

A STUDY OF PLEURAL FLUID BILIRUBIN/SERUM BILIRUBIN RATIO FOR DIFFERENTIATING EXUDATIVE AND TRANSDUATIVE EFFUSIONS IN TERTIARY CARE CENTRE

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ABSTRACT

Introduction : Pleural effusion, the pathologic accumulation of fluid in the pleural space is a common clinical problem with a broad differential that ranges from heart failure and cirrhosis to infection, malignancy and pulmonary embolism. The first critical step in evaluation is to distinguish transudates (due to systemic factors altering hydrostatic/oncotic pressures) from exudates (due to increased pleural permeability or impaired lymphatic drainage), because this classification directs subsequent diagnostic testing and management. Contemporary guidelines continue to recommend routine biochemical analysis of pleural fluid alongside clinical context to make this distinction. **Objectives :** To study the pleural fluid bilirubin to serum bilirubin ratio for differentiating exudative and transudative effusions. **Materials and Methods:** This cross sectional study involving 75 patients who met specific inclusion and exclusion criteria was done from June 2024 to November 2025. **Results:** Among the 75 patients, transudative effusion was observed in 23 patients (30.6%), while 52 cases (69.3%) had Exudative effusion. The mean Pleural fluid/Serum Bilirubin ratio in exudative effusions (1.42) is significantly higher than in transudative effusions (0.35). A p-value of < 0.0001 indicates highly statistical significance. **Conclusion:** In conclusion, the study demonstrates that the pleural fluid to serum bilirubin ratio is a highly effective and cost-efficient method for distinguishing exudative from transudative pleural effusions. This diagnostic tool provides a non-invasive and readily accessible approach that complements traditional diagnostic criteria like Light's criteria. With an impressive sensitivity of 94.23% and specificity of 91.30%, the PF/SB ratio shows promise, especially in settings where access to advanced biochemical testing might be limited.

KEYWORDS

Pleural effusion, Pleural fluid bilirubin, Serum bilirubin.

INTRODUCTION

Pleural effusion—the pathologic accumulation of fluid in the pleural space is a common clinical problem with a broad differential that ranges from heart failure and cirrhosis to infection, malignancy and pulmonary embolism. The first critical step in evaluation is to distinguish transudates (due to systemic factors altering hydrostatic/oncotic pressures) from exudates (due to increased pleural permeability or impaired lymphatic drainage), because this classification directs subsequent diagnostic testing and management. Contemporary guidelines continue to recommend routine biochemical analysis of pleural fluid alongside clinical context to make this distinction.^{1,2}

For five decades, Light's criteria—using pleural fluid and serum protein and LDH thresholds—have been the standard approach. They are highly sensitive for identifying exudates but can misclassify ~20–25% of transudates (particularly in patients on diuretics), prompting interest in adjunctive indices that might improve specificity or help in borderline cases. Serum–pleural albumin/protein gradients are often used to “rescue” suspected pseudo-exudates, but additional inexpensive markers have also been explored.^{3,4}

One such candidate is the pleural fluid bilirubin to serum bilirubin ratio (PF/SB). Bilirubin behaves as a relatively large, protein-bound molecule; in inflammatory states with increased pleural capillary permeability, higher bilirubin transudation into pleural fluid would be expected, potentially differentiating exudates from transudates. Early reports in CHEST proposed that the PF/SB ratio correlates with exudative physiology, suggesting a practical cut-off around 0.6 (≥ 0.6 exudate; < 0.6 transudate). Subsequent clinical laboratory references and small clinical series have echoed this threshold, though they also note overlap between groups, meaning PF/SB should be considered an adjunct rather than a replacement for Light's criteria.^{5,6}

More recent small studies—from single-centre cohorts—have compared PF/SB with conventional indices and reported moderate diagnostic accuracy and good concordance with Light's criteria, with suggested utility where Light's results are equivocal or where diuretic use raises concern for pseudo-exudates. However, sample sizes are limited and the studies are heterogeneous in aetiology mix and analytical methods; thus, PF/SB is best positioned as a supportive marker in a standardized pleural fluid panel in tertiary-care settings, rather than a standalone discriminator.⁷

It is also important to recognize a distinct entity—bilious (bilothorax) effusion—in which the PF/SB ratio exceeds 1.0, usually reflecting direct translocation of bile into the pleural space (e.g., after

hepatobiliary procedures, biliary leaks, or subphrenic collections). This scenario is rare but clinically significant and should not be conflated with routine exudate/transudate discrimination.⁸

Rationale for the Present Study (Tertiary-care Context). In high-volume tertiary centres, pleural effusions often present with complex, mixed aetiologies and prior treatment exposure (e.g., diuretics), increasing the risk of misclassification by standard criteria alone. A low-cost, easily available analyte such as bilirubin, already measured routinely in most biochemistry labs, could add incremental value to frontline differentiation when interpreted alongside Light's criteria, albumin/protein gradients, and clinical context. This study therefore evaluates the diagnostic performance of the PF/SB ratio for differentiating exudative and transudative pleural effusions in a tertiary-care population and explores a suitable cut-off for local practice.⁹

Transudative effusions result primarily from systemic factors that alter the Starling forces (such as increased hydrostatic pressure, decreased oncotic pressure), without primary pleural pathology. Common causes include heart failure, liver cirrhosis and nephrotic syndrome. On the other hand, exudative effusions are caused by alterations in pleural capillary permeability and/or lymphatic obstruction, reflecting pleural surface or lung disease (e.g., infection, malignancy, inflammation), and thus contain higher concentrations of protein, LDH and other markers of pleural inflammation. The widely-used criteria for this differentiation are Richard W. Light's criteria (1972) — namely, a pleural fluid to serum protein ratio > 0.5 , a pleural fluid to serum LDH ratio > 0.6 , or a pleural fluid LDH greater than two-thirds of the upper limit of normal for serum LDH. While Light's criteria have high sensitivity, their specificity — particularly in certain clinical situations remains sub optimal, leading to a significant proportion of misclassifications.

Bilirubin is the end-product of heme metabolism, carried in serum, and its presence in body fluids (including pleural fluid) is recognized. The hypothesis underlying the use of the pleural fluid/serum bilirubin ratio is that in exudative conditions (with increased vascular and pleural capillary permeability, pleural inflammation or pleural surface involvement) there may be greater leakage or diffusion of bilirubin (or its conjugates/complexes) into the pleural space compared to transudative conditions, where simple ultrafiltrate of plasma predominates. In this way, the pleural fluid bilirubin value, and particularly its ratio to serum bilirubin might reflect the pleural-membrane permeability status and hence help distinguish exudates from transudates.

Several studies have evaluated the pleural fluid/serum bilirubin ratio and reported promising diagnostic performance. For example, in one study the pleural fluid to serum bilirubin concentration ratio was found to discriminate exudates from transudates with high sensitivity and specificity. In resource-limited settings, the use of a simple ratio like this may have practical utility.

OBJECTIVE

To study the diagnostic utility of the pleural fluid bilirubin to serum bilirubin ratio in differentiating exudative from transudative pleural effusions in patients with pleural effusion.

MATERIALS AND METHODS

Cross sectional study has been performed on patients getting admitted in Basaveshwar Teaching and General Hospital attached to Mahadevappa Rampure Medical College, Kalaburagi from June 2024 to November 2025 on 75 patients admitted in ipd, department of General Medicine with Pleural effusion.Data was Analysed using appropriate inferential statistics.

Informed and written consent was obtained in patients own vernacular language.The purpose of the study was explained to the patient. Detailed history, clinical examination and laboratory data of these patients was recorded as per the Proforma after applying inclusion and exclusion criteria. Prognosis is assessed by pleural fluid bilirubin and serum bilirubin ratio for differentiating transudative and exudative effusion

Duration of study: 18 months

Inclusion Criteria:

- 1. All patients who have definite clinical diagnosis and radiological evidence of pleural effusion
- 2. Age above 18 yrs.

Exclusion Criteria:

- 1. Patients with Jaundice, dyslipidemia ,hypoproteinemia ,pulmonary embolism , Traumatic effusion.
- 2. Age <18yr
- 3. Pregnancy And Lactation.

RESULTS AND OBSERVATIONS

Table 1: Comparison of Basic Pleural Fluid Parameters

Parameter	Exudative Mean (SD)	Transudative Mean (SD)	p-value
Fluid Protein (g/dL)	4.2 ± 0.8	1.8 ± 0.6	< 0.001*
Cell Count(cells/mm³)	1450 ± 850	320 ± 150	< 0.001*

As expected by standard patho physiological principles, pleural fluid protein and cell counts were significantly elevated in the exudative group compared to the transudative group.

Table 2: Comparison of Mean Bilirubin Ratio (PF/S)

Type of Effusion	Number of Cases (n)	Mean Bilirubin Ratio (PF/S)	Standard Deviation (SD)	p-value
Exudative	52	1.42	± 0.38	<0.0001
Transudative	23	0.35	± 0.16	

The mean PF/S Bilirubin ratio in exudative effusions (1.42) is significantly higher than in transudative effusions (0.35). A p-value of <0.0001 indicates highly statistical significance.

Mean Bilirubin Ratio (PF/S)

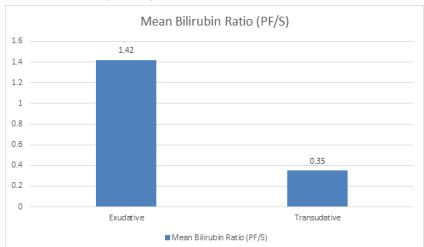


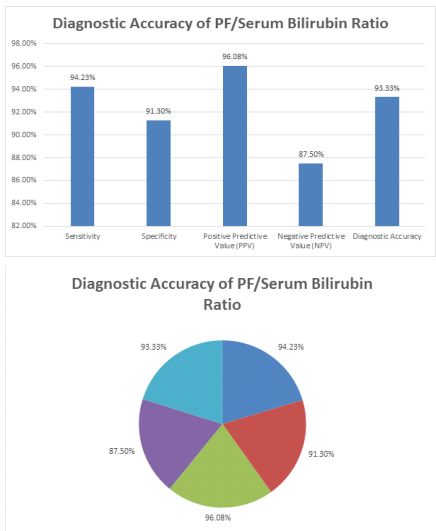
Table 3: The 2x2 Contingency Table (Using a cut-off of > 0.6)

PF/Serum Bilirubin Ratio	Exudative (Gold Standard)	Transudative (Gold Standard)	Total
> 0.6 (Test Positive)	TP = 49	FP = 2	51
≤ 0.6 (Test Negative)	FN = 3	TN = 21	24
Total	Total Exudates = 52	Total Transudates = 23	75

> 0.6 (Test Positive)	TP = 49	FP = 2	51
≤ 0.6 (Test Negative)	FN = 3	TN = 21	24
Total	Total Exudates = 52	Total Transudates = 23	75

Table 4: Diagnostic Accuracy of PF/Serum Bilirubin Ratio

Parameter	Formula	Value (%)
Sensitivity	TP / (TP + FN) × 100	94.23 %
Specificity	TN / (TN + FP) × 100	91.30 %
Positive Predictive Value (PPV)	TP / (TP + FP) × 100	96.08 %
Negative Predictive Value (NPV)	TN / (TN + FN) × 100	87.50 %
Diagnostic Accuracy	(TP + TN) / 75 × 100	93.33 %



DISCUSSION

The present study was a cross-sectional observational study conducted on 75 patients presenting with pleural effusion. The primary objective was to evaluate the diagnostic efficacy of the Pleural Fluid to Serum (PF/S) Bilirubin ratio in distinguishing exudative from transudative pleural effusions, offering a simpler and highly specific alternative to Light's criteria. The clinical, biochemical, and demographic parameters observed in our cohort were systematically analyzed and compared with established landmark and contemporary medical literature.

Demographic Profile

In the present study, the mean age of the study population was 54.2 ± 14.5 years, with the highest incidence of pleural effusion observed in the 46 to 60 years age group (34.66%), closely followed by the elderly population over 60 years (32.00%). This demographic pattern strongly correlates with the findings of Agrawal P et al. (2018), who similarly reported the highest prevalence of exudative effusions in the fifth and sixth decades of life. As noted in their literature, this age distribution is clinically anticipated due to the increasing incidence of underlying etiologies such as malignancies, chronic inflammatory conditions, and reactivation of tuberculosis with advancing age. Regarding gender distribution, a clear male predominance was observed, with males constituting 60.0% of the total study population. This gender profile is in strong concordance with the demographic data reported by Yadav M et al. (2021) and Chauhan A et al. (2021), where male subjects similarly accounted for the majority of the study cohort. This higher prevalence in males is historically attributed to greater occupational exposure to pulmonary irritants, higher rates of smoking, and a proportionately higher incidence of chronic lung diseases and tuberculosis, as extensively documented by Porcel JM et al.

Diagnostic Efficacy of the PF/S Bilirubin Ratio

The core variable of this thesis—the Pleural Fluid to Serum Bilirubin ratio—yielded profound results. The pathophysiological basis for this test relies on the fact that bilirubin is tightly bound to albumin. In the setting of pleural inflammation (exudates), increased capillary permeability allows the diffusion of these larger protein-bound

molecules into the pleural space. Our results strongly reflect this: the mean PF/S Bilirubin ratio for exudates was significantly higher (1.42 ± 0.38) compared to transudates (0.35 ± 0.16) with a p-value of < 0.0001 . This highly significant difference perfectly replicates the foundational results published by **Meisel S et al. (1990)**.

Applying the standard cut-off value of > 0.6 , the PF/S Bilirubin ratio demonstrated an outstanding **Sensitivity of 94.23%**, a **Specificity of 91.30%**, a **Positive Predictive Value (PPV) of 96.08%**, and an overall **Diagnostic Accuracy of 93.33%**.

These diagnostic metrics are in excellent agreement with landmark and contemporary studies:

1. Meisel S et al. (1990): In their seminal study proposing the > 0.6 cut-off, they reported a sensitivity of 96% and a specificity of 83%. Our study's sensitivity (94.23%) is in near-perfect agreement, though we observed a higher specificity (91.30%), reinforcing the parameter's reliability in ruling out transudates.

2. Agrawal P et al. (2018): In a similar evaluation, they reported a sensitivity of 88.00% and a specificity of 93.00%. Our results closely mirror these findings. The high PPV in both studies confirms that a PF/S Bilirubin ratio of > 0.6 is highly indicative of an exudative etiology.

3. Yadav M et al. (2021) & Chauhan A et al. (2021): The primary limitation of Light's criteria is the misclassification of transudates as exudates, particularly in patients receiving diuretic therapy. Recent literature by **Yadav et al.** and **Chauhan et al.** emphasized that the bilirubin ratio results in significantly fewer false positives. In our study, only 2 out of 23 transudates (8.6%) were misclassified as exudates. This corroborates the observations by **Chauhan et al.** that the bilirubin ratio is highly specific and effectively mitigates the false-positive limitations associated with Light's criteria.

The findings of the present study, when compared with established literature, solidify the standing of the Pleural Fluid to Serum Bilirubin ratio as an excellent, cost-effective diagnostic adjunct. With a diagnostic accuracy of 93.33%, while circumventing the need for expensive multi-parameter testing, making it highly advantageous in routine clinical practice and resource-limited tertiary care centers.

CONCLUSION:

In conclusion, the study demonstrates that the pleural fluid to serum bilirubin ratio is a highly effective and cost-efficient method for distinguishing exudative from transudative pleural effusions. This diagnostic tool provides a non-invasive and readily accessible approach that complements traditional diagnostic criteria like Light's criteria. With an impressive sensitivity of 94.23% and specificity of 91.30%, the PF/SB ratio shows promising results, especially in settings where access to advanced biochemical testing might be limited. The study emphasizes the potential of this ratio as a supplementary marker, enhancing the diagnostic process for pleural effusion differentiation. Given the results, it is suggested that the PF/SB ratio to be considered as a routine diagnostic marker alongside other tests in clinical settings to improve the accuracy of pleural effusion classification and subsequent management.

Limitations:

1. Small Sample Size: The study included 75 patients, which may not be large enough to generalize the findings to the broader population. Larger, multi-center studies with a more diverse sample size are needed to confirm the results.

2. Single-Center Study: The study was conducted in a single tertiary care center, which may limit the generalizability of the results to other hospitals or healthcare settings. Further validation in different centers and regions is necessary to evaluate the broader applicability of the findings.

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