

Gastric Aspirate Shake Test for Prediction of Hyaline Membrane Disease in Preterm Babies

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ABSTRACT

Introduction: Hyaline Membrane Disease (HMD) remains a major cause of neonatal death and morbidity in infants of less than 37 weeks gestation. HMD is an important cause of RDS in newborns. To evaluate whether the Gastric Aspirate Shake Test in Preterm babies can predict the likelihood of Hyaline Membrane Disease.

Methods: The Shake Test for prediction of Hyaline Membrane Disease was evaluated in 81 preterm newborns at NICU and Nursery, Patan Hospital. Over 0.5 ml of gastric aspirate was obtained within 1 hour of birth and mixed with an equal amount of normal saline for 15 seconds; 1 ml of 95% alcohol was then added and the mixture was agitated for the next 15 seconds. Then after 15 minutes, the air-liquid interface was examined for bubbles.

Results: Among 81 neonates, 46 developed HMD. 56.8% (26/46) of neonates with negative shake test developed HMD which was statistically significant ($p < 0.05$). The sensitivity, specificity, positive predictive value, and negative predictive value were 96.29%, 76.47%, 86.6%, and 92.8% respectively.

Conclusion: The gastric aspirate shake test is a rapid, simple, and inexpensive procedure and useful in predicting HMD and facilitating early transfer to the neonatal intensive care unit.

Keywords: Hyaline Membrane Disease; Shake test.

INTRODUCTION

Despite major advances in the understanding & management of respiratory distress in the newborn, hyaline membrane disease (HMD) remains a major cause of neonatal death and morbidity in infants of less than 37 weeks gestation.¹ HMD is an important cause of RDS in newborns. It is generally believed that the incidence of HMD in South Asia is low. This is partly because of the difficulty in confirming the clinical diagnosis in the absence of an autopsy. With advances in neonatal care, there is an increase in the survival of preterm babies and many of them develop HMD. The incidence of HMD in India is reported to be 10-15/1000 live births.² and it increases with decreasing gestation.³ The medical practitioner is therefore often faced with the inevitable delivery of a preterm and or low birth weight infant without knowing whether the infant is likely to develop HMD due to pulmonary immaturity. The importance of identifying infants who are at risk

to develop HMD as soon as possible after delivery is to facilitate their early transfer to a NICU.^{4,5} A simple reliable test of pulmonary maturity in the newborn infant at risk would therefore be of great value, especially in a setting where high-risk newborns have to be transferred to another facility where the surfactant is given or available. It is now well accepted that HMD is caused by a deficiency of surfactant due to pulmonary immaturity. Assessment of pulmonary maturity by determining the lecithin-sphingomyelin (L/S) ratio in the amniotic fluid described by Gluck et al.⁶ have been widely used and highly reliable. However, estimation of the L/S ratio has to be done by thin-layer chromatography which is an expensive and slow technique and needs trained personnel. Clements et al.⁷ developed an inexpensive yet sensitive shake test on amniotic fluid to predict fetal lung. It is now well accepted that HMD is caused by a deficiency of surfactant due to pulmonary immaturity. Assessment

of pulmonary maturity by determining the lecithin-sphingomyelin (L/S) ratio in the amniotic fluid described by Gluck et al.⁶ have been widely used and highly reliable. However, estimation of the L/S ratio has to be done by thin-layer chromatography which is an expensive and slow technique and needs trained personnel. Clements et al.⁷ developed an inexpensive yet sensitive shake test on amniotic fluid to predict fetal lung maturity. This test too can be performed only in centers where facilities for amniocentesis are available. It has been postulated that surfactant enters the stomach by direct swallowing of pulmonary secretions rather than by ingestion of amniotic fluid. A single-step gastric aspirate shake test has been described to predict HMD.⁸ The shake test is a quick, simple, and inexpensive bedside test that depends on the principle of stability of bubbles in amniotic or gastric aspirate fluid when mixed with the respective diluents in a solution.^{9,10} This test is based upon the ability of pulmonary surfactant to generate stable foam in the presence of ethyl alcohol.

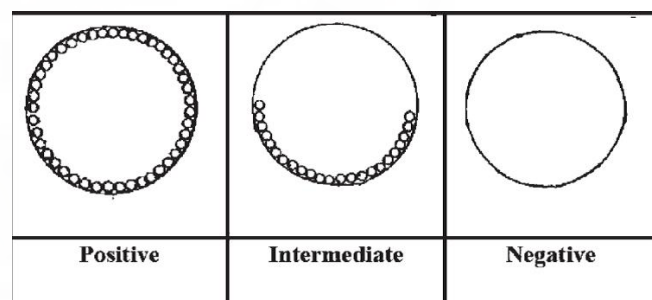
The shake test was originally found to be comparable with the L/S ratio in predicting fetal lung maturity. Thereafter many studies have been conducted comparing the tap test and shake test with the standard phospholipids profile to determine the reliability of these tests as compared to the standard tests.¹¹⁻¹⁵ The ideal test for fetal lung maturity should be rapid, inexpensive, and capable of being done at the patient's bedside, with high predictive value for both positive and negative results.^{16,17} Fetal lung maturity can be determined as soon as the baby is born from gastric aspirate at the bedside and can be decided accordingly with the referral of the patients to the higher center where all neonatal facilities are available. Studies about the feasibility of a single-step shake test on gastric aspirates in the rapid evaluation of pulmonary surfactant maturity at birth in Nepali neonates have so far been not done. Indian studies in this regard are also scanty.

METHODS

This descriptive, cross-sectional study was done in the Patan Hospital Neonatal Intensive Care Unit (NICU) and Nursery over a period of one year in the Department of Paediatrics at Patan Hospital from August 2009 to July 2010. All babies greater than or equal to 28 weeks and less than 37 weeks (36+6) with or without respiratory distress after birth were included in the study. The gestational age was estimated according to the criteria of New Ballard scoring. Neonates with more than 1 hour, who received breastfeeding or any other feeds, neonates with severe congenital anomalies or incompatible with life, neonates whose gastric aspirates obtained through

NG tube were <0.5 ml or samples mixed with meconium or blood were excluded from the study. Neonates were defined with Hyaline Membrane Disease if respiratory rate >60/ min, expiratory grunting, suprasternal, intercostal, subcostal retraction, or cyanosis occurred within 6 hours of life and persisted for >24 hours, and if chest x-ray showed hypo-aeration, diffuse reticular-granular pattern with air bronchogram. Over 0.5 ml of gastric aspirate was obtained within 1 hour of birth and mixed with an equal amount of normal saline for 15 seconds; 1 ml of 95% alcohol was then added and the mixture was agitated for the next 15 seconds. Then after 15 minutes, the air-liquid interface was examined for bubbles.¹⁸⁻²⁰

- 1.If no bubbles were present then the test is **NEGATIVE**. This result indicates that the infant's lungs are probably immature and that very little surfactant is present. As a result, the infant is at high risk of developing hyaline membrane disease.
- 2.If bubbles are seen around the top of the fluid but not enough bubbles are present to completely cover the surface, then the test is **INTERMEDIATE**. This result indicates that only some surfactant is present in the lungs and the infant may still develop mild hyaline membrane disease.
- 3.If bubbles are present right across the surface of the fluid, then the test is **POSITIVE**. This indicates that the lungs are mature and are producing adequate amounts of surfactant.



The result of the test was correlated with clinical data and the outcome of the disease. The parents were informed and explained about the procedure, and who agree to participate in the study were included. An informed verbal and written consent was taken. Data were analyzed using SPSS software, Student T-test, and Chi-square test or Fisher exact test were used for analysis. P-value <0.05 will be considered significant.

RESULTS

A total of 7678 live babies were delivered to Patan Hospital during the study period of one year from August 2009 to July 2010. Among the preterm neonates, 104 were

enrolled in the study. Out of that 81 preterm neonates who met the inclusion criteria were enrolled in the study.

All the newborn babies had shake tests performed within 1 hour of life. 56.8% (26/46) of neonates with a negative shake test developed HMD which was statistically significant ($p < 0.05$) as shown in table 1. However, 37 babies had an intermediate shake test which was 45.7% of the total enrolled population. Out of that 19/37 (23.45%) developed HMD and 18/37 (22.2%) did not develop HMD as shown in table 1.

Table 1: HMD and shake test

Confirmed HMD	Shake Test			Total
	Positive	Intermediate	Negative	
Yes	1	19	26	46
No	13	18	4	35

Among the preterm neonates, one neonate expired at 41 days of life due to sepsis. The baby who expired received surfactant therapy and this is the first neonate of this study receiving surfactant with negative shake test results. Among the preterm neonates, 5 (6.1%) died due to severe prematurity and Hyaline Membrane Disease. Among the eighty-one preterm neonates, nine received surfactant therapy which is 25.71% of the gestation age of 28-32 weeks of gestation and 11.11% of the whole enrolled population. All babies qualifying for surfactant treatment could not receive surfactant because of financial reasons.

Table 2 shows that among the 81 preterm neonates 44 neonates have positive or negative shake tests, of which 27 neonates developed Hyaline Membrane Disease. Among these 27 neonates, 26 were correctly predicted by gastric aspirate shake test (as a negative test).

Table 2: Validity of shake test result and HMD

Result of Shake test	HMD Confirmed	
	Yes	No
Positive	1	13
Negative	26	4

Sensitivity: 96.29%, Specificity: 76.47%

Positive predictive value: 86.6%, Negative predictive value: 92.8%

Table 3: Gestational age and Shake Test

Gestational Age	Shake Test			Total
	Positive	Intermediate	Negative	
28-31 weeks		13	22	35
32-35 weeks	6	18	7	31
36-37 weeks	8	6	1	15

The lower the gestational age, the more likely the neonate was to have a negative shake test (with corresponding increased likelihood of hyaline membrane disease). This was a statistically significant finding ($p < 0.05$).

Table 4: Birth weight and HMD

Confirmed HMD	Birth weight		
	<2000gms	2000-2499gms	>2500gms
Yes	45	1	>2500gms
no	13	10	12

Table 4 showed that the study population of less than 2000 gms preterm neonates were more likely to develop HMD which is 76.6%. likewise increased birth weight decrease the prevalence of developing HMD.

DISCUSSION

This study shows that the neonates who developed HMD had negative shake test results which are 56.8% of the neonate with negative shake test results which are statistically significant ($p < 0.05$). the sensitivity, specificity, positive predictive value, negative predictive value were 96.29%, 76.47%, 86.6%, 92.8% respectively. This study also indicates that the lower the gestational age more likely to develop HMD.

The present study included the babies whose gestation period was 28 weeks to less than 37 weeks (36+6 weeks) of gestation. Similar age groups of neonates were also included in studies conducted by Tanswell.¹⁸ P Parekh, et al.¹⁹ All the newborn babies had shake tests performed within 1 hour of life 56.8% (26/46) of neonates with negative shake tests developed HMD which was statistically significant ($p < 0.05$), the result of the current study had sensitivity, specificity, positive predictive value and negative predictive value 96.29%, 76.47%, 86.6%, and 96.29% respectively, that was similar with the study done by Parekh et al.¹⁹ that is from eighty-five percent of the preterm neonate (17/20) with a negative shake test developed HMD, this was statistically significant ($p < 0.001$).

As expected this study showed that the study population of less than 2000 gms preterm neonates (71.6%) were more likely to develop HMD. Likewise, increased birth weight decreases the prevalence of developing HMD. A similar study and result were also given by Chaudhari et al.²⁰ and J. Teeratakulpisarn et al.²¹ The neonates who received surfactant therapy had a better outcome and they did not develop HMD. Administration of surfactant reduces the cost and stay in the hospital. A study done by Fiori HH et al.²² showed that surfactant therapy reduces the cost and unnecessary

intervention and decreases hospital stay. It may also be done for our patients. The sensitivity of the shake test was 96.27% which is similar to the study done by Wu TJ et al.²³ (95%), and Pena-Camarena et al.²⁴ (97.5%).

An intermediate shake test indicating the partial presence of surfactant did not offer protection for developing HMD. To predict HMD, it might be best to regard an intermediate test result as negative so at increased risk of HMD. In the current study, thirty-seven neonates had intermediate shake test results which were 45.7% of the total enrolled population. Out of that 19/37(23.45%) developed HMD and 18/37(22.2%) did not develop. The result of the shake test when intermediate is considered positive has sensitivity, specificity, positive predictive value, and the negative predictive value of 56.52%, 88.57%, 86.6%, and 60.78% respectively and while as negative then the sensitivity, specificity, positive predictive value, and negative predictive value were 97.82%, 37.14%, 67.1%, and 92.85% respectively. This shows that a positive intermediate shake test indicating the partial presence of surfactant did not offer protection for developing HMD as 23.45% of cases in this group developed the disease. To predict HMD it might be best to regard an intermediate test result as negative. A similar result was observed by Chaudhari et al.²⁰ where all 12 neonates with an intermediate test developed HMD and also suggest that it was best to regard an intermediate test result as negative.

Compared with other studies on gastric aspirate shake tests performed in the Indian population, the results were similar. Gupta et al.²⁵ found that the gastric aspirate shake test had a predictive value of 96% for HMD and also showed that the test was comparable to the L:S ratio of pharyngeal aspiration. Arya et al.²⁶ found a predictive value of 97%, Singh et al.²⁷ found sensitivity and specificity of 94.5% and 71% respectively, Park et al.¹⁹ found a predictive value of 92.3%, and R. Chaudhari et al.²⁸ found sensitivity, specificity and positive predictive value of 100%, 70%, and 100% respectively for developing HMD.

CONCLUSION

The gastric aspirate shake test is a rapid, simple, and inexpensive procedure and useful in predicting HMD and facilitating early transfer to the neonatal intensive care unit. The result of the study suggests high sensitivity and specificity and makes this a good test for fetal lung maturity.

This test is also useful in primary care hospitals to distinguish between HMD and other causes of respiratory failure and therefore to decide on early transfer to the specialized hospital for those candidates for prophylactic surfactant treatment, which is an important part of the management of preterm infants.

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