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RAPID DIAGNOSIS OF RESPIRATORY DISTRESS SYNDROME BY ORAL ASPIRATE IN PREMATURE NEWBORNS – A PROSPECTIVE COMPARATIVE STUDY

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ABSTRACT **Background and Objectives:** Respiratory distress syndrome is common in premature infants; frequency is inversely proportional to gestation and birth weight. RDS is mostly caused by surfactant deficiency. For the diagnosis of RDS in newborns, the stable microbubble test on gastric aspirate and amniotic fluid has been employed. The major goal of this study was to assess how well the stable microbubble test might predict RDS from oral aspirates of preterm babies. **Methodology:** A prospective comparative study was done on 73 inborn preterm neonates of AJIMS, Mangalore over the period of 18 months. Neonates with gestation <37weeks were included in the study. Oral sample was collected as soon as baby delivered. Stable microbubble test was done for all the babies, number of stable microbubbles were compared between newborns with RDS and newborns without RDS. Number of stable microbubbles were also compared with requirement of surfactant, use of CPAP and ventilator. **Results:** The mean number of stable microbubbles in those with RDS was 17.77 SD ± 6.746 and in those without RDS was 31.14 SD ± 8.26. At a cut-off level of ≤25 microbubbles with Sensitivity 87%, specificity 78.57%, PPV 75% and NPV 89.2%. The findings of our study suggest that sensitivity of chest x-ray in detecting RDS was 77.4%, specificity 92.86%. The negative and positive predictive value of chest x-ray in detecting RDS were 84.78% and 88.89% respectively. **Conclusion:** In comparison to Chest X ray in detection of RDS, stable microbubble test was found to be more sensitive at a cut off value of <25 stable microbubbles. However, specificity was found to be better with chest x-ray. Hence, stable microbubble test can be considered as a better screening test for RDS in preterm.

KEYWORDS : Respiratory distress syndrome, Stable microbubble test, Preterm Newborns

INTRODUCTION

Respiratory distress syndrome (RDS) occurs predominantly in premature babies; its occurrence is negatively related to gestational age and birth weight. It occurs in 60-80% of infants <28weeks of gestation, in 15-30% between 32-36 weeks of gestation, and rarely in those >37weeks of gestation. Surfactant insufficiency is the major cause of RDS (1).

Deficient production or release of surfactant, combined with tiny respiratory units and a compliant chest wall, creates atelectasis and resulting in perfused but not vented alveoli producing hypoxia. Reduced lung compliance, limited tidal volumes, increased physiological dead space and insufficient alveolar ventilation eventually culminates in hypercapnia. Symptoms include tachycardia, grunting, intercostal and subcostal retractions, nasal flaring and cyanosis and progress to respiratory failure. The severity of RDS can be assessed by Downe's scoring, chest x-ray and blood gas analysis (2). The clinical history, chest x ray findings, and blood gas and acid base levels help establish the clinical diagnosis. Nonetheless, blood gas and acid base values recognized as gold standard for the diagnosis of RDS (3).

Continuous airway pressure (CPAP) is used early to stabilise at-risk preterm newborns, starting as early as in the delivery room, which lowers the need for ventilators, as recommended.

Consequently, there has been a revived interest in quick diagnostic procedures to measure the surfactant system function, such as the stable micro bubble test (SMT), which may be explained by the pursuit of refining indications for early exogenous surfactant therapy (2,3,4).

It has been recommended that stable micro bubble (SMB) count in gastric aspirates collected in the delivery room immediately after birth was useful to predict the need for exogenous pulmonary surfactant in preterm newborns not requiring mechanical ventilation in a study conducted prior to the recommendation for routine use of CPAP in the delivery room (2).

A research by Bhatia et al. demonstrated that RDS-affected, extremely preterm infants receiving CPAP and having a high micro bubble count on their gastric aspirate (>8SMB/mm2) developed normally and didn't need mechanical ventilation (2).

Oral fluid samples are commonly and easily obtainable. This rapid diagnostic test will be very helpful in a situation without the availability of CPAP or mechanical ventilation to determine the baby's prognosis very early on and to move the baby to a higher centre.

In order to determine the diagnostic effectiveness of stable micro bubble testing in the early detection of respiratory distress syndrome, we are doing this study.

METHODOLOGY

A prospective comparative study included 73 inborn preterm neonates of AJIMS, Mangalore during the study period of 18 months. (November 2018 – April 2020). Inclusion criteria was Inborn preterm neonates (<37weeks) were included in the study and Exclusion criteria was (1) out born neonates, (2) Newborns with congenital anomalies,(3) Newborns of those parents who aren't willing to participate in the study.

Preterm neonates fulfilling the inclusion criteria were included as study subjects after obtaining detailed informed consent from the parents.

Oral aspirate was collected using single use sterile catheter with mucus extractor connected to vacuum immediately after birth. And the sample was used to perform stable micro bubble test. Firstly, sample of nearly 4mL of fluids were taken with the calibrated pipette. With the pipette held vertically and placed with the tip practically touching the counting chamber (Neubauer chamber), the aliquot was swiftly suctioned in and ejected out for approximately 6sec(20times) in the pipette, in order to increase aeration of samples. The chamber was then turned over and a binocular microscope was placed inside to create a hanging drop. The count area was examined at 100x magnification after 4 minutes to determine the quantity of SMB (bubbles less than 50microns in diameter) present per square millimetre. Non-spherical and black bubbles was not included. Then later, number of stable microbubbles were compared with preterm newborns who developed RDS, required surfactant, or use of CPAP/ Ventilator.

The decision of using surfactant, CPAP, ventilation or any other medication was decided by the treating pediatrician.

RESULT

In our study, Data was collected from 73 preterm neonates and statistically analyzed.

Out of 73 patients, 35 male and 38 were females which is comparable with previous study. However, there is no direct correlation between sex and mode of delivery prevalence of RDS in our study.

Table No.1. Baseline Characteristics

S.No			Number	Percentage (%)
1.	Sex	Female	38	52.1
		Male	35	47.9
		Total	73	100
2.	Mode of delivery	LSCS	35	47.9
		VD	38	52.1
		Total	73	100
3.	Gestation	Early preterm	28	38.4
		Late preterm	45	61.6
		Total	73	100
4.	RDS	Early preterm	24	85.7
		Late preterm	7	15.6
		Total	31	42.5

Table No.2. Distribution according to the Exposure

S.No			Mean	SD	P value
1.	Steroids	Received	25.76	9.48	0.561
		Not received	23.82	13.56	
2.	Hood Oxygen	Required	24.67	10.69	0.427
		Not required	26.60	9.27	
3.	CPAP	Required	18.67	8.80	<0.001
		Not required	29.46	8.64	
4.	Ventilator	Required	18.87	8.64	0.004
		Not required	27.17	9.81	
5.	Surfactant	Required	18.29	8.11	0.001
		Not required	27.64	9.68	
6.	Chest x-ray (RDS)	Present	18.81	7.97	<0.001
		Absent	29.37	9.20	
7.	Stable microbubble test	Positive	17.77	6.75	<0.001
		Negative	31.14	8.26	

Among early preterm 85.7% had RDS and among late preterm only 15.6% had RDS P Value <0.001, there was a statistically significant difference found between early preterm and late preterm with respect to RDS.

Mean number of stable micro bubbles among subjects who Received antenatal steroids was 25.76 ± 9.48 and Mean number of stable microbubbles among subjects who didn't Received antenatal steroids was 23.82 ± 13.56. There was no statistically significant difference found between number of stable microbubbles and antenatal steroids. Mean number of stable micro bubbles among subjects who required hood Oxygen was 24.67 ± 10.69 and Mean number of stable microbubbles among subjects who didn't required hood Oxygen was 26.60 ± 9.27. There was no statistically significant difference found between number of stable microbubbles and hood Oxygen. Mean number of stable micro bubbles among subjects who Required CPAP was 18.67± 8.80 and Mean number of stable micro bubbles among subjects who didn't required CPAP was 29.46 ± 8.64. There was a statistically significant difference found between number of stable micro bubbles and CPAP (p value <0.001). Mean stable micro bubbles among subjects who required ventilator was 18.87± 8.64 and Mean number of stable micro bubbles among subjects who didn't required ventilator was 27.17 ± 9.81. There was a statistically significant difference found between stable micro bubbles and ventilator requirement (p value 0.004). Mean stable micro bubbles among subjects who required surfactant was 18.29 ± 8.11 and Mean number of stable microbubbles among subjects who didn't required surfactant was 27.64 ± 9.68.There was a statistically significant difference found between number of stable microbubbles and surfactant (p value 0.001). Mean number of stable microbubbles among subjects who had x-ray features of RDS was 18.81 ± 7.97 and Mean number of stable microbubbles among subjects didn't had x-ray features of RDS was 29.37 ± 9.20. There was a statistically significant difference found between number of stable microbubbles and x-ray features of RDS (p value <0.001).

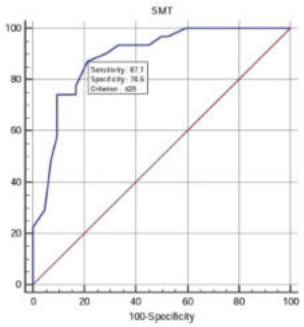
Table 3: Comparison of chest x ray in diagnosis of RDS in preterm newborn

Sensitivity	77.42%
Specificity	92.86%
Positive Predictive Value	88.89%
Negative Predictive Value	84.78%

The findings of our study suggest that sensitivity of chest x-ray in detecting RDS was 77.4% while specificity was 92.86%. When compared to stable microbubble test the specificity was found to be more with the chest x ray. The negative and positive predictive value of chest x-ray in detecting RDS were 84.78% and 88.89% respectively.

Graph 1:- Receiver operating characteristic (ROC) curve for the number of stable microbubbles in predicting RDS.

An area-under-the-curve (AUC) value of 0.888 was obtained using number of stable microbubbles for predicting RDS.



At a cut-off level of <25 SMT Sensitivity was 87%, specificity was 78.57%, PPV was 75%, NPV was 89.2%.

STATISTICALANALYSIS:

The SPSS 22 version of software was used to analyse the data, which was entered into a Microsoft Excel data sheet. Data that was categorical was displayed as frequencies and proportions. Chi-square test or Fischer's exact test was used as test of significance for qualitative data. Mean and standard deviation were used to depict continuous data. To determine the mean difference between two quantitative variables, the independent t test was employed as a measure of significance.

The receiver operating characteristic (ROC) and appropriate cut-off points were chosen for the computation of sensitivity, specificity, positive and negative predictive values.

A test with an area under the ROC curve of 0.5 predicts a result no better than by chance. An area under the ROC curve exceeding 0.8 indicated pretty excellent prediction Graphical depiction of data: We used MS Word and MS Excel to create a variety of graphs. P value (Probability that the result is true) of <0.05 was determined as statistically significant after adopting all the rules of statistical tests.

Statistical software: Microsoft Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, \sUSA) was used to analyse data.

DISCUSSION

Respiratory distress syndrome (RDS), is a common problem in preterm infants. This disorder is caused by deficiency of pulmonary surfactant in an immature lung. RDS is a major cause of morbidity and mortality in preterm infants. The major cause of morbidity and mortality is due to the delay in initiation of treatment, or lack of infrastructure and equipment's for the required treatment in the developing country. Hence there is a requirement of rapid and easily available technique to prevent the delay in initiation of treatment or to shift the baby to hospital where the facilities are available.

In our study, Data was collected from 73 preterm neonates and statistically analyzed. Out of 73 patients, were 35 male and 38 were females which is comparable with previous studies. However, there is no direct correlation between sex and prevalence of RDS in our study.

In our study, the study subjects were less than 37weeks of age. A study done by Manoel Antonio da Silva Ribeiro et al study considered 64 newborns which were <34weeks only (11). The study included 23 males while in our study we included 35males and 38 females. In a similar study by S Chida et al 105 study subjects were included. The included patients were less than 35 weeks of gestation (12). In a study

done by Schoichi chida et al, 101 infants of gestation between 24 and 35 weeks were included (13).

During our study out of 73 infants 18 required CPAP, 18 required ventilators. In our study we tried to assess the relation between the stable microbubble test score with the mode of ventilation required following delivery. However no significant difference was found in the stable microbubble test score between the two groups. The cut off score in both the groups were noted to be 18.87 +/- 8.64. In the study done by Manoel Antonio da Silva Ribeiro out of 64, 9 required CPAP and 3 required mechanical ventilator (11).

Our study findings suggested that at a cutoff level of less than or equal to 25 stable microbubbles the sensitivity for detection of RDS was found to be 87% while specificity was 78.57%. The PPV was found to be 75% and NPV was 89.2%. These findings were comparable with the study by Manoel Antonio da Silva Ribeiro et al, in which they found the sensitivity to be 81.4% and specificity was 87.5%(11). In a similar study done by S Chida et al the stable microbubble test was done on gastric aspirate and amniotic fluid to predict RDS considering the cut off value of 10 microbubbles. In their study PPV for stable microbubble test on amniotic fluid sample was found to be 100% while that on gastric aspirate was found to be 96%. NPV for the same was 91% and 84% respectively (12). A study done by Schoichi chida et al considered a cut off level of 20 microbubbles. The sensitivity and specificity were 93.5 % and 95.7% respectively while PPV was 90.7% and NPV was 97.1%.

In our study using the stable microbubble test we have co related the incidence of RDS with the administration of antenatal steroids. Since the p value was > 0.05 the results were considered insignificant. However, there are not many studies comparing these parameters. Hence this becomes one of the strengths of our study.

In our study, we compared number of stable microbubbles with respiratory distress syndrome using oral aspirate. We have not correlated with gastric aspirate or amniotic fluid which becomes a limitation of the study.

CONCLUSION

This non-invasive method for early detection and rapid diagnosis of RDS can replace routinely used chest x ray for diagnosis thereby avoiding unnecessary radiation exposure in new born.

Testing the stable microbubble in oral aspirate at birth in preterm, can predict the possibility of a preterm having RDS at a cutoff value of <25 number of stable microbubbles with PPV of 75%, NPV of 89.2% with a good sensitivity of 87% and specificity of 78.5%.

In comparison to chest x ray in detection of RDS, stable microbubble test was found to be more sensitive at a cut off value of <25 stable microbubbles.

The possibility of need of surfactant in a case of RDS can be predicted using number of stable microbubbles.

This test aids to choose the right mode of ventilation, helping us prevent aggressive ventilator management or even under treatment and forms a basis of treatment. Helps in early initiation of treatment and timely management which decrease the overall neonatal mortality and morbidity.

This study can be a guide to form new recommendation for RDS screening which is simple, non-invasive, cost effective and with no radiation exposure or any side effects.

REFERENCES

1. Singh M. Care of Newborn; Revised 8th edition; 2017; 359-362.
2. Waldo N. Text book of Paediatrics, 1st south asia ed. 2017;1: 850-858.
3. Stark , Cloherty .manual of neonatal care. 8th edition.1:437-445.
4. Fiori HH, Fiori RM. Why not use a surfactant test for respiratory distress syndrome? Neonatology. 2015; 107:312.
5. Daniel IW, Fiori HH, Piva JP, Munhoz TP, Nectoux AV, Fiori RM. Lamellar body count and stable microbubble test on gastric aspirates from preterm infants for the diagnosis of respiratory distress syndrome. Neonatology. 2010; 98:150---5.4.
6. Fiori HH, Henn R, Baldisserotto M, Bica IG, Fiori RM. Evaluation of surfactant function at birth determined by the stable microbubble test in term and near term infants with respiratory distress. Eur J Pediatr. 2004;163:443-448.
7. Fiori HH, Fritscher CC, Fiori RM. Selective surfactant prophylaxis in preterm infants born at < or =31 weeks' gestation using the stable microbubble test in gastric aspirates. J Perinat Med.2006; 34:66-70.
8. Bhatia R, Morley CJ, Argus B, Tingay DG, Donath S, Davis PG. The stable microbubble test for determining continuous positive airway pressure (CPAP) success in very preterm infants receiving nasal CPAP from birth. Neonatology. 2013;104(3):188-193.
9. Pediatric Acute Lung Injury Consensus Conference Group. Pediatric acute respiratory distress syndrome: consensus recommendations from the Pediatric Acute Lung Injury Consensus Conference. Pediatr Crit Care Med 2015;16:428-439.
10. De Luca D, van Kaam AH, Tingay DG, et al. The Montreux definition of neonatal ARDS: biological and clinical background behind the description of a new entity. Lancet Respir Med 2017;5:657-666.
11. da Silva Ribeiro MA, Fiori HH, Luz JH, Garcia PC, Fiori RM. Rapid diagnosis of respiratory distress syndrome by oral aspirate in premature newborns. Jornal de Pediatria (Versão em Português). 2019 Jul 1;95(4):489-94.
12. Chida S, Fujiwara T, Konishi M, Takahashi H, Sasaki M. Stable microbubble test for predicting the risk of respiratory distress syndrome: II. Prospective evaluation of the test on amniotic fluid and gastric aspirate. European journal of pediatrics. 1993 Feb 1;152(2):152-6.
13. Ma, L.-Y and Ye, Z.-Z and Lu, G.-J and Chida, Shoichi and Shimada, S. Early diagnosis of neonatal respiratory distress syndrome by the stable microbubble test on gastric aspirates. Chinese Journal of Contemporary Pediatrics; 2005.