

# KOMBINIMI I ADENOSINE DEAMINAZES (ADA) DHE PROTEINES C-REAKTIVE (PCR) NE DIAGNOZEN E LIKIDEVE PLURALE

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## Summary

### COMBINED ADENOSINE DEAMINASE (ADA) AND C-REAKTIVE PROTEIN (PCR) IN DIAGNOSIS OF PLEURAL EFFUSIONS

**Background:** Pleural effusion is common complication of various diseases. Malignant diseases and tuberculous pleurisy are two most common in developing country like our country. The diagnosis of pleural effusions remains challenge for clinician. A variety of biological markers have been proposed to facilitate noninvasive differential diagnosis including concentration of adenosine deaminase (ADA), C-reactive Protein (CRP), INF gamma TB recently. CRP concentration has been studied in pleural fluid and been found to be higher in benign exudates and lower in malignant exudates. Usefulness of adenosine deaminase (ADA) estimation in pleural fluid has been shown as a reliable chemical biomarker specially when there is suspicion of tuberculosis in endemic areas. But in countries with low incidence of TB the diagnostic value of ADA have to be discussed because of high falls positivity. The combination of adenosine deaminase and C - reactive protein levels might be helpful for discrimination between sub groups of exudative pleural effusion: malignant effusion, tuberculous pleurisy and par pneumonic effusion.

**The Aim:** The aim of this study was to explore the value of combined biomarkers (ADA and C - reactive protein) on discrimination between different pleural effusions groups.

**Materials and methods:** In this study, prospective one, were enrolled 123 patients with pleural effusion at the University Hospital for Lung Disease "Sh. Ndroqi", Tirana, Albania between May 2009 and June 2011. Samples were obtained from the first successful thoracentesis and before any treatment were initiated. In all the cases pleural fluid tested for glucose, proteins, LDH, cholesterol-reactive Protein, total ADA, microscopy, cytology and microbial testing (Grams staining, Z N Staining, cultures). Pleural biopsy was done in selected cases of tuberculosis and malignancy. Concentrations of CRP in the pleural fluid were measured using an immunoturbidimetric assay with COBAST INTEREGA 400+ Roche device. Adenosine deaminase estimation was done by photometric method. A comparison of serum and pleural effusion C-reactive protein and ADA levels in different subgroups of patients with effusion was made.

**Statistical analysis:** Results are expressed as Mean  $\pm$  SD. We assessed sensitivity, specificity, positive and negative predictive value, Positive Likelihood ratio, Negative Likelihood ratio, Youden index and accuracy of the test separately and in combination of two markers. We used Student's paired t-Test with a two-tailed distribution and chi square (r-value) to evaluate differences in means and distributions. P values  $< 0.05$  were considered significant. Cut-off points of parameter values for discriminating between the three exudative groups were based on the area under the ROC-curve.

**Results:** The study group included 86 (70 %) males and 37 (30%) females with a mean age of  $61.7 \pm 17$  years. In transudative effusions the level of ADA was very low. The range of ADA was 55.7 (28.5-166) and mean  $\pm$  SD was  $61.4 \pm 42.3$  U/L. In tuberculous group the range of ADA was 163 (39.2-495) and mean  $\pm$  SD was  $189 \pm 124$  while collectively in non-tuberculous group it was  $64.17 (26.8 - 206)$  and  $70.6 \pm 39.69$  ( $p = 0.00031$ ). CRP level in malignant effusion was lower  $14.3 \pm 11.8$  mg/L with the range of CRP 9.9 (0.7-43) comparing with parapneumonic effusion  $123.8 \pm 80.1$ , with a range of 111.7(23-293) and tuberculous effusion  $36.4 \pm 18.5$  mg/L with a range of 28.9 (16-77.4). CRP values were compared between different exudative groups and difference in these values was statistically significant, ( $p < 0001$ ,  $p = 0.00033$  respectively). The sensitivity of CRP for diagnosis of malignant effusions at cut-off  $< 20$  mg/L was 71% and specificity 85.7%, positive predictive value 88%. The sensitivity of ADA for diagnosis of TB effusions at cut-off  $> 90$  U/L was 85.7% and specificity of 80.5%. The negative predictive value of ADA for the diagnosis of non-tuberculous etiology was 92.3%. Sensitivity for malignant effusions at ADA level cut-off  $< 70$  U/l was 71.4%, specificity 91.3%, Positive Likelihood ratio of 8.2 and Negative likelihood ratio of 0.31. Sensitivity for parapneumonic effusions at cut-off level of  $> 70$  U/L was 100%, specificity 48.5% with NPV of 100%. When we estimated accuracy of various