Am J Blood Res 2023;13(2):71-76
www.AJBlood.us /ISSN:2160-1992/AJBR0148311

Original Article

Pattern and predictors of mortality among inborn and out born neonates on ventilatory support: an unmatched case-control study

Manoj Kumar[1], Swati[1], Bijit Biswas[1], Avinash Kumar[2], Anjali Kumari[3], Rajan Kumar[1]

[1]All India Institute of Medical Sciences, Deoghar, Jharkhand, India; [2]All India Institute of Medical Sciences, Patna, Bihar, India; [3]Anugrah Narayan Magadh Medical College, Gaya, Bihar, India

Received December 7, 2022; Accepted April 10, 2023; Epub April 15, 2023; Published April 30, 2023

Abstract: Background: Limited literature was available on the pattern and determinants of mortality among inborn neonates in comparison to the out born ones. The study's goal was to investigate the patterns and risk factors for mortality among hospitalised, on-ventilator inborn and out born neonates. Materials and methods: It was an unmatched, case-control, pilot study conducted between January and December 2020 using information retrieved from the medical records of patients attending the neonatal intensive care unit (NICU) of a tertiary healthcare facility, namely Narayan Medical College & Hospital, situated in eastern India. Results: Congenital pneumonia was the leading cause of death in inborn neonates, with an overall mortality rate of 33.4%. Meanwhile, the overall fatality rate for out born neonates was found to be 43.3%, with birth hypoxia being the most common cause. The only significant attribute affecting mortality in inborn neonates was low arterial blood gas (ABG) pH, whereas in out born neonates they were prematurity, thrombocytopenia, low ABG pO_2, and high pCO_2. Overall, new-borns with thrombocytopenia, low ABG pO_2, and high pCO_2 were observed to be at higher risk for mortality compared to others. Conclusion: The mortality rate of out born neonates was higher than inborn ones. The attributes affecting mortality were observed to be prematurity, thrombocytopenia, low ABG pH, pO_2, and high pCO_2.

Keywords: Infant, new-born, intensive care, neonatal, mortality, disease attributes, arterial blood gas

Introduction

The neonatal period is the most vulnerable one in a child's life. India has made considerable progress in reducing the neonatal mortality rate (NMR) from 29.5 (2016) to 24.9 (2020) per 1000 live births, although this was still high than the reported global average for the year 2020 (17 per 1000 live births) [1, 2]. The majority of these neonatal deaths were attributed to preterm birth, intrapartum-related issues (birth asphyxia or lack of breathing at birth), infections, and birth abnormalities [3].

In hospital settings, Neonatal intensive care units (NICUs) are the most likely place of such deaths. Although indications of NICU admissions has differed in developed (i.e., congenital abnormalities) and developing countries (i.e., prematurity, infections, jaundice, birth asphyxia, pneumonia etc.) [4]. As per available literature in this regard, predominant causes of NICU admissions in India were sepsis, perinatal asphyxia, prematurity, respiratory distress syndrome (RDS), meconium aspiration syndrome (MAS) and jaundice with the first three being the leading causes of mortality [4-7].

Out born neonates were more vulnerable to death compared to inborn ones as per the existing reports [6]. The attributes affecting neonatal mortality were reported to be prematurity, gestational age, hypoglycaemia, apnoea, pulmonary and intracranial haemorrhage, sepsis, hypoglycaemia, thrombocytopenia, pneumothorax, shock etc. [5, 7-12]. Sadly, no such relevant literature is available from the eastern part of India. There is also a paucity of data about predictors of mortality for inborn in comparison to out born neonates. Therefore, this pilot unmatched case-control study was planned to investigate patterns and predictors of mortality among inborn and out born neonates on venti-

latory support, admitted in a tertiary care health facility in eastern India.

Materials and methods

It was an unmatched, case-control, pilot study carried out between January and December 2020 utilizing information retrieved from the medical records of patients attending the neonatal intensive care unit (NICU) of a tertiary healthcare facility, namely Narayan Medical College & Hospital, situated in Rohtas district of Bihar, India. An inborn neonate was considered as a case in this study, while an out born ne was recruited as a control. Notably, a newborn, delivered by a skilled birth attendant (SBA) in the study healthcare facility was considered as inborn. All other births including home deliveries who were referred from outside to the study healthcare facility for seeking NICU care were considered out born.

The minimum sample size for the study was calculated to be 179 for cases and 358 for controls using OpenEpi (an online sample size calculator), taking into account the death rates of inborn and out born neonates as 14.9% and 25.4%, respectively, as reported by a prior study from Uttarakhand by Rakholia R et al. [6], two controls for one case, 95% confidence, and 80% power [13]. Although considering the feasibility and logistic constraints, a record-based pilot study conducted among 20% of the smallest required sample (30 cases and 60 controls) to investigate the issue and explore the feasibility of a larger study.

All the inborn and out born neonates admitted to the SNCU of the Narayan Medical College & Hospital during the study period were the potential study participants. Incomplete medical records of neonates with missing study variables were excluded. Although, there was no such incomplete medical record found within the sampling frame. During the study period, in total 56 inborn and 103 out born neonates attended the concerned healthcare facility. Using simple random sampling (SRS), the predetermined number of samples was chosen from the serially numbered census list for both groups. Random numbers generated using an OpenEpi random number generator [14]. Indications for SNCU admission, birth weight, gestational age, hypoglycaemia, intraventricular haemorrhage, seizures, pulmonary haemorrhage, shock, ventilator-associated pneumonia (VAP), pneumothorax, thrombocytopenia, and arterial blood gas (ABG) readings (pH, pO_2 and pCO_2) were the variables that were documented from medical records for the study. These variables were considered based on review of the literature and their documentation status in the study hospital [5-12] (**Figure 1**).

Ethical issues

Institutional ethics committee (IEC) of the concerned tertiary healthcare facility approved the study (reference number: NMCH/IEC/07/2020). Since this was a retrospective study using hospital records, informed written consent from the study participants cannot be taken. During data collection and reporting, anonymity of the study participants was assured. The study abided all the principles of the Declaration of Helsinki.

Statistical analysis

Microsoft Excel was initially used to enter the data, which was later imported for analysis into the statistical package for social sciences (SPSS) (version 16.0). The quantitative variables of the study were expressed as n (%). Assess the difference regarding ventilatory support indications between cases and controls, the chi-square test of proportion was applied. Univariate logistic regression analysis was used to determine the relevant factors associated with mortality among the study participants, and odds ratios (ORs) were used to express the strength of the association. The 95% confidence level was taken as the default for all inferential statistics.

Results

The overall mortality rate for inborn neonates was 33.4%, with congenital pneumonia, persistent pulmonary hypertension of the new-born (PPHN) and hyaline membrane disease (HMD) accounting for 50.0%, 40.0%, and 37.5% of deaths respectively. Although, birth asphyxia (47.6%), MAS (46.7%), and HMD (44.5%) were the most frequent causes of death among out born neonates with an overall mortality rate of 43.3%. However, there was no discernible difference in the overall and cause-specific mortality rates of inborn and out born neonates (**Table 1**).

Figure 1. Map of India showing the location of the study hospital.

Table 1. Distribution of neonates as per indication of ventilatory support and treatment outcome

Indication of Ventilatory Support	Inborn [N=30]		Out born [N=60]		*P*-value*
	Survivor N (%)	Death N (%)	Survivor N (%)	Deaths N (%)	
Birth Asphyxia	4 (66.6)	2 (33.4)	11 (52.4)	10 (47.6)	0.54
HMD	5 (62.5)	3 (37.5)	5 (55.5)	4 (44.5)	0.78
MAS	3 (75.0)	1 (25.0)	8 (53.3)	7 (46.7)	0.45
Sepsis	2 (66.6)	1 (33.4)	5 (62.5)	3 (37.5)	0.90
CP	1 (50.0)	1 (50.0)	2 (66.6)	1 (33.4)	0.74
AOP	2 (100.0)	0 (0.0)	1 (100.0)	0 (0.0)	#
PPHN	3 (60.0)	2 (40.0)	2 (66.6)	1 (33.4)	0.85
Overall	20 (66.6)	10 (33.4)	34 (56.7)	26 (43.3)	0.36

*chi-square test of proportion; #could not be calculated as outcome was null; BA: Birth Asphyxia; HMD: Hyaline membrane disease; MAS: meconium aspiration syndrome; CP: Congenital Pneumonia; AOP: Apnoea of prematurity; PPHN: Persistent Pulmonary Hypertension of the New-born.

The only significant attribute affecting mortality in inborn neonates was ABG pH (≤7.1) [OR=6.0 (1.1-31.9)], although for out born neonates it was gestational age (<37 weeks) [OR=3.1 (1.0-9.5)], thrombocytopenia (yes) [OR=13.2 (3.6-48.2)], ABG pO_2 (<50) [OR=7.7 (2.3-25.5)], as well as pCO_2 (≥60) [OR=11.0 (3.3-36.7)]. Overall, those with thrombocytopenia (yes) [OR=5.8 (2.1-16.1)], ABG pO_2 (<50) [OR=5.1 (2.0-13.1)], and pCO_2 (≥60) [OR=3.1 (1.3-7.5)] was observed to be at higher risk for death compared to others (**Table 2**).

Table 2. Univariate logistic regression analysis showing predictors of mortality among the study population

Predictors	Total n (%)	Inborn [N=30]		Out born [N=60]		Total [N=90]	
		Death n (%)	OR (95% CI)	Death n (%)	OR (95% CI)	Death n (%)	OR (95% CI)
Birth weight: (In Kg)							
<2.5 kg	56 (62.2)	6 (33.3)	1.0 (0.2-4.7)	16 (42.1)	0.6 (0.2-1.7)	22 (39.2)	0.7 (0.3-1.7)
≥2.5 kg	34 (37.8)	4 (33.3)	Ref.	12 (54.5)	Ref.	16 (47.1)	Ref.
Gestational age: (In weeks)							
<37	36 (40.0)	3 (18.7)	0.2 (0.1-1.2)	13 (65.0)	3.1 (1.0-9.5)	16 (44.4)	1.2 (0.5-2.7)
≥37	54 (60.0)	7 (50.0)	Ref.	15 (37.5)	Ref.	22 (40.7)	Ref.
Hypoglycaemia							
Yes	37 (41.1)	5 (41.7)	1.8 (0.4-8.7)	8 (32.0)	0.4 (0.1-1.0)	13 (35.1)	0.6 (0.2-1.4)
No	53 (58.9)	5 (27.7)	Ref.	20 (57.1)	Ref.	25 (47.1)	Ref.
Intraventricular haemorrhage							
Yes	18 (20.0)	4 (50.0)	2.7 (0.5-14.2)	5 (50.0)	1.2 (0.3-4.6)	9 (50.0)	1.5 (0.5-4.2)
No	72 (80.0)	6 (27.3)	Ref.	23 (46.0)		29 (40.3)	Ref.
Seizure							
Yes	22 (24.4)	2 (28.6)	0.7 (0.1-4.8)	4 (26.7)	0.3 (0.1-1.1)	6 (27.3)	0.4 (0.1-1.2)
No	68 (75.6)	8 (34.8)	Ref.	24 (53.3)	Ref.	32 (47.0)	Ref.
Pulmonary Haemorrhage							
Yes	12 (13.3)	3 (75.0)	8.1 (0.7-91.8)	3 (37.5)	0.6 (0.1-2.9)	6 (50.0)	1.4 (0.4-4.8)
No	78 (86.7)	7 (26.9)	Ref.	25 (48.1)	Ref.	32 (41.0)	Ref.
Shock							
Yes	29 (32.2)	3 (33.3)	1.0 (0.2-5.2)	6 (30.0)	0.4 (0.1-1.1)	9 (31.0)	0.5 (0.2-1.3)
No	61 (67.8)	7 (33.3)	Ref.	22 (55.0)	Ref.	29 (47.5)	Ref.
Ventilator-Associated Pneumonia							
Yes	11 (12.2)	1 (33.3)	1.0 (0.1-12.5)	4 (50.0)	1.2 (0.3-5.2)	5 (45.4)	1.2 (0.3-4.1)
No	79 (87.8)	9 (33.3)	Ref.	24 (46.1)	Ref.	33 (41.8)	Ref.
Pneumothorax							
Yes	5 (5.5)	1 (50.0)	2.1 (0.1-37.7)	2 (66.6)	2.4 (0.2-27.8)	3 (60.0)	2.1 (0.3-13.5)
No	85 (94.5)	9 (32.1)	Ref.	26 (45.6)	Ref.	35 (41.2)	Ref.
Thrombocytopenia							
Yes	57 (63.3)	8 (34.8)	1.3 (0.2-8.5)	24 (70.6)	13.2 (3.6-48.2)	32 (56.1)	5.8 (2.1-16.1)
No	33 (36.7)	2 (28.5)	Ref.	4 (15.4)	Ref.	6 (18.2)	Ref.
pH							
≤7.1	33 (36.7)	6 (60.0)	6.0 (1.1-31.9)	8 (34.8)	0.5 (0.1-1.3)	14 (42.4)	1.0 (0.4-2.4)
>7.1	57 (63.3)	4 (20.0)	Ref.	20 (54.1)	Ref.	24 (42.1)	Ref.
pO_2							
<50	49 (54.5)	6 (42.8)	2.2 (0.5-10.6)	23 (65.7)	7.7 (2.3-25.5)	29 (59.2)	5.1 (2.0-13.1)
≥50	41 (45.5)	4 (25.0)	Ref.	5 (20.0)	Ref.	9 (21.9)	Ref.
pCO_2							
<60	40 (44.4)	5 (50.0)	Ref.	6 (20.0)	Ref.	11 (27.5)	Ref.
≥60	50 (55.6)	5 (25.0)	0.3 (0.1-1.6)	22 (73.3)	11.0 (3.3-36.7)	27 (54.0)	3.1 (1.3-7.5)

OR: odds ratio; CI: confidence interval.

Discussions

According to our knowledge, this was the first study from eastern India to investigate patterns and predictors of mortality among hospitalised inborn and out born neonates on ventilatory support in a tertiary care hospital in eastern India. The mortality rate of out born neonates (two out of every five) observed to be higher in comparison to inborn ones (one out of every three) in the present study. Our observations were similar to research from Uttarakhand by

Rakholia et al. [6], which found that out born NMR (N=98) (66.2%) was statistically greater than inborn NMR (N=50) (33.8%). Although, due to un-attainment of the smallest desired sample size for the study, we were unable to detect a statistically significant difference between the two rates. The probable reasons for higher mortality among out born infants might be unclean birth practices (especially in the case of home deliveries), delayed presentation, mismanagement by faith healers etc.

Contrary to the findings of a study from Northern India by Rakholia et al. [6], which revealed that respiratory distress syndrome (RDS) was the most frequent reason for SNCU admission among inborn new-borns, we found that congenital pneumonia was the most common cause in the present study. Similarly, we found that birth asphyxia accounted for the majority of SNCU admissions for out born neonates, which differed from the observations of Rakholia et al. [6] in which RDS was reported to be the most common cause for the same. The variations in the study population, their health-seeking behaviour, and other unexplored factors could handle the variability of observations.

We found that those who were premature, thrombocytopenic, low ABG pH, pO_2 and high pCO_2 had significantly higher mortality risk. Other Indian research has identified perinatal asphyxia, sepsis, preterm, birth asphyxia, hypothermia, shock at presentation, severe low birth weight, convulsion, and cyanosis as significant predictors of neonatal mortality [4, 6-10]. Although except Rakholia et al. [6], none of the studies evaluated the determinants of death for inborn in comparison to out born neonates. When taking into account international literature concerning this, a study from Egypt by G. Hany et al. [15] found that haemorrhage, sepsis, and pneumothorax were the three most important factors in determining mortality risk among neonates. This finding was like our observations as we found neonates with pulmonary and intraventricular haemorrhage had a higher risk of death. However, these associations were not statistically significant. We have also documented variability between predictors of inborn and out born mortality alone and overall mortality. On the other hand, neonatal hypothermia, lack of antenatal care (ANC) visits, and a delayed start to breastfeeding were listed as important determinants of neonatal mortality in a different study from Ethiopia by Tolossa et al. [16]. Due to the lack of availability of these data in our hospital records, the effect of these variables on neonatal mortality could not be decided in the current investigation.

The limitations of the study were first, the recruitment of study participants from only one tertiary healthcare facility. Secondly, non-attainment of the desired sample size. This was a monocentric pilot study conducted among a 20% sample of the desired minimum number of samples. The full sample size for the study could not met considering the feasibility and logistic constraints. Lastly, the use of unmatched case-control design leads to possible selection bias and limits generalisability. Although, the use of SRS for recruitment might have eliminated chances of any selection bias.

Conclusion

Out born neonates were found to be at higher risk for mortality compared to the inborn ones. Overall, premature neonates with thrombocytopenia, low ABG pH, pO_2, and high pCO_2 were observed to be at higher risk for death compared to others. Studies with a larger sample size are required to give more insights into the issue.

Disclosure of conflict of interest

None.

Address correspondence to: Bijit Biswas, All India Institute of Medical Sciences, Deoghar, Jharkhand, India. E-mail: drbijitbiswas@gmail.com

References

[1] National family health survey-5: state fact-sheet, India fact sheet. Ministry of Health and Family Welfare, GOI; 2019. Available from: http://rchiips.org/nfhs/NFHS-5_FCTS/Jharkhand.pdf.

[2] Neonatal mortality. UNICEF Data. [cited 2022 Nov 25]. Available from: https://data.unicef.org/topic/child-survival/neonatal-mortality/.

[3] Newborns: improving survival and well-being. [cited 2022 Nov 25]. Available from: https://www.who.int/news-room/fact-sheets/detail/newborns-reducing-mortality.

[4] Murtaza M, Ali MN, Khan IS and Zargar MH. Causes of mortality and morbidity among neonates admitted to the neonatal intensive care

unit in Ladakh, India. J Mahatma Gandhi Inst Med Sci 2021; 26: 42-45.
[5] Bokade CM and Meshram RM. Morbidity and mortality patterns among outborn referral neonates in central India: prospective observational study. J Clin Neonatol 2018; 7: 130-135.
[6] Rakholia R, Rawat V, Bano M and Singh G. Neonatal morbidity and mortality of sick newborns admitted in a teaching hospital of Uttarakhand. CHRISMED J Health Res 2014; 1: 228-234.
[7] Nair NS, Lewis LE, Dhyani VS, Murthy S, Godinho M, Lakiang T and Venkatesh BT. Factors associated with neonatal pneumonia and its mortality in India: a systematic review and meta-analysis. Indian Pediatr 2021; 58: 1059-1066.
[8] Meshram RM, Gajimwar VS and Bhongade SD. Predictors of mortality in outborns with neonatal sepsis: a prospective observational study. Niger Postgrad Med J 2019; 26: 216-222.
[9] Singh J, Dalal P and Gathwala G. Clinical profile and predictors of mortality among the referred neonates at a tertiary care centre in north India: a prospective observational study. Trop Doct 2020; 50: 221-227.
[10] Narang M, Kaushik JS, Sharma AK and Faridi MM. Predictors of mortality among the neonates transported to referral centre in Delhi, India. Indian J Public Health 2013; 57: 100-104.
[11] Iqbal Q, Younus MM, Ahmed A, Ahmad I, Iqbal J, Charoo BA and Ali SW. Neonatal mechanical ventilation: indications and outcome. Indian J Crit Care Med 2015; 19: 523-527.
[12] Ranjit S and Natraj R. BESTFIT-T3: a tiered monitoring approach to persistent/recurrent paediatric septic shock - a pilot conceptual report. Indian J Crit Care Med 2022; 26: 863-870.
[13] OpenEpi - Sample size for unmatched case-control studies. [cited 2022 Nov 22]. Available from: http://www.openepi.com/SampleSize/SSCC.htm.
[14] OpenEpi - Toolkit shell for developing new applications. Available from: http://www.openepi.com/Random/Random.htm.
[15] Hany MG. Predictors of mortality in the neonatal intensive care unit of El-Galaa teaching hospital. J Med Sci Res 2021; 4: 104-113.
[16] Tolossa T, Wakuma B, Mengist B, Fetensa G, Mulisa D, Ayala D, Feyisa I, Fekadu G, Jara D, Bikila H and Getahun A. Survival status and predictors of neonatal mortality among neonates admitted to Neonatal Intensive care Unit (NICU) of Wollega University referral hospital (WURH) and Nekemte Specialized hospital, Western Ethiopia: a prospective cohort study. PLoS One 2022; 17: e0268744.