characteristics

That neonates who developed neonatal nec-

rotizing enterocolitis had lower birth weights, lower gestational age than neonates who did not develop birth asphyxia and neonatal sepsis. Neonates whose were surgically treated had lower birth weights, low gestational age, and lower Apgar scores at 1 min than neonates who were managed medically.

Analysis univariate also showed that neonates who developed necrotizing enterocolitis were often exposed to several different medications: pre and postnatal glucocorticoids, surfactant, erythropoietin, etc. They were exposed to invasive procedures such as umbilical vessel catheterization and mechanical ventilatory support than neonates who did not develop necrotizing enterocolitis. Neonates in the surgically were also often exposed to several different medications.

And invasive procedures than neonates of medically treated. Breast milk use was less frequent in neonates who developed Birth asphyxia or necrotizing enterocolitis when compared to neonates who did not develop necrotizing enterocolitis

a. Demographics

Table 1 show that a total of 2,287 neonate's outcome status was included in the analysis. Out of those, out born babies were admitted higher (57.97%) compared to inborn babies (42.03%). There is statistically significant difference among the distribution of cases depending on mode of admission. The majority of 96.76 % of the neonates were born at the hospital compared to home deliveries (3.24%). Male babies are admitted more (56.05%) compared to female babies (43.95%). There is no statistically significant difference among the distribution of cases according to gender. Study mothers were mostly from rural areas (84.3%) compared to urban areas (15.7%).

b. Obstetrics characteristics

Table 1 show that the majority of the neonates were born at the hospital. More than half (51.98%) of neonates were term while

48.02% of neonates were preterm and there is statistically significant difference among the distribution of cases depending on Gestational Age ($p < 0.05$). Most of the babies born through normal vaginal delivery in 71.7%, followed by LSCS in 21%.

c. Clinical characteristics of neonates

Table 1 show that majority of the neonates were admitted within 24 hour of life. Regarding admission problems, majority of admissions were due to neonatal sepsis which account 30.66%, followed by birth asphyxia HIE (29.04%), hyaline membrane disease (11.03%) and neonatal jaundice (9.68%), meconium aspiration syndrome (7.69%),

congenital malformations (2.79%), and hemorrhagic disease of newborn (1.68%). There is statistically significant difference among the distribution of cases depending on disease pattern. Bulk of the problems encountered by neonates are on the 1st day of life (51%) and then there is gradual decline in the admission rate with increasing age of the baby. Majority, 62% of neonate admissions were low birth weight (LBW), and 38.0% neonatal baby weight > 2.5 kgs. Even in term babies small for gestational age babies were present. There is statistically significant difference among the distribution of cases depending on birth weight.

Table 1. Results of demographic characteristics

Characteristic	Variable	Frequency (N)	Percentage (%)
Age of the neonate on admission	1 day	1162	50.8
	2-7 days	807	35.3
	>7 days	318	13.9
Gender	Male	1282	56.05
	Female	1005	43.95
Gestational Age at birth	<34 weeks	642	28.08
	34-37 weeks	456	19.94
	Term (>37 weeks)	1189	51.98
Weight on admission	≥ 2500 g	868	38.0
	1500-2499 g	892	39.0
	1000-1499g	483	21.0
	<1000 g	44	2.0
Place of delivery	Health Institution	2213	96.76
	Home	74	3.24
Type of delivery	NVD	1641	71.7
	LSCS	481	21.0
	AVD	91	4.0
	Home	74	3.3
Mode of Admission	In born	961	42.03
	Out born	1326	57.97
Dwelling Place	Urban	359	15.7
	Rural	1928	84.3

2. Analysis Univariate

Table 2 show that a total admission, 448 deaths accounting for 19.58% of total neonatal mortality. Neonatal mortality is more in male babies ($n = 277$) compared to female babies ($n = 171$). Neonatal mortality is more in outborn babies ($n = 308$) com-

pared to Inborn babies ($n = 140$) with statistically significant difference ($p < 0.05$). Neonatal mortality is more in pre-term babies ($n = 318$) compared to term babies ($n = 130$) with statistically significant difference. Neonatal mortality is more in low-birth-weight babies ($n = 362$, 80.8%) compared to

normal baby weight >2.5 kgs (n= 86,19.2%) with statistically significant difference among the distribution of neonatal deaths according to birth weight.

Table 4 show that regarding morbidities, neonatal sepsis (35.49%) is the most common cause of death followed by prematurity (27.23%), birth asphyxia HIE (25.89%), Meconium aspiration syndrome (7.81%) and there is a statistically significant difference among the distribution of neonatal deaths according to cause of death. In the total of 2,287 babies who were enrolled in the study, 1,839 babies were discharged and 448 babies were died.

3. Analysis multivariate

Multivariate logistic regression showed that the most important variable associated with

the development of necrotizing enterocolitis was birth weight. Variables other than birth weight were found to be independently associated with an increased risk for necrotizing enterocolitis, those were being on a ventilator during the first week of life. Neonates were highest risk for necrotizing enterocolitis weighed <1 kg body weight and received higher medications during the first week of life. Delivered by cesarean section and a history of surgical intervention were associated with a decreased risk of necrotizing enterocolitis independent of birth weight (Table 5). Delivery by cesarean section and have received breast milk during first week of life were associated with a decreased risk for birth asphyxia or necrotizing enterocolitis.

Table 2. Results of univariate analysis

Variable	Survival		Deaths		p
	N	%	N	%	
Total	1839	80.41	448	19.59	
Gender					
Male	1005	43.95	277	21.6	0.020
Female	834	17.45	171	17	
Mode of Admission					
Inborn	1186	43.47	140	14.5	<0.001
Outborn	653	18.83	308	23.2	
Gestational age (weeks)					
Term (>37 weeks)	1059	46.3	130	29.02	< 0.001
34-37 weeks	317	13.8	139	31.03	
<34 weeks	463	20.2	179	39.95	
Birth weight (kg)					
> 2.5 kg	782	34.19	86	19.20	< 0.001
1.5-2.499 kg	736	32.18	156	34.82	
1-1.499	311	13.6	172	38.40	
<1 kg	10	0.43	34	7.58	

Table 3. Results of univariate analysis (data continuous)

Variable	Survival		Deaths		p
	Mean	SD	Mean	SD	
Birth weight	1.7	0.8	1.2	0.7	<0.010
Gestational age	31.5	5.5	29.5	4.2	<0.010
Apgar at 1 min, Median (25 th -75 th percentile)	7 (6-8)	-	6 (4-8)	-	0.900
Apgar at 5 min, Median (25 th -75 th percentile)	9 (8-9)	-	8 (7-9)	-	0.900

Table 3. Cause of morbidity and mortality

Disease	Outcome			
	Live		Deaths	
	N	%	N	%
Neonatal sepsis	542	23.7	159	35.49
Birth asphyxia HIE	548	23.97	116	25.89
Hyaline membrane disease	130	5.69	122	27.23
Meconium aspiration syndrome	141	6.16	35	7.81
Hemorrhagic disease of newborn	38	1.68	-	-
Neonatal jaundice	222	9.68	-	-
Congenital malformations	55	2.40	9	2.02
Others	163	7.12	7	1.56

Table 4. Multivariate logistic analysis for neonates with and without necrotizing enterocolitis or birth asphyxia

Variable	OR	95% CI	p
Delivered by cesarean section	0.6	0.5 to 0.8	<0.001
Neonates exposed to medications	1.6	1.3 to 2.0	<0.001
Neonates exposed to surgical interventions	0.7	0.5 to 0.8	<0.001
Birth weight	Increased with decreasing weight	-	<0.001
Apgar at 5 min	Increased with decreasing score	-	0.04

DISCUSSION

The present study is conducted over a period of one year from September 2014 to August 2015. During this study period a total of 2287 babies were admitted, and 448 deaths were occurred during study period.

In the present study more than half of the babies were admitted on day one of post-natal life. This indicates problems were started in antenatal period or during delivery. Similar results were observed in study by Prasad et al. (2011) in this study 85.53% of babies were admitted in the first ten days of postnatal life(Prasad and Singh 2011).

In the present study more number of term babies were admitted than preterm babies, more number of male babies were admitted compared to female babies. Similar reports were observed as 59.23% (Thammanna et al., 2015).

In the present study more number of male babies were admitted (56.05%) compa-

red to female babies (43.95%). Similar results were observed in study done by Sridhar et al. (2015) (M: 59.23%), Kumar et al. (2012) (M: 59.8%) (Kumar et al., 2012).

In the present study 42.03% were inborn babies and 57.97% were outborn babies. Similar results were observed with study done by Prasad et al. (2011) (41.73%), Gauchan et al. (2011) in Nepal (32.4%) (Gauchan et al., 2011).

In a study by PV Sridhar et al., Inborn admissions are more compared to outborn admissions. But in our study outborn admissions are more compared to inborn admissions. This is because our Govt Maternity Hospital has attached Special Newborn Care Unit (SNCU) with Level-II care services, so baby's requiring Level-II care services are admitted in SNCU and babies requiring Level-III Care are being referred to our NICU.

In the present study low birth weight babies are observed more in number

(62.05%). Similar results were observed in the study done by Prasad et al. (2011) (65.63%), and (Zulfqar, 2009) (60.83%).

This may be due to poor maternal health status and poor antenatal checkup. According to UNICEF "The State of World's Children 2010" report, 28% neonates are born with Low Birth Weight in India. Similar rate of low birth weight and preterm admission have been reported by study conducted by Garg et al. (2005) in New Delhi (Garg et al., 2005).

In the present study most common cause of neonatal morbidity is neonatal sepsis (30.65%) followed by HIE (29.08%) and hyaline membrane disease. Results were compared with study done by Sridhar et al., (2015) in which morbidity in neonatal sepsis (28.8%), Hyaline membrane disease (23.85%), HIE (17.72%). In study done by Rubina Zulfqar et al, neonatal sepsis is the leading cause for neonatal admission. In study by Dr. Gauri Shankar Shah et al. (2012) neonatal sepsis, prematurity and birth Asphyxia are the leading causes of neonatal admissions.

According to National Neonatal Perinatal Database (NNPD 2002-03), Sepsis is the most common morbidity responsible for admission followed by prematurity and perinatal Asphyxia. Neonatal sepsis acts as an important cause for morbidity and mortality especially among low birth weight and preterm babies.

In the present study neonatal mortality is more in male babies compared to female babies and similar results were observed in study done by Kumar et al. (2012) (M: 56.25%; F: 43.75%).

In the present study neonatal mortality is more in out born babies (23.2%) compared to inborn babies (14.5%). Similar results were observed in study done by Sridhar et al. (2015) (I: 6.69%, O:8.36%).

In our study out born babies have a

significantly higher mortality when compared to Inborn babies. This comparison highlights the babies which have been referred for the requirement of NICU care have higher mortality. This can be due to problems associated with neonatal transport. Various complications of neonatal transport such as hypothermia, hypoglycemia and others have been reported. Even intra hospital transports are associated with increased risk of clinical complications. Pankaj reported a mortality of 32.2% in transported neonates (Huang et al., 2010; Pankaj et al. 2012). Goldsmit et al. (2012) reported that 28 of 160 transported Neonates died.

In the present study neonatal mortality is more in low-birth-weight babies (80.81%) compared to babies' weight >2.5 kgs. Similar results were observed in study done by Prasad et al. (2011) (80.32%), Kumar et al. (2012) (59.2%).

High proportion of mortality in low-birth-weight babies may be due to poor antenatal care, poor nutritional status of pregnant mother and delayed referral from peripheral hospitals. Neonatal sepsis acts as an important cause for morbidity and mortality in low birth weight and preterm babies.

In the present study neonatal sepsis is the most common cause of neonatal mortality followed by hyaline membrane disease and birth asphyxia HIE. Similar results were observed in study done by Prasad et al. (2011) (sepsis 34.3%). In study done by Shah et al. (2012) neonatal sepsis is the leading cause of death (32.6%) followed by prematurity (27.2%) and birth asphyxia (25.9%). In study by Jan et al. (2013) neonatal sepsis is the leading cause death (41.36%) (Jan et al., 2013).

According to NNPD (2002-03), neonatal sepsis is one of the commonest causes of neonatal mortality. in the study report published by ICMR reports sepsis (32.8%)

as the major cause for neonatal mortality followed by birth asphyxia (22.3%) and prematurity (16.8%). In the study done at JIPMER, Sepsis was the cause for death in 52.3% of neonates followed by birth asphyxia and injuries (Augustine et al., 1994). In our study overall mortality is 19.58%. Which was comparable (18.69%) with study done by Prasad et al. (2011).

Mortality rate in our study is higher when compared to other Indian studies. Because in our study majority of deaths in outborn babies because they were brought to NICU in critical condition due to delay in referral and poor transport facilities. Deaths due to hyaline membrane disease and birth asphyxia may probably be due to poor antenatal care, malnourished pregnant women, delivery in a facility with poor resuscitation, delay in referral from peripheral hospitals.

In our study overall most common cause of neonatal mortality is neonatal sepsis. In preterm hyaline membrane disease is most common cause of neonatal mortality. In term, neonatal sepsis followed by birth asphyxia are the most common causes of deaths.

In present study majority of admissions were on day one of life. So major problems were encountered in either antenatal period or during delivery. Morbidity and mortality may be decreased by better antenatal care, institutional deliveries and good perinatal monitoring. Majority of admissions in NICU are due to neonatal sepsis followed by birth asphyxia and prematurity. Neonatal mortality is more common with Neonatal Sepsis followed by prematurity and Birth asphyxia. Neonatal sepsis is the most common cause of neonatal mortality and morbidity this is addressed by creating awareness among health personnel of district hospitals and primary health centers about the importance of hand washing and use of sterile technique for delivery has to be

emphasized to minimize the risk of sepsis. Strict aseptic protocols should be implemented in tertiary care center. Significant mortality in out born babies as compared to Inborn highlights the need for better transport facilities and early referral of the Newborns requiring NICU care. There is a need to establish Neonatal care facilities especially in rural and remote areas so that the problems of Neonatal transport can be minimized. Care facilities at district/ sub-district level may be strengthened to decrease mortality. Deaths due to prematurity and Birth Asphyxia can be decreased by better Antenatal Care, Perinatal monitoring and hospital delivery. Most of the morbidities and subsequently mortalities can be prevented by improving and effective implementation of important preventive services like maternal care and IMNCI, timely interventions and timely referral to tertiary care centers for delivery of high risk pregnancies and care of neonates in high risk situation.

The large sample size is the major strength of this study with thorough follow-up for every neonate. Data regarding mortality and morbidity pattern in NICU admissions can be useful and applicable to set major prospective studies at other centres.

AUTHOR CONTRIBUTION

MK, and ZUR were involved in conception, collection of data, and in drafting of the manuscript. SSB, and SAK were involved in analysing the data. MK, SSB, SAK and ZUR were involved in critical revision of the manuscript.

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CONFLICT OF INTEREST

There are no conflicts of interest.

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