Predictors of Outcome in Neonates with Respiratory Distress

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Abstract

Introduction: Many of the parameters utilised in scoring systems used to predict disease severity in respiratory distress in neonates are not readily available in the primary care facility of developing countries. This study was carried out to assess the utility of birth weight, gestational age, APGAR score at 5 min, baseline oxygen saturation and Downe's score in prediction of requirement of respiratory support and mortality in neonates with respiratory distress. **Material and Methods:** A prospective study was carried out in the neonatal intensive care unit of a tertiary teaching hospital. 165 consecutively admitted neonates presenting with respiratory symptoms were included in the study. The relevant parameters and investigations were documented in a structured performa. The neonates were followed up for outcomes which included requirement of respiratory support and mortality. **Results:** A higher mortality was associated with birth weight of ≤ 1620 grams, gestational age of ≤ 31 weeks, APGAR score of ≤ 6, Downe's score of > 3 and baseline oxygen saturation of ≤ 86 % (p values < 0.001). The requirement of mechanical ventilation was more with birth weight of ≤ 2000 grams, gestational age of ≤ 32 weeks, APGAR score of ≤ 7, Downe's score of > 4 and baseline oxygen saturation of ≤ 87 % (*p* value < 0.001). The requirement of any respiratory support at 72 hours was associated with birth weight of ≤ 1894 grams, gestational age of ≤ 37 weeks, APGAR score of ≤ 7, Downe's score of > 3 and baseline oxygen saturation of ≤ 89 % (*p*-value <0.001). **Conclusions:** Readily available parameters like birth weight, gestational age, APGAR score, oxygen saturation and Downe's score could together be used to predict mortality and requirement of respiratory support in the resource limited setting.

Key words: Neonates, respiratory distress, respiratory support, predictors, outcome

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Introduction

Respiratory distress is one of the commonest causes of admission of a neonate to the neonatal intensive care unit (NICU). It is a challenging problem and accounts for significant morbidity and mortality. In various Indian studies, it occurred in up to four to seven percent of the neonates[1,2]. There are various factors which determine the progress and outcome in neonatal respiratory distress. The birth weight, gestational age and the degree of respiratory compromise are the key factors which decide the level of care the neonate would require. Clinical monitoring is most important as sophisticated equipments may

not always be available in resource limited settings. Clinical scores such as Downe's score[3], Silverman score[4], APGAR score[5] and ACoRN respiratory score[6] are being used for assessing the severity of respiratory distress while CRIB (Clinical risk index for babies)[7] and SNAPPE (Score for neonatal acute physiology-perinatal extension)[8] are being used for determining illness severity. Calculation of some of the above mentioned scores need estimation of fractional inspired oxygen, arterial blood gas analysis and monitoring of vitals including blood pressure. However, invasive monitoring and ventilator facilities are not available in all the neonatal care units. There is a dearth of studies on role of simple clinical parameters like Downe's score and pulse oximetry early on during the course of respiratory distress in predicting which neonates may have a higher mortality, need mechanical ventilation and need higher duration of respiratory support. Simple clinical scores if meticulously documented could be useful to determine the progression of the respiratory distress. This would then enable timely transfer of these neonates to higher centres from the primary neonatal care facility available in most of the developing countries.

This study was therefore conducted to assess the suitability of simple parameters like birth weight, gestation age, baseline oxygen saturation, APGAR score at five minutes and Downe's score as predictors of certain short term outcomes like requirement of respiratory support and mortality.

Material and Methods

Over a period of 18 months, all consecutively admitted neonates developing respiratory distress were studied. *Inclusion Criteria*: Neonates delivered in the hospital, which developed respiratory distress within 6 hours of birth, irrespective of gestational age and aetiology. *Exclusion Criteria*: All neonates admitted for indication other than respiratory distress and neonates with congenital anomalies.

Any newborn showing one or more of the following signs within 06 hours of birth was considered to have respiratory distress: (i) Respiratory rate of sixty per minute or more (ii) grunting (iii) intercostal or subcostal retraction (iv) cyanosis

Following data was recorded: Birth weight (babies were weighed as soon as possible after birth, nude, using standardized digital weighing scale), Gestational age (as per expected date of delivery (EDD) and confirmed by USG report mentioned in the antenatal follow up card), APGAR score at five minutes after birth, Downe's score (at admission and after 2 hours, 6 hours, 12 hours and 24 hours), SpO_2 at admission (in room air) and after 2 hours, 6 hours, 12 hours and 24 hours. Neonates in the study group were treated as per unit protocol which had specified indications for oxygen therapy, continuous positive airway pressure (CPAP), mechanical ventilation, surfactant therapy, antibiotics, fluid therapy, thermoregulation and supportive care. The neonates were followed up for the following outcomes: Need for mechanical ventilation at any stage during admission, Need for any respiratory support in the form of oxygen therapy, CPAP or mechanical ventilation at 72 hours after admission. Mortality and survival data was recorded at time of discharge.

For this study, neonates were divided into four groups based on their birth weight and gestational age for differential analysis as depicted in Table 1.

The diagnostic criteria for various causes of respiratory distress were adopted from the recommendations made by National Neonatology Forum and also published in National Neonatology Perinatology database report 2002-03 [1].

Data analysis was done by using SPSS (Statistical package for social sciences) version 17.0. Fisher's exact test, Chi-square test, Odds ratios were used to find out the relationship between various parameters. Binary logistic regression analysis was used to find out the relationship between defined predictors and outcomes. Receivers Operating Characteristic curves were used to find the cut off values of the predictors for the specified outcomes. All the statistical tests were used at 95% confidence interval (C.I.) (5 % level of significance) and *p*-value of < 0.05 was considered as a significant relation between studied parameters.

Results

During the study period, a total of 165 neonates having respiratory distress fulfilled the inclusion criteria of the study. They were followed up for studying the relationship between the specified predictors and the outcomes. The demographic profile of the studied population is depicted in Table 1.

In univariate analysis along with ROC curves : Birth weight $\leq$ 1620 gram, gestational age of $\leq$ 31 weeks, APGAR score of $\leq$ 6, Downe's score of >3 and baseline oxygen saturation of $\leq$ 86 % were found to be significantly associated with mortality (Table 2),

Birth weight $\leq$ 2000 gram, gestational age of $\leq$ 32 weeks, APGAR score of $\leq$ 7, Downe's score of >4 and

baseline oxygen saturation of ≤ 87 % were significantly associated with requirement of mechanical ventilation (Table 3) .Birth weight ≤ 1894 gram, gestational age of ≤ 37 weeks, APGAR score of ≤ 7, Downe's score of >3 and baseline oxygen saturation of ≤ 89 % were significantly associated with requirement of respiratory support (O_2, CPAP, mechanical ventilation) at 72 hrs of life (Table 4).

On multivariate analysis by binary logistic regression, the following odds ratios were noted for various predictors:

Predictors versus mortality - Birth weight (OR-1.002, 95% CI: 1.00- 1.004), gestational age (OR-0.60,95% CI: 0.42-0.86), APGAR score (OR-0.59,95% CI: 0.30-1.15), Downe's score at baseline (OR-1.42, 95% CI: 0.85- 2.36) and oxygen saturation at baseline (OR-1.02, 95% CI: 0.86- 1.21).

Predictors versus mechanical ventilation- Birth weight (OR-0.99, 95% CI: 0.99- 1.00), gestational age(OR-1.33,95% CI: 1.06-1.67),APGAR score at 5 mins (OR-1.98,95% CI: 1.14-3.42), Downe's score at baseline (OR-0.87, 95% CI: 0.60- 1.25) and oxygen saturation at baseline (OR- 1.09, 95% CI: 0.97- 1.22).

Predictors versus respiratory support at 72 hours- Birth weight (OR-1.00, 95% CI: 0.99- 1.00), gestational age (OR-0.84, 95% CI: 0.71-1.01), APGAR score at 5 minutes (OR-0.76,95% CI: 0.48-1.19), Downe's score at baseline (OR-1.28, 95% CI: 0.96- 1.72) and oxygen saturation at baseline (OR- 0.96, 95% CI: 0.87- 1.07)

Table 1: Demographic characteristics of the studied population

Variables		Number	Percentage
Birth weight (grams)	≤ 1000	8	4.8
	1001 – 1500	36	21.8
	1501 – 2500	45	27.3
	> 2500	76	46.1
Gestational age (weeks)	≤ 28	6	3.6
	28 weeks 01 day – 32 weeks	40	24.2
	32 weeks 01 day- 36 weeks	25	15.2
	> 36 weeks	94	57
APGAR score (at 5 minutes)	≤3	1	6
	4 to 6	24	14.5
	≥ 7	140	84.5
Sex	Male	97	58.8
	Female	68	41.2
Etiology	RDS	67	40.60
	TTNB	62	37.58
	MAS	19	11.52
	Sepsis	7	4.24
	Birth asphyxia	5	3.03
	Hypoglycemia	3	1.82
	Pneumonia	2	1.21
Requirement of Mechanical ventilation		49	29.7
Survival/ Mortality	Survival	141	85.5
	Death	24	14.5
Respiratory support (O_2, CPAP, Mechanical Ventilation) requirement at 72 hrs of life		97	58.7

Table 2: Predictors and Mortality

		Survival/ mortality		Total	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Odds ratio	95% C.I for Odds ratio	
		Survive	Death							Lower	Upper
Birth weight (grams)	> 1620	106	6	112	75.18%	75.00%	94.64%	33.96%	9.09	3.34	24.69
	≤ 1620	35	18	53							
Gestational age (weeks)	> 31	124	8	132	87.94%	66.67%	93.94%	48.48%	14.59	5.42	39.2
	≤ 31	17	16	33							
APGAR score (at 5 minutes)	> 6	129	11	140	91.49%	54.17%	92.14%	52.00%	12.70	4.68	34.44
	≤ 6	12	13	25							
Downe's score	≤ 3	74	2	76	52.48%	91.67%	97.37%	24.72%	12.15	2.75	53.62
	> 3	67	22	89							
SpO2 (%)	≤ 86	107	8	115	75.89%	66.67%	93.04%	32.00%	6.29	2.47	15.98
	>86	34	16	50							

Table 3: Predictors and mechanical ventilation

		Mechanical ventilation		Total	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Odds ratio	95% C.I for Odds ratio	
		Required	Not required							Lower	Upper
Birth weight (grams)	≤ 2000	33	36	69	67.35%	68.97%	47.83%	83.33%	4.58	2.24	9.36
	> 2000	16	80	96							
Gestational age (weeks)	≤ 32	27	19	46	55.10%	83.62%	58.70%	81.51%	6.27	2.96	13.23
	> 32	22	97	119							
APGAR score (at 5 minutes)	≤ 7	41	43	84	83.67%	62.93%	48.81%	90.12%	8.70	3.73	20.27
	> 7	8	73	81							
Downe's score	> 4	26	26	52	59.09%	77.39%	50.00%	83.18%	4.94	2.35	10.39
	≤4	18	89	107							
SpO2 (%)	≤ 87	28	21	49	57.14%	81.90%	57.14%	81.90%	6.03	2.88	12.6
	> 87	21	95	116							

Table 4: Predictors and respiratory support at 72 hours of life

Yes		Respiratory support at 72 hr		Total	Sensitivity	Specificity	PPV	NPV	Odds ratio	95% C.I for Odds ratio	
		No								Lower	Upper
Birth weight (grams)	≤ 1894	49	16	65	50.52%	76.47%	75.38%	52.00%	3.32	1.66	6.59
	> 1894	48	52	100							
Gestational age (weeks)	≤ 37	59	21	80	60.82%	69.12%	73.75%	55.29%	3.47	1.8	6.69
	> 37	38	47	85							
APGAR score (at 5 minutes)	≤ 7	64	20	84	65.98%	70.59%	76.19%	59.26%	4.65	2.38	9.09
	> 7	33	48	81							
Downe's score	> 3	60	23	83	65.22%	65.67%	72.29%	57.89%	3.59	1.85	6.95
	≤ 3	32	44	76							
SpO2 (%)	≤ 89	62	20	82	63.92%	70.15%	75.61%	57.32%	4.16	2.13	8.11
	> 89	35	47	82							

Discussion

In India, and many developing nations, only few 'Neonatal intensive care units' have level III facilities for newborn care. Most of the centres, especially in the rural districts, have only level II care facilities. Respiratory distress is among the most common symptom complexes seen in the newborn infant. It may result from pulmonary and non pulmonary causes[1,2,9,10,11,12,13]. Prognosis depends not only on the birth weight and gestational age, but also on other perinatal factors and physiological conditions of the individual neonate, in particular the disease severity in the first hours of life[14,15]. The prediction of requirement of higher level of care like mechanical ventilation and prolonged requirement of oxygen support is of paramount importance at the peripheral level where sophisticated medical equipments are not available. This study was therefore conducted to assess the utility of birth weight, gestational age, baseline oxygen saturation, Downe's score and APGAR score at 5 min as predictors of mortality and requirement of respiratory support/ mechanical ventilation at 72 hours in neonates with respiratory distress. In our study, the main causes of respiratory distress requiring mechanical ventilation were Respiratory distress syndrome (61%) and meconium aspiration syndrome (14%). The study results are similar to other Indian studies[16,17]. The overall mortality was 14.5 % which was similar to another Indian study by Bhat et al (18%)[2] .

Predictors versus defined outcomes:

Mortality- In our study birth weight of ≤ 1620 grams was associated with higher mortality (sensitivity 75 %, positive predictive value (PPV) 94.64 %, Odds ratio (OR)-9, confidence interval (95% CI): 3.3-24.6). Our birth weight associated with higher mortality was comparatively lower in value compared to earlier studies done by Mathur et al[18] and Malhotra et al[16] showing birth weight of <2000 gram associated with higher chance of mortality. This shows the trend that with better neonatal care facilities younger neonates are surviving well. Gestation age of≤31 weeks was predictive of mortality (sensitivity- 88%, PPV- 94%, OR-14.5, 95% CI: 5.42-39.2), which is comparable to studies done by Gera et al (30.4 weeks)[19] . Our gestation age cut off value was lesser than as observed by Monir et al (34 weeks)[20]. APGAR score of ≤6 was associated with higher odds of mortality compared to higher scores (sensitivity- 92%, PPV- 92%, OR- 12.7, 95% CI: 4.6-34.4). Our score predictive of mortality was comparable to study by Onama et al (APGAR score ≤6)[21] but our value of APGAR score was higher than many previous studies[22,23,24,25]. Downe's score of >3 had a sensitivity of 52.48 % with positive predictive value of 97.37 % for mortality. And there was 12.1 times odds (95% CI: 2.7-53.6) of dying with Downe's score of > 3. Neonates having oxygen saturation of ≤ 86 % at admission had higher mortality (sensitivity- 76%, PPV- 93%, OR-6.29, 95% CI: 2.47-15.9). In our study mortality was 49 % in the ventilated neonates which is higher than study by MA Xio et al (15.4 %)[6].

Mechanical ventilation- Our study has showed that birth weight of ≤2000 grams is associated with higher requirement of mechanical ventilation (sensitivity-67 %, PPV- 48%). The odds of requirement of mechanical ventilation with birth weight of ≤ 2000 grams was 4.58 times (95% CI: 2.24- 9.36).This was comparable to the study by Mathur et al [18]. Gestation age of ≤ 32 weeks was predictive of higher requirement of mechanical ventilation (sensitivity- 55%, PPV- 59%, OR- 6.27, 95% CI: 2.96-13.23). APGAR score of ≤ 7 had a sensitivity of 83.67 % with positive predictive value of 48.8 % and a high negative predictive value of 90.12 meaning thereby that APGAR score of >7 significantly excludes requirement of mechanical ventilation. Eugene et al[26] and MA Xiao et al[6] also had similar findings with 5 minute APGAR score of < 7 predicting requirement of mechanical ventilation. In our study Downe's score of >4 had sensitivity of 59% and PPV of 50 % towards predicting ventilator support with an OR of 4.94 (95% CI: 2.35-10.39). Baseline oxygen saturation of ≤ 87 % had a sensitivity and PPV of 57.14% and an OR of 6.03(95% CI: 2.88-12.60) predicting the likely requirement of mechanical ventilation.

Respiratory support (O_2, CPAP, ventilation) requirement at 72 hrs of life- Birth weight of <1894 grams had higher chances of requiring respiratory support compared to birth weight of > 1894 grams (Odds ratio- 3.32, 95% CI: 1.66-6.59). The corresponding values for gestational age was 37 weeks (OR-3.47, 95% CI: 1.80-6.69), APGAR score-7 (OR-4.65, 95% CI: 2.38-9.09), Downe's score-3 (OR-3.59, 95% CI: 1.85-6.95) and baseline oxygen saturation -89% (OR-4.16, 95% CI: 2.13-8.11) .These were associated with requirement of respiratory support at 72 hours with variable sensitivity and specificity as shown in Table 4.

However on multivariate analysis, only gestational age and birth weight were independent predictors of mortality (*p*-value <0.05). For requirement of mechanical ventilation, gestation age and APGAR score were independent predictors of ventilation (*p*-value <0.05). No studied parameter significantly predicted requirement of respiratory support (O2, CPAP, ventilation) at 72 hours on multivariate analysis. This may have been because of the limited sample size

or type of sample population which was a limitation of the study.

Conclusion

Neonatal respiratory distress is one of the common causes of NICU admission in India and other developing countries. Illness severity assessment is important for the management. The APGAR score, Downe's score and SpO2 monitoring can be done non invasively with relative ease. The suggested cut offs for the observed (Birth weight and gestation age) and monitored (Downe's score, APGAR score and oxygen saturation) parameters may be together used to predict the requirement of respiratory support, mechanical ventilation and mortality in neonates with respiratory distress thereby guiding the decisions for treatment of these babies in a given neonatal care facility as against referral to a higher centre.

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