Determinant factors of immediate outcomes of Neonatal Respiratory Distress Syndrome in Gondar, Ethiopia

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ABSTRACT

Introduction: Respiratory Distress Syndrome (RDS) is a frequent neonatal emergency worldwide. The prevalence varies with gestational age (GA) being higher among preterm babies. Preterm birth is the world's primary cause of newborn deaths and RDS is the leading cause of death in premature infants, including in Ethiopia.

Objectives: To identify the determinant factors of the immediate outcomes of RDS in the neonatal intensive care unit (NICU), University of Gondar Specialized and Comprehensive Hospital (UoGSCH).

Method: A hospital-based prospective descriptive analytical cross-sectional study was conducted from February to September 2020.

Results: A total of 162 neonates were enrolled; there were 87 (53.7%) males and 75 (46.3%) females. Of these 106 (65.4%) were discharged with improvement, 4 (2.5%) discharged with complications, and 52 (32.0%) died; 50% of deaths occurred within the first 24 hours of age. The odds of mortality for those admitted below 6 hours of age was 6.14 times higher (AOR=6.14, 95% CI:1.63 23.03) than those admitted aged 6 hours and above. Babies born to primiparous mothers were more than twice as likely to die (AOR=2.49, 95% CI:1.05 5.87) than babies born to multiparous mothers. Neonates who were delivered in other facilities had 3.78 times increased odds of mortality (AOR=3.78, 95% CI: 1.23 11.57).

Conclusion: Age at admission, site of referral, parity and gestational age (GA) had a significant association with neonatal mortality due to RDS.

Keywords: Respiratory Distress Syndrome, preterm, neonatal mortality, Ethiopia.

INTRODUCTION

Annually about 15 million preterm babies are born around the world and more than one million die soon after birth mainly due to respiratory complications.[1] Respiratory Distress Syndrome (RDS) is a common and serious complication of preterm birth accounting for 50% of preterm deaths.[1] RDS is responsible for 30-40% of admissions in the neonatal period.[2] The prevalence of RDS varies with gestational age (GA), 30% among preterm, and 20% among post terms to 4% in term babies.[3]

A large multicentre study, done in 2016-2018 in Ethiopia, reported the mortality related to RDS of 45%.[4] However, determinate outcome factors were not clearly addressed, other than the use of continuous positive airways pressure (CPAP), hypothermia and X-ray findings.

Therefore, in our study multiple determinant factors (gestational age (GA), birth weight, mode of delivery, steroids given to the mother, if the baby was grunting,

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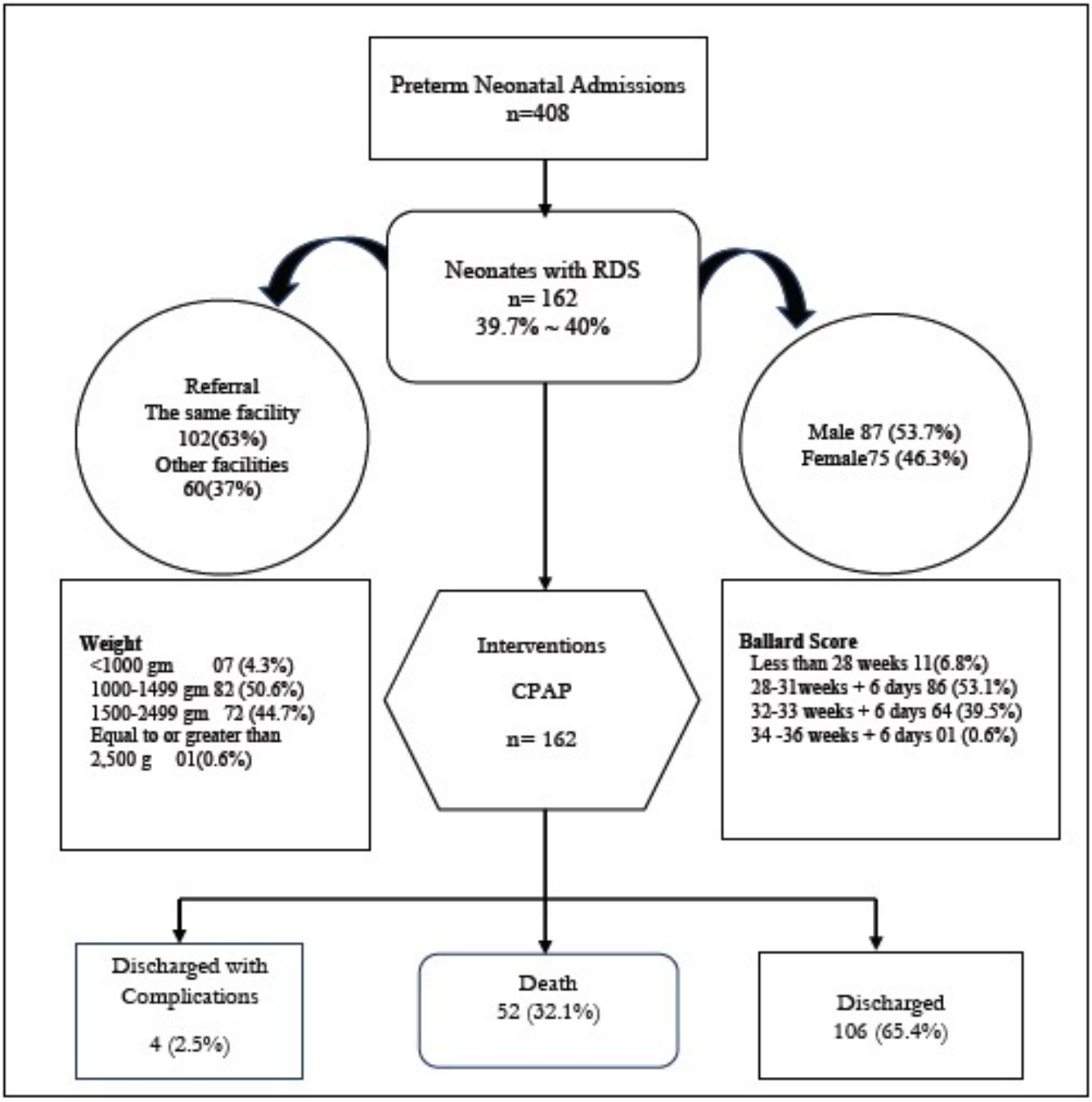

Figure 1. Flow diagram of the study

apnoea, maternal diabetes mellitus, multiple pregnancy and use of CPAP) were recorded. These findings may lead to future improvements in care.

METHOD

This was a hospital-based prospective descriptive and analytical cross-sectional study conducted to assess determinant factors and immediate outcomes of RDS in preterm neonates that were hospitalized in the neonatal intensive care unit (NICU) of University of Gondar Specialized and Comprehensive Hospital (UoGSCH), Ethiopia from 1 February 2020 to 30 September 2020. All preterm neonates with RDS seen during the study period were included. The sample size was calculated according to the equation: $N= Z^2(PQ)/d^2$.

Using the prevalence of RDS 7% from a previous study[5] and 95% CI, and 4% margin of error, the final sample size became 156.

Where: N=sample size; Z=statistical certainty (1.96 at 95% level of confidence); P=prevalence =7% or 0.07, Q= probability of failure =1-P = 1 - 0.07= 0.93; d= desired margin of error = 0.04 or 4%; $N = (1.96)^2\ 0.07(1 – 0.07)/(0.04 \times 0.04) = 156$.

Table 1. Socio-demographic characteristics

Variable		n (%)
Neonatal age on admission(hours)	Below 6 hours	119(73.5)
	6-11.9 hours	14(8.6)
	12-23.9 hours	19(11.7)
	24 hours and above	10(6.2)
Sex	Male	87(53.7)
	Female	75(46.3)
Residence	Urban	72(44.4)
	Rural	90(55.6)
Sites of referral	The same facilities	102(63)
	Other hospital	22(13.6)
	Local health centres	34(21)
	Home	4(2.5)
Maternal age	Below 18 years	0(0)
	18 - 25 years	5(3.1)
	25 - 30 years	80(49.4)
	30 -35 years	49(30.2)
	Above 35 years	28(17.3)

The actual sample size was 162 as this was the number admitted with RDS.

A pretested and later modified questionnaire was filled in daily. The information (demographic data and detailed history) was collected after informed consent was obtained and was crossed-checked with that in the medical files. A physical examination was carried out and cross-checked for completeness and accuracy and the results of investigations such as chest X-ray, random blood sugar (RBS), and complete blood count (CBC) were collected from the patients' files. After the data were compiled and data quality was cross-checked, coded and entered it into EpiData version 3.1(8), it was analysed by Adjusted Odds Ratio by using SPSS Version 20.

RESULTS

Figure 1 summarizes the interventions and outcomes of this study.

From a total of 408 preterm neonates admitted over the study period, 162 with clinical picture of RDS were included in this study (i.e. more than the determined sample size of 156). Neonates with severe congenital anomalies, malformations or dysmorphic features (due to

Table 2. Clinical and maternal Characteristics

Variable		n (%)
Chief complaint/ Reason for referral	Prematurity and LBW	88 (54.3)
	Fast breathing	67 (41.4)
	Fast breathing with grunting	30 (18.5)
	Twin evaluation	20 (12.3)
	Triplet evaluation	4 (2.5)
Gestational age	Unknown	7 (4.3)
	Less than 28 weeks	14 (8.6)
	28 weeks -31 weeks plus 6 days	67 (41.4)
	32- weeks33 weeks plus 6 days	51 (31.5)
	≥34 weeks	23 (14.2)
Parity	Primiparous	47 (29.0)
	Multiparous	115 (71.0)
Mode of delivery	Spontaneous vaginal delivery	128 (79.0)
	Caesarean section	28 (17.3)
	Induced	3 (1.9)
	Assisted	3 (1.9)
Problems during pregnancy	Antepartum haemorrhage	15 (9.3)
	Pregnancy Associated Hypertension	11 (6.8)
	Gestational diabetes mellitus	2 (1.2)
	Urinary tract infections	3 (1.9)
	Chorioamnionitis	7 (1.8)
Previous obstetrics history	Early neonatal death	7 (4.3)
	Premature birth	9 (5.6)
Duration of labour	Normal (18 hours or less)	147 (90.7)
	Prolonged (above 18 hours)	15 (9.3)
Rupture of membrane	Normal (18 hours or less)	151 (93.8)
	Prolonged (above 18 hours)	10 (6.2)

Table 3. Newborn characteristics

Variable		n (%)
Conscious level	Conscious	114 (70.4)
	Lethargic	46 (28.4)
	Comatose	2 (1.2)
	Cardio-Respiratory distress	162 (100)
	Cyanosis	34 (21)
	Apnoea	20 (12.3)
	Pallor	13 (8)
Respiratory rate	Less than 60 BPM	51 (31.5)
	60-80 BPM	105 (64.8)
	More than 80 BPM	6 (3.7)
Weight of the neonate	Less than 1,000 g	7 (4.3)
	1,000-1,499 g	82 (50.6)
	1,500-2,499 g	72 (44.7)
	Equal to or greater than 2,500 g	1 (0.6)
Ballard score*	Less than 28 weeks	11 (6.8)
	28-31weeks + 6 days	86 (53.1)
	32-33 weeks + 6 days	64 (39.5)
	34 -36 weeks + 6 days	1 (0.6)

*see https://perinatology.com/calculators/Ballard.htm

Table 4. Systemic review

Variable		n (%)
Pattern of breathing	Normal	22 (13.6)
	Laboured	129 (79.6)
	Gasping	06 (3.7)
	Apnoeic	5 (3.1)
	Cyanosis	34 (21)
	Nasal flaring	133 (82.1)
	Grunting	135 (83.3)
	Intercostal retraction	158 (97.5)
	Subcostal retraction	156 (96.3)
	Bilateral decreased breath sounds	162 (100)
Central nervous system	Alert	133 (82.1)
	Lethargic	28 (17.3)
	Comatose	1 (0.6)
Neonatal reflexes	Intact	3 (1.9)
	Depressed	157 (96.9)
	Absent	2 (1.2)
	32-33 weeks + 6 days	64 (39.5)
	34 -36 weeks + 6 days	1 (0.6)

other contributories for the distress) or those who died before settling the cause of RD were excluded.

The highest rate of admissions was of those aged below 6 hours 119 (73.5%) (Table 1); 53.7% were males, with a male:female ratio of 1.2:1. There were 102 (63%) referred from within the facility. Neonates whose mothers resided in rural areas accounted for 90 (55.6%) of referrals (Table 1).

The main reason for referral or chief complaint was prematurity and low birth weight (LBW) 88(54.3%), followed by fast breathing 67(41.4%) and fast breathing with grunting 30(18.5%); 45.2% of neonates had a GA between 28 weeks to 31 weeks and 6 days, while 34.4% were between 32 weeks to 33 weeks plus 6 days (Table 2).

Nearly three-quarters (74.1%) of newborns cried immediately after delivery, and 28.4%, 21.0%, 12.3% and 8.0% were lethargic, cyanosed, apnoeic or pale respectively at time of admission.

Note the time of admission was not always immediately after delivery because we had referrals from other facilities. Reasons for apnoea could include prematurity or immature lungs as in case of RDS. Usually we found 2-3 signs of distress in one patient, for instance increased respiratory rate, cyanosis, and/or grunting.

About half of the newborns (50.6%) had birth weights between 1,000 g and 1,499g (Table 3).

At admission, 79.6% of neonates had a laboured breathing pattern, while 3.7% of them were gasping (note some babies were admitted more than 1 hour after delivery); 83.3% were grunting, and all of them had decreased breath sounds bilaterally (Table 4).

Results of chest X-Rays done for 18 (11.1%) of the neonates showed that 10 (6.2%) were normal, 5 (3.1%) were Stage I, 3 (1.9%) were Stage II and none were Stage III or IV, where Stage I=Reduced lung volume, II=Air bronchograms, III=Reticulogranularity, IV=Increased lung opacification.[6] Taking chest X-rays was challenging due to the critical condition of the neonates and lack of portable X-Ray. For more information see Trotter et al.

Final outcomes

Out of 162 admitted neonates with RDS, 106 (65.4%) were discharged improved, 4 (2.5%) were discharged with complications, and 52 (32%) died.

Table 5. Final outcomes

Variable		n (%)
Final outcomes	Discharged with improvement	106 (65.4)
	Discharged with complication	4 (2.5)
	Death	52 (32.1)
Discharged with complications	Asphyxia with encephalopathy	3 (1.9)
	Discharged against medical advice	1 (0.6)
Immediate cause of death	Respiratory failure	41 (25.3)
	Multiple organ failure	6 (3.7)
	Pulmonary Haemorrhage	4(2.5)
	Severe sepsis with disseminated intravascular coagulation (DIC)*	1(0.6)
Underlying cause of death	RDS	45 (27.8)
	Asphyxia with encephalopathy	4 (2.5)
	Severe sepsis	1 (0.6)
	Severe sepsis with DIC	1 (0.6)
	Severe sepsis or/and Hospital Acquired Sepsis **	1 (0.6)
	Severe sepsis with necrotising enterocolitis stage III	1 (0.6)
	Absent	2 (1.2)
	32-33 weeks + 6 days	64 (39.5)
	34 -36 weeks + 6 days	1 (0.6)

**Evidence suggesting DIC was bleeding from umbilical stump and complete blood count (Reference value (SI)) showed WBCs of 2.4 x 10^ 9 cells/L, Haematocrit 0.28. platelet 65 x 10^9 /L)*

***A diagnosis of sepsis based on clinical judgement, systemic inflammatory response syndrome (SIRS) Criteria and complete blood count.*

Further details of the causes of death and outcomes are given in Table 5. The immediate causes of death were 41(25.3%) due to respiratory failure, and 6 (3.7%), 4 (2.5%), 1(0.6%) were due to multiple organ failure (MOF), pulmonary haemorrhage and severe sepsis with disseminated intravascular coagulation (DIC) respectively.

The identified underlying causes of death were RDS, perinatal asphyxia (PNA) with hypoxia ischaemic encephalopathy (HIE) (where the baby's brain does not get enough oxygen around the time of birth) and sepsis which were constituted 45(27.8%), 4(2.5%), 4(2.5%) respectively. Half (50%) of the deaths occurred within 24 hours of age and 32.7% died within 24 to 72 hours.

Factors associated with mortality

From logistic regression analysis parity, place of delivery, tachypnoea, age at admission, GA and mode of delivery were associated with neonatal mortality in bivariate analysis (p value 0.2). In the multivariate analysis parity, tachypnoea, GA and place of delivery had a statistically significant association with mortality (p value 0.05). Thus, in neonates below six hours of age, the odds of mortality were 6.14 times higher than those aged six hours and above at admission (AOR=6.14, 95% CI:1.63 - 23.03). Neonates from primipara mothers had risks of mortality 2.49 times higher than neonates from multiparous mother (AOR 2.49, 95% CI:1.05 - 5.87).

Babies delivered in other facilities had 3.78 times greater risk of death (AOR= 3.78, 95% CI:1.23 - 11.57). Compared to GA less than 28 weeks, those between 28-31 weeks plus 6 days, 32-33 weeks plus 6 days and above 34 weeks, had decreased odds of mortality by 90%, 92%, and 86% respectively. Similarly, if the neonate was tachypnoeic the risk of death decreased by 69% compared to non-tachypnoeic (AOR= 0.31, 95% CI: 0.14 - 0.71). Table 6.

DISCUSSION

In this study the proportion of preterm deaths due to RDS was 31.5%, which is lower than studies done in Tanzania (52%)[7], Jimma, Ethiopia (41%)[8] and a multi-Centre Prospective Observational Study in Ethiopia (Study of illness in preterm) (45%).[5] This might be due to earlier interventions like CPAP but this finding is higher than a study done in Italy which showed a mortality of 24%.[9]

This study showed those preterm neonates who were delivered and referred from other facilities had a 3.78 times higher risk of mortality than those who were delivered and referred from the same facility (UoGSCH); this finding was supported by a study done in the United States which showed a reduction in mortality from 63% in the late-treated infants to 21% in early-treated infants.[10] A study conducted in Jimma-Ethiopia showed that those who resided outside of Jimma had significantly ?higher mortality rates.[8] This may be due to the distance and no CPAP on referral.

Neonates who were admitted within 6 hours of age have 6.14 times higher risk of mortality than those above six hours of age at admission (AOR= 6.14, 95% CI:1.63 -

Table 6. Factors associated with mortality

Characteristics	Mortality	COR 95% CI*	AOR 95% CI*	p-value	
	Yes	No			
Parity					
Primipara	24	23	3.24 (1.58-6.61)	2.49 (1.05-5.87)	0.037
Multipara	28	87	1	1	
Place of delivery					
The same facility	32	70	1	1	
Other facilities	20	40	1.09 (0.55-2.15)	3.78 (1.23-11.57)	0.020
Tachypnoea					
Yes	28	83	0.37 (0.18-0.76)	0.31 (0.14 - 0.71)	0.006
No	24	27	1	1	
Age of neonate at admission					
Below 6 hours	46	73	3.88 (1.52 - 9.92)	6.14 (1,63-23.03)	0.007
6 hours and above	6	37	1	1	
Gestational Age					
Below 28 weeks	11	3	1	1	
Between 28 weeks and 31 weeks and 6 days	19	48	0.10 (0.02 - 0.43)	0.10 (0.02-0.48)	0.004
Between 32 weeks and 33 weeks and 6 days	12	39	0.08 (0.02 - 0.35)	0.08 (0.018-0.42)	0.003
Between 34 weeks and 36 weeks and 6 days	6	17	0.09 (0.01 - 0.46)	0.14 (0.025-0.85)	0.032
Mode of delivery					
Caesarean section	9	19	1.0 (0.41 - 2.39)	1.55 (0.54-4.42)	0.408
Vaginal	43	91	1	1	

**COR 95% CI = Crude odds ratios and its 95% confidence interval. AOR = Adjusted odds ratio and its 95% confidence interval*

23.03), which was a surprising result that may be due to underlying problems, or a comorbid condition like perinatal asphyxia.

This study showed that mortality is inversely related to GA, and being male is associated with increased risk of death which is in line with a study done in Italy[9] and Tanzania.[7] This is related to prematurity of the lungs and less surfactant production.

This study showed that primiparous pregnancy is associated with 2.49 times increased risk of mortality compared to multipara mothers, and this is in line with a study done in Italy.[9]

This study showed the odds of mortality decreased by 69% in tachypnoeic babies as compared to non-tachypnoeic (AOR=0.31, 95% CI:0.14 0.71). This finding was surprising; it demonstrates the value scaling of early interventions and strict follow up and use of CPAP.

This study showed that those delivered through Caesarean section had 1.5 times risk of mortality as compared to their counterpart who delivered through vaginal delivery, the association was not statistically significant. (AOR= 1.55, 95% CI:0.54 4.42). Similarly, maternal diabetes, birth weight and giving women in premature labour steroids to mature the baby's lungs were not associated with significant risk of mortality in neonates with RDS.

CONCLUSION

RDS is the major cause of mortality in preterm neonates. The main reasons for referral were prematurity and LBW followed by tachypnoea. Mortality due to RDS was significantly associated with the age of the baby at admission, parity, gestational age and place of delivery. It is interesting to speculate whether primiparous women have difficulty in accessing quick appropriate care when in premature labour.

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