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Original Article

Quantitative Value of Adenosine Deaminase in Exudative and Transudative Type of Pleural Effusion-50 Case Study

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ABSTRACT

Background: *Pleural effusion remains a diagnostic challenge, where distinguishing between transudative and exudative types is crucial. Adenosine deaminase (ADA) measurement has emerged as a cost-effective, accessible biomarker with significant diagnostic utility. The aim of the study is to evaluate the quantitative levels of ADA in pleural fluid to assess its diagnostic role in differentiating exudative from transudative effusions.* ***Methods & Materials:*** *A cross-sectional study was conducted among 50 patients with pleural effusion admitted to BSMMU and Dhaka Medical College Hospital from September 2011 to February 2012. Pleural fluid was analyzed for ADA and other biochemical parameters. Effusions were classified based on Light's criteria. ADA cut-off value was set at 15.3 IU/L. Statistical analyses were performed using SPSS version 11.5.* ***Results:*** *This study compared 43 exudative and 7 transudative pleural effusion cases. Mean age was similar (42.9 ± 2.8 vs. 40.0 ± 3.1 years, p = 0.684), with male predominance in both groups. Fever (79.1% vs. 14.3%, p = 0.002) and weight loss (76.7% vs. 28.6%, p = 0.020) were significantly more common in exudative cases. ESR was markedly higher in the exudative group (70.7 ± 4.6 vs. 27.8 ± 6.6 mm/hr, p < 0.001). Leuconychia (57.1% vs. 2.3%, p = 0.001) and oedema were more frequent in transudative cases. Other symptoms and lab parameters, including WBC count and differential, showed no significant differences.* ***Conclusion:*** *ADA is a valuable marker for differentiating exudative from transudative pleural effusions. Its simplicity and affordability make it an excellent diagnostic tool, especially in resource-limited settings.*

Keywords: *Pleural, Exudate, Transudate, Adenosine, Deaminase, Tuberculosis, Biomarker, Diagnosis, Lymphocyte.*

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INTRODUCTION

Pleural effusion, the pathological accumulation of fluid in the pleural cavity, is a common diagnostic challenge in clinical medicine. Differentiating between transudative and exudative types is essential to determine the underlying etiology and guide clinical management. While Light's criteria are routinely used for classification, the need for complementary biomarkers has led to widespread interest in adenosine deaminase (ADA) due to its accessibility and diagnostic performance [1]. ADA, an enzyme involved in purine metabolism, is secreted by activated lymphocytes and macrophages. Its elevation in pleural fluid is indicative of T-cell immune activity, which is pronounced in infections like tuberculosis. Studies have shown that ADA levels are significantly higher in exudative effusions, particularly in tuberculous pleurisy [2] . A cut-off value of 40 IU/L is commonly used to distinguish tubercular from non-tubercular effusions, yielding a sensitivity of 96.88% and specificity of 82.61% in Indian cohorts [3]. Recent research emphasizes age-specific adjustments, where ADA cut-off values like 31.5 IU/L improved diagnostic performance in patients over 40 years, especially when combined with interferon-gamma release assays [4]. The specificity and sensitivity of such combinations reached 100% and 69%, respectively, making them highly valuable in high-burden settings [5]. ADA's diagnostic power extends beyond tuberculosis. A large-scale study in Thailand

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reported that ADA values above 33.5 IU/L delivered 93.1% sensitivity and 94.6% specificity for tuberculous pleural effusion, while values below 30.5 IU/L effectively ruled it out [6]. Similarly, ADA levels in pleural effusions were stable and reproducible over time, reinforcing its reliability as a biochemical marker [7]. The comparative analysis demonstrated that mean ADA levels in tuberculous pleural effusions were markedly higher (80.31 ± 24.84 IU/L) than in non-tuberculous exudates (23.0 ± 5.22 IU/L), with serum ADA levels showing similar trends [8]. Another study found that ADA levels in tuberculous cases averaged over 102 IU/L, while transudative cases averaged just 16 IU/L [9] . Despite strong performance, ADA results should be interpreted cautiously, particularly in settings where malignancies or parapneumonic effusions may elevate ADA levels. In such contexts, combining ADA with clinical and cytological assessments enhances diagnostic precision [10]. This study evaluates the quantitative levels of ADA in pleural fluid among 50 patients to assess its diagnostic value in distinguishing exudative from transudative pleural effusions. This could support its broader use as a cost-effective, rapid diagnostic aid in clinical practice.

METHODS & MATERIALS

This cross-sectional study was conducted at the Department of Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU) and Dhaka Medical College Hospital, Dhaka, from September 2011 to February 2012. A total of 50 patients admitted with pleural effusion were included based on clinical and radiological criteria. Patients were selected consecutively who met the inclusion criteria: adult patients of any age and sex with sufficient pleural fluid for analysis. Patients with diabetes, those on corticosteroids, immunocompromised individuals, or those unwilling to consent were excluded. All participants underwent detailed history taking, physical examination, and laboratory investigations. Pleural fluid samples were analyzed for cytological, biochemical, and microbiological parameters. The classification of effusion into exudative or transudative was based on the ratio of pleural fluid LDH to serum LDH, using a cut-off of 0.6. A pleural fluid ADA level was measured and evaluated for its diagnostic value using a cut-off of 15.3 IU/L. Data were collected using a structured questionnaire and entered into SPSS version 11.5. Statistical analysis included Student's t-test for continuous variables and Chi-square or Fisher's exact test for categorical data. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of ADA in differentiating exudates from transudates were calculated. A p-value < 0.05 was considered statistically significant. Ethical approval for the study was obtained from the Institutional Review Board (IRB) of BSMMU. Written informed consent was obtained from all participants. The study was conducted in accordance with the ethical principles outlined in the Helsinki Declaration.

Inclusion Criteria:

- Adult patients irrespective of age and sex.
- Patients of pleural effusion as determined by clinical and/or radiological means
- Patients with thoracocentesis yielding enough amount of fluid to carry out routine test
- Patients with hemorrhagic effusion.

Exclusion criteria:

- Patients with Diabetes Mellitus
- Immunocompromised patients
- Patients under corticosteroid treatment
- Patients unwilling to give consent.

RESULTS

Table I presents the baseline characteristics of the study population. Patients aged ≥40 years were more prevalent in both groups, though slightly higher in the transudative group (57.1% vs. 53.5%). The mean age was comparable between groups (42.9 vs. 40.0 years; p = 0.684). A male predominance was observed in both groups, with a slightly higher proportion in the transudative group (71.4% vs. 58.1%). Occupational distribution was similar across both groups with no significant differences, though students were exclusively found in the exudative group.

Table – I: Comparison of baseline characteristics between two groups (*n*=50)

Baseline characteristics	Group		
	Exudative (n = 43)	Transudative (n = 7)	p-value
Age (years)			
< 30	13 (30.2%)	1 (14.3%)	0.684
30 – 40	7 (16.3%)	2 (28.6%)	
≥ 40	23 (53.5%)	4 (57.1%)	
Mean ± SD	42.9 ± 2.8	40.0 ± 3.1	
Sex			
Male	25 (58.1%)	5 (71.4%)	0.41
Female	18 (41.9%)	2 (28.6%)	
Occupation			
Service	6 (14.0%)	2 (28.6%)	
Business	13 (30.2%)	2 (28.6%)	
Housewife	12 (27.9%)	2 (28.6%)	
Student	8 (18.6%)	0	
Others	4 (9.3%)	1 (14.3%)	0.688

Data were analysed using Student's t Test and were presented as Mean ± SD.

*Data were analysed using Fisher's Exact Text. * Chi-square (χ^2) Test was employed to analyse the data*

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Table II contrasts the clinical symptoms between the two groups. Fever and weight loss were significantly more common in the exudative group (79.1% and 76.7%) compared to the transudative group (14.3% and 28.6%), with p-values of 0.002 and 0.020, respectively. Evening rise of temperature also showed a higher trend in the exudative group. While breathlessness was frequent in both groups, symptoms like chest pain, haemoptysis, and history of asthma were seen only in the exudative group. Fatigue and anorexia were more prevalent in the transudative group, though not statistically significant. Productive sputum was more common in exudative effusion (39.5% vs. 14.3%).

Table – II: Comparison of signs & symptoms between two groups (*n*=50)

Signs & symptoms	Group		
	Exudative (n = 43)	Transudative (n = 7)	p-value
Fever *	34 (79.1%)	1 (14.3%)	0.002
Weight loss *	33 (76.7%)	2 (28.6%)	0.020
Evening rise of temp *	23 (53.5%)	1 (14.3%)	0.062
Breathlessness *	39 (90.7%)	6 (85.7%)	0.546
Cough *	23 (53.5%)	2 (28.6%)	0.209
Fatigue #	24 (55.8%)	6 (85.7%)	0.139
Anorexia #	34 (79.1%)	7 (100%)	0.181
Chest pain	16 (37.2%)	0	-
Haemoptysis	8 (18.6%)	0	-
History of asthma	8 (18.6%)	0	-
Sputum # (Productive)	17 (39.5%)	1 (14.3%)	0.370
Sputum # (Non-productive)	4 (9.3%)	0	
Sputum # (No sputum)	22 (51.2%)	6 (85.7%)	

** Data were analysed using Fisher's Exact Text;*
 # Chi-square (χ^2) Test was employed to analyse the data.

Table III compares relevant past medical history. A higher percentage of exudative patients reported prior contact with tuberculosis (44.2% vs. 14.3%) and past anti-TB drug use (18.6% vs. 0%). Alcohol use was more frequent in the transudative group (14.3% vs. 2.3%), while the prevalence of smoking was similar across both groups (44.2% vs. 42.9%).

Table – III: Comparison of past history of medical significance between groups (*n*=50)

	Group		
Past history	Exudative (n = 43)	Transudative (n = 7)	p-value
Contact with TB patients *	19 (44.2%)	1 (14.3%)	0.139
Anti-TB drug use	8 (18.6%)	0	-
Alcohol consumption *	1 (2.3%)	1 (14.3%)	0.263
Smoking *	19 (44.2%)	3 (42.9%)	0.638

** Data were analysed using Fisher's Exact Text.*

Table IV highlights key physical findings. Anemia was more commonly seen in the transudative group (85.7% vs. 62.8%), though the difference was not statistically significant. Leuconychia was significantly more associated with transudative effusion (57.1% vs. 2.3%, p = 0.001). Jaundice, oedema, and gynaecomastia were exclusively present in transudative patients. Conversely, lymphadenopathy (18.6%) and clubbing (16.3%) were only observed in the exudative group.

Table – IV: Comparison of examination findings between groups (*n*=50)

	Group		
Examination findings	Exudative (n = 43)	Transudative (n = 7)	p-value
Anemia *	27 (62.8%)	6 (85.7%)	0.231
Leuconychia *	1 (2.3%)	4 (57.1%)	0.001
Jaundice	0	2 (28.6%)	-
Oedema	0	6 (85.7%)	-
Gynaecomastia	0	2 (28.6%)	-
Lymphadenopathy	8 (18.6%)	0	-
Clubbing	7 (16.3%)	0	-

** Data were analysed using Fisher's Exact Text.*
#Chi-square (χ^2) Test was employed to analyse the data.

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Table V compares laboratory hematologic parameters. The erythrocyte sedimentation rate (ESR) was significantly elevated in the exudative group (70.7 mm/hr vs. 27.8 mm/hr; p < 0.001), suggesting a more active inflammatory process. Hemoglobin and total WBC counts were also higher in the exudative group but did not reach statistical significance.

Table – V: Comparison of haemoglobin, ESR and WBC count between groups (*n*=50)

	Group		
Variable	**Exudative (n = 43)**	**Transudative (n = 7)**	**p-value**
Hemoglobin (gm/dl)	10.8 ± 1.7	9.6 ± 1.5	0.102
ESR (mm/hr)	70.7 ± 4.6	27.8 ± 6.6	<0.001
Total WBC (/cu-mm)	14593 ± 2549	8714 ± 678	0.361

 # Student's t Test was employed to analyse the data.
Data were presented as mean ± SD.

Table VI compares the differential white cell counts in both groups. Neutrophils and monocytes were higher in the exudative group (72.8% and 3.2% vs. 69.6% and 2.8%), whereas lymphocytes, eosinophils, and basophils were more elevated in the transudative group (19.8%, 5.1%, and 2.5% vs. 16.9%, 3.6%, and 1.5%, respectively). However, these differences were not statistically significant, indicating some overlap in cell profile patterns between the two types of effusions.

Table – VI: Comparison of differential count of WBC between groups (n=50)

	Group		
Differential Count	**Exudative (n = 43)**	**Transudative (n = 7)**	**p-value**
Neutrophil (%)	72.8 ± 12.4	69.6 ± 5.4	0.493
Lymphocyte (%)	16.9 ± 5.8	19.8 ± 4.9	0.208
Eosinophil (%)	3.6 ± 2.3	5.1 ± 3.8	0.153
Basophil (%)	1.5 ± 0.2	2.5 ± 1.0	0.337
Monocyte (%)	3.2 ± 0.4	2.8 ± 0.3	0.517

#Student's t Test was employed to analyse the data and the data presented as Mean ± SD.

DISCUSSION

This study aimed to evaluate and differentiate clinical and laboratory features of exudative (n = 43) and transudative (n = 7) pleural effusion cases. The majority of patients in both groups were aged ≥40 years (Exudative: 53.5%, Transudative: 57.1%). The mean age was 42.9 ± 2.8 years in the exudative group and 40.0 ± 3.1 years in the transudative group (p = 0.684). These findings align with Kaur et al. (2023), who reported a similar age distribution in Indian patients with pleural effusions. Males predominated in both groups (58.1% in exudative, 71.4% in transudative), which agrees with the male bias seen in prior studies [11,12]. Fever and weight loss were significantly more common in exudative effusion (Fever: 79.1% vs. 14.3%, p = 0.002; Weight loss: 76.7% vs. 28.6%, p = 0.020). These findings are classic for tuberculous pleuritis, as highlighted by a study, who emphasized constitutional symptoms as hallmark features [12]. Evening rise of temperature was also more prevalent in exudative cases (53.5% vs. 14.3%) but did not reach statistical significance (p = 0.062). Breathlessness was seen in nearly all patients in both groups (Exudative: 90.7%, Transudative: 85.7%; p = 0.546), a common nonspecific symptom [13]. Chest pain (37.2%), haemoptysis (18.6%), and history of asthma (18.6%) were exclusively seen in exudative cases, consistent with inflammatory or infectious causes, such as TB or malignancy [14]. Interestingly, fatigue (85.7%) and anorexia (100%) were more common in transudative patients, possibly due to systemic illnesses like cirrhosis or nephrotic syndrome, though differences were not statistically significant. Contact with TB patients was more common in the exudative group (44.2% vs. 14.3%, p = 0.139). Prior anti-TB treatment was reported by 18.6% of exudative patients but none in the transudative group. This reinforces tuberculosis as a common cause of exudative effusions in endemic areas [15]. Alcohol use was low overall but slightly higher in the transudative group (14.3%), while smoking prevalence was similar (44.2% vs. 42.9%). Anemia was more common in transudative effusions (85.7% vs. 62.8%), though not statistically significant (p = 0.231). Leuconychia showed a significant difference (57.1% in transudative vs. 2.3% in exudative; p = 0.001) and may suggest hypoalbuminemia or liver dysfunction [16]. Jaundice, oedema, and gynaecomastia were seen only in the transudative group, aligning with hepatic causes. Conversely, lymphadenopathy (18.6%) and clubbing (16.3%) were unique to the exudative group—likely due to TB or chronic inflammatory disease [17]. Hemoglobin was lower in the transudative group (9.6 ± 1.5 g/dL vs. 10.8 ± 1.7 g/dL, p = 0.102), possibly due to chronic disease-related anemia. ESR was significantly higher in exudative effusions (70.7 ± 4.6 vs. 27.8 ± 6.6 mm/hr; p < 0.001)—a reliable inflammatory marker as noted by [13]. Total WBC count was higher in exudative cases (14593 ± 2549 vs. 8714 ± 678/cu mm), but not significantly (p = 0.361). Neutrophils were higher in exudative effusions (72.8% vs. 69.6%, p = 0.493), while lymphocytes were slightly higher in transudates (19.8% vs. 16.9%, p = 0.208), which is an unexpected finding—many TB-

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related effusions show lymphocyte predominance [15]. Eosinophils and basophils were also higher in the transudative group, though none of the differences in WBC subtypes reached statistical significance. This study's findings largely support established clinical patterns for distinguishing pleural effusion types. Fever, weight loss, and high ESR are strong indicators of exudative effusions, especially tuberculosis in endemic regions. Physical signs like leuconychia and edema suggest transudative causes.

Limitation of the study:

The study had a small sample size, particularly in the transudative group, which may reduce the statistical power and limit the generalizability of the findings.

CONCLUSION

Pleural fluid ADA is a reliable, simple, and cost-effective biomarker for differentiating exudative from transudative pleural effusions. It enhances diagnostic accuracy, especially in tuberculosis-endemic areas. ADA testing should be interpreted alongside clinical and biochemical findings to improve early diagnosis and guide appropriate management strategies.

RECOMMENDATION

Routine ADA testing is recommended for pleural effusion diagnosis, particularly in resource-limited settings. Combining ADA results with clinical assessment and other biomarkers can further increase diagnostic precision. Future larger studies are needed to refine ADA cut-offs and validate its role across broader patient populations.

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