The accuracy of lamellar body count and lecithin/sphingomyelin ratio in the prediction of neonatal respiratory distress syndrome: a meta-analysis


Authors' objectives
To compare the performance of the lecithin-to-sphingomyelin (L/S) ratio and the lamellar body count (LBC) in the prediction of neonatal respiratory distress syndrome (RDS).

Searching
MEDLINE was searched for articles published between January 1966 and August 1999. The bibliographies of the included studies were also checked for further articles meeting the inclusion criteria.

Study selection
Study designs of evaluations included in the review
No inclusion criteria relating to the study design were specified. The included articles reported diagnostic cohort studies.

Specific interventions included in the review
Studies evaluating both the L/S ratio and LBC were eligible for inclusion. The reported cut-off values for L/S ratio were between two and three. The reported cut-off values for LBC ranged from 10,000 to 46,000 per microL.

Reference standard test against which the new test was compared
The included studies were required to compare the test results with the occurrence of RDS. RDS was defined by a combination of clinical and radiological criteria and therapy.

Participants included in the review
No inclusion criteria relating to the study participants were specified. The studies were of pregnant women, but no further details (e.g. gestation at testing) were reported.

Outcomes assessed in the review
Studies were excluded if there were insufficient data to construct a 2x2 table of test results and the occurrence of neonatal RDS. The prevalence of RDS and the sensitivity and specificity were calculated and reported for each included study.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed the articles and a third reviewer resolved any disagreements.

Assessment of study quality
The methodological quality of the included studies was scored on the basis of the following characteristics:

Sampling (consecutive versus other);

data collection (prospective versus retrospective);

study design (cohort versus case-control);

diagnostic review bias (blinding to test results when the diagnosis was made);

verification bias;
inclusion of an appropriate patient spectrum (minimal and maximal gestational age, inclusion of multiple pregnancies, diabetic pregnancies, and women with ruptured membranes and use of corticosteroids); method of amniotic fluid collection and whether samples contaminated with blood or meconium were excluded; time between testing and delivery; and criteria by which RDS was defined.

Two reviewers independently assessed the articles and a third reviewer resolved any disagreements.

**Data extraction**
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Data on the study design, index test and reference standard methods, and outcome measures (2x2 data) were extracted.

**Methods of synthesis**
How were the studies combined?
Summary receiver operating characteristic (ROC) curves were constructed for L/S ratio and LBC. The constructed curves were tested for statistically significant differences using a linear regression model.

How were differences between studies investigated?
A Spearman correlation coefficient was calculated for the association between sensitivity and specificity (for each test) to explore possible heterogeneity due to variation in the cut-off levels (threshold effect). Linear regression was used to determine whether study characteristics were associated with the diagnostic performance of either test. A P-value of less than 0.05 was considered statistically significant.

**Results of the review**
Six studies were included in the analysis. The total number of women included in these studies was unclear; a total of 600 women were tested using the L/S ratio, and a total of 680 were tested using LBC. The minimum gestational age varied between 25 and 29 weeks, while the maximum gestational age varied between 40 and 42 weeks. No study explicitly excluded women with multiple pregnancies, gestational diabetes, or ruptured membranes. None of the studies reported the use of corticosteroids.

All the studies were diagnostic cohorts and the presence of verification bias could not be excluded in any study. Two of the six included studies were prospective evaluations in which investigators making the diagnosis were blind to the test results.

The sensitivity of the L/S ratio ranged from 64% (specificity 95%) to 92% (specificity 89%), while the specificity ranged from 81% (sensitivity 71%) to 100% (sensitivity 75%).

The sensitivity of LBC ranged from 71% (specificity 93%) to 100% (specificity 89 and 100%), while the specificity ranged from 73% (sensitivity 88%) to 100% (sensitivity 100%).

There was no statistically significant difference between the summary ROC curves for the two tests.

The linear regression analysis indicated that none of the study characteristics had a statistically significant impact on the performance of either of the two tests.

**Authors' conclusions**
The performance of the LBC in the prediction of neonatal RDS was equal, if not superior, to the L/S ratio. Since the LBC is less time-consuming and expensive than the L/S ratio, it may be considered as the test of first choice in the
assessments of foetal lung maturity.

CRD commentary
The review addressed a clearly stated research question and was generally well conducted and reported. The inclusion criteria used were broad but appropriate to the question addressed. The literature search was very limited and no attempt to identify unpublished studies was reported; relevant data may therefore have been overlooked. The approach to the data analysis was appropriate and clearly reported. However, although the data presented indicate equivalence of diagnostic performance between L/S ratio and LBC, the authors' conclusions favoured the use of LBC on the grounds of cost and possibly greater accuracy. No cost data were presented and the data reported do not support the promotion of either test on the grounds of diagnostic performance.

Implications of the review for practice and research
Practice: The authors recommended that LBC be used as the test of first choice in the assessment of foetal lung maturity. They further stated that this test should be interpreted with caution in women with oligohydramnion or polyhydramnion.

Research: The authors stated that studies are required to assess the effect of the presence of oligohydramnion or polyhydramnion, gestational age and other clinical factors on the diagnostic performance of tests of foetal lung maturity.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.