Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: www.saspublishers.com

OPEN ACCESS

Pulmonary Medicine

Role of Alkaline Phosphatase in Distinguishing Between Tuberculous and Non Tuberculous Pleural Effusions

MD Moiz Lalani[1*], M Sravan Kumar[2], B Phani Kumar[3], R Suresh[4], P Sunitha[4], P Ravi[4]

[1]Post Graduate, Department of Pulmonary Medicine, Kakatiya Medical College, Telangana, India
[2]Professor and Head of Department, Department of Pulmonary Medicine, Kakatiya Medical College, Telangana, India
[3]Associate professor, Department of Pulmonary Medicine, Kakatiya Medical College, Telangana, India
[4]Assistant professor, Department of Pulmonary Medicine, Kakatiya Medical College, Telangana, India

***Corresponding author:** MD Moiz Lalani
| **Received:** 27.02.2019 | **Accepted:** 06.03.2019 | **Published:** 30.03.2019
DOI: 10.36347/sjams.2019.v07i03.010

Abstract | **Original Research Article**

The standard investigations to elucidate the etiology of pleural effusions are most often rewarding, but sometimes they do not yield the exact etiologic cause of effusion, particularly in tuberculous pleural effusion. The most important aspect of evaluating an exudative pleural effusion is differentiation between tubercular and non tubercular effusion as management strategy is different in each of these cases. Tuberculous pleural effusion (TPE) is the second most common form of extra pulmonary tuberculosis next only to lymph node involvement. Accurate diagnosis of pleural effusion is challenging because even after thoracentesis and/or closed pleural biopsy, 25-30% of pleural effusion remain undiagnosed. The proportion of TPE among total pleural effusions diagnosed by medical thoracoscopy is 23.5%. Alkaline phosphatase is a cell membrane derived enzyme and one of the biochemical markers found in pleural effusion. A prospective analytical study was conducted among 50 patients admitted in Department of Pulmonary Medicine, government chest diseases and tuberculosis hospital, and kakatiya medical college. Detailed history, general physical and systemic examination was done in all cases. Routine and specific investigations like chest Xray/CT scan, USG chest, Pleural fluid analysis, pleural fluid ALP, Serum ALP were done. Out of the total 50 cases 35 (70%) were diagnosed with Tuberculous pleural effusion. ROC curve analysis of Pleural fluid to serum ALP ratio showed a significance level of <0.001 with an area under curve of 87.2%. A sensitivity of 83.3% and specificity of 87.5% was seen at a cut off value of 0.49.ROC curve analysis of Pleural fluid ALP showed a significance level of <0.001 with an area under curve of 87.1%. A sensitivity of 83.7% and a specificity of 69.2% were seen at a cutoff value of 75.8 U/L.

Keywords: Pleural fluid alkaline phosphatase, serum Alkaline phosphatises, tuberculous pleural effusion, non-tuberculous pleural effusion, and ratio.

INTRODUCTION

Pleural effusions are associated with a number of medical conditions causing fluid accumulation by different synergestic mechanisms like increased pleural membrane permeability, increased pulmonary capillary pressure, decreased oncotic pressure and lymphatic obstruction. The standard investigations to elucidate the etiology of pleural effusions are most often rewarding, but sometimes they do not yield the exact etiologic cause of effusion, particularly in tuberculous pleural effusion. The most important aspect of evaluating an exudative pleural effusion is differentiation between parapneumonic, malignant and tubercular effusion as management strategy is different in each of these cases.

According to global Tuberculosis (TB) report 2018 by World Health Organisation (WHO) there were estimated 10 million incident cases of tuberculosis globally in 2017: 5.8 million among men, 3.2 million among women and 1.0 million among children. Worldwide, TB is one of the top 10 causes of death and leading cause from single infectious agent. In 2017, TB caused an estimated 1.3 million deaths among HIV negative people and additional 0.3 million deaths from TB among HIV positive people [1].

Alkaline phosphatase (ALP) is a cell membrane derived enzyme and one of the biochemical markers found in pleural effusion. Efficacy of ADA as a marker of TPE has already been proved in previous studies. Previous studies have also used ALP either to differentiate between exudates and transudates [2-6] or to differentiate tuberculous from non-tuberculous effusion [7].

This study was thus undertaken to find out the usefulness of ALP levels in pleural fluid and serum to differentiate tuberculous from nontuberculous pleural effusion, and also to reduce the need of invasive and expensive procedures like thoracoscopy for diagnosis of undiagnosed pleural effusion.

MATERIALS AND METHODS

A prospective analytical study conducted with the aim to evaluate

1. The role of pleural fluid alkaline phosphatase in the diagnosis of tuberculous pleural effusion and
2. Pleural fluid/serum alkaline phosphatase ratio for the purpose of differentiating tuberculous from non-tuberculous pleural effusion, among 50 patients admitted in Department of Pulmonary Medicine, government chest diseases and tuberculosis hospital, and kakatiya medical college. Cases were selected on the basis of inclusion and the exclusion criteria. A brief history of presenting complaints, past medical ailments, history of previous hospitalization, personal history, drug usage and medication history, history of allergies, smoking history, other habits and addictions, general physical and systemic examination has been done on all cases. Routine examination and specific investigations when required like chest Xray/CT scan, USG chest, sputum for AFB, Pleural fluid analysis, pleural fluid ALP, Serum ALP were done. 35cases were diagnosed to have tubercular pleural effusion based on clinical examination, lights criteria, ADA levels and pleural biopsy in doubtful cases. The same Pleural fluid samples were subjected for ALP levels. Samples were centrifuged at 3000 RPM/sec for 15 minutes. Approximately 300-400 µl of supernatant was pipetted and kept in auto analyser. The reagent used here is P-nitrophenol phosphate. ALP breaks the phosphate group of reagent and the resultant compound i.e P- nitrophenol gives yellow colour with increased absorbance at 405nm. The auto analyser uses the colorimetric method to determine the ALP activity which is displayed on the computer screen at the end of 6 minutes. Clearance from institutional ethical committee was obtained.

Numerical data have been represented by Mean ± SD, and categorical data was compared and analysed between tuberculous and non-tuberculous effusion cases. The data was interpreted by means of the Pearson's Chi square test using the statistical software SPSS version 21.0. Sensitivity, specificity, area under curve, receiver operating curve and odds ratio for pleural fluid parameters were calculated.

RESULTS AND DISCUSSION

Total number of cases in present study were 50 out of which 35 (70%) were diagnosed as Tuberculous pleural effusions. Age distribution ranged from 20-80 years with a mean age of 39.06±14.68 years. Majority of the cases (70.5%) fell in the age group of 31-40 years. Majority of cases (40%) of tubercular pleural effusion fell in 21-30 age group and 33.3% of non-tubercular pleural effusion fell in 31-40 age groups [Table 1]. Majority of the cases in our study were men who constituted 34 (68%) when compared to 16 (32%) women [Table 2]. Out of them, 21 men and 14 women were diagnosed as having tuberculous pleural effusion.

Out of the total 50 cases, 35 (70%) were diagnosed with Tuberculous pleural effusion. Out of the remaining 15 cases (30%) in which, 7 were of malignant etiology and the remaining 8 constituted other etiologies like empyema, parapneumonic effusions[Table 3]. Right sided effusions constituted a total of 30 cases (60%), 22(62.9%) Out of 30, were of tuberculous etiology. 13(37.1%) out of the 20(40%) cases involving the left side were tuberculous [Table 4]. Right sided effusions constituted a total of 30 cases (60%), 22(62.9%) Out of 30, were of tuberculous etiology. 13(37.1%) out of the 20(40%) cases involving the left side were tuberculous [Table 5].

Alkaline Phosphatase levels in tuberculous effusions showed a mean of 89.74±23.14 IU/l when compared to a mean of 56.47±16.21 IU/l in non TB effusions. This difference was found to be statistically significant. Difference in the serum ALP levels between TB (120.49±21.48) and non TB (202.27±31.48) was also found to be statistically significant. The overall ratio of Pleural fluid to serum ALP was found to be 0.69±0.21 in TB effusions and 0.38±0.16 in non TB effusions. The difference in these ratios was also found to be statistically significant [Table 6].

ROC curve analysis of Pleural fluid to serum ALP ratio showed a significance level of <0.001 with an area under curve of 87.2%. A sensitivity of 83.3% and specificity of 87.5% was seen at a cut off value of 0.49 [Figure 1]. ROC curve analysis of Pleural fluid ALP showed a significance level of <0.001 with an area under curve of 87.1%. A sensitivity of 83.7% and a specificity of 69.2% was seen at a cutoff value of 75.8 U/L[Figure 2]. Based on the ROC curve analysis, a cutoff value of 75.8 U/L was chosen for pleural fluid alkaline phosphatase values. A pleural to serum ALP ratio of 0.49 was chosen as a cutoff to differentiate between tuberculous and non-tuberculous effusions. Applying these cutoff values, P/S ALP ratio showed a total of 27 out of 35 cases as having a tuberculous effusion and, ALP levels also showed the same i.e 27 out of 35 cases as having a TB effusion [Table 7].

Table-1: Age distribution

Age	Non-TB		TB		Total	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
≤ 20	0	0.0	2	5.7	2	5.7
21 – 30	1	6.7	14	40.0	15	46.7
31 – 40	5	33.3	13	37.1	18	70.5
41 – 50	1	6.7	3	8.6	4	15.2
51 – 60	4	26.7	1	2.9	5	29.5
> 60	4	26.7	2	5.7	6	32.4
Total	15	100.0	35	100.0	50	200.0

Table-2: Sex distribution

Sex	Frequency	Percent
Female	16	32.0
Male	34	68.0
Total	50	100.0

Table-3: EtiologicalCause

Etiology	Frequency	Percet
Non-TB	15	30.0
TB	35	70.0
Total	50	100.0

Table-4: Side of effusion

Side of effusion	Frequency	Percent
Left	20	40.0
Right	30	60.0
Total	50	100.0

Table-5: Frequency of side of effusion

Side of effusion	Non-TB		TB		Total	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Left	7	46.7	13	37.1	20	40
Right	8	53.3	22	62.9	30	60
Total	15	100.0	35	100.0	50	100

Table-6: Pleural fluid alkaline phosphatase

Alkaline phosphatase	TB (n=35)		Non-TB (n=15)		P-value
	Mean	SD	Mean	SD	
P ALP	89.74	23.14	56.47	16.21	<0.01*
S ALP	120.49	21.48	202.27	31.48	<0.01*
P/S	0.69	0.21	0.38	0.16	<0.01*

Table-7: Cutoff points for alkaline phosphatase

Criteria	Cut off	Non-TB		TB	
		Frequency	Percent	Frequency	Percent
P ALP	≤ 75.8	11	73.3	8	22.9
	> 75.8	4	26.7	27	77.1
P/S	≤ 0.49	11	73.3	8	22.9
	> 0.49	4	26.7	27	77.1

Table-8: Statistical indices of diagnostic criteria

	P ALP	P/S
Sensitivity	83.7%	83.3%
Specificity	69.2%	87.5%
PPV	88.6%	91.4%
NPV	60.0%	66.7%
Area under the curve	87.1%	87.2%
Cut off value	75.8	0.49

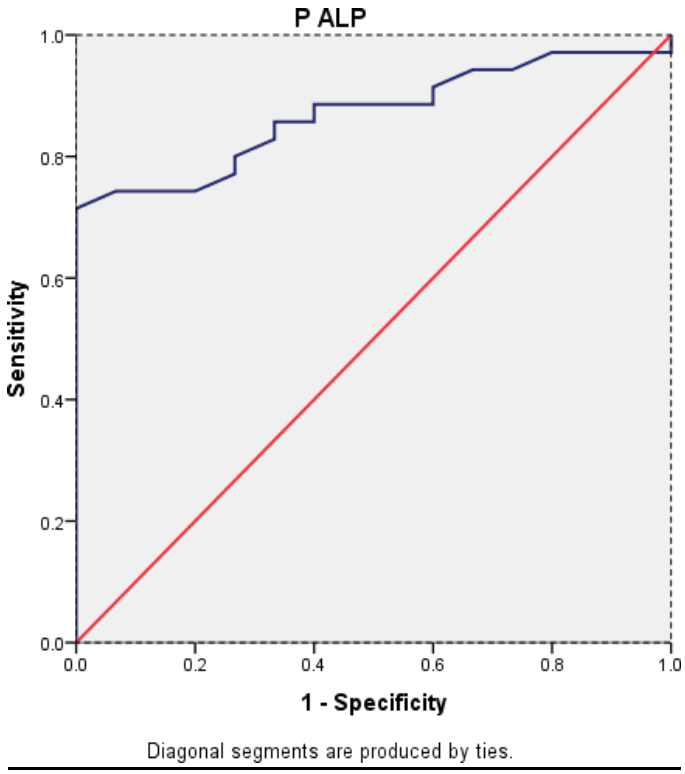

Fig-1: ROC OF P/S RATIO

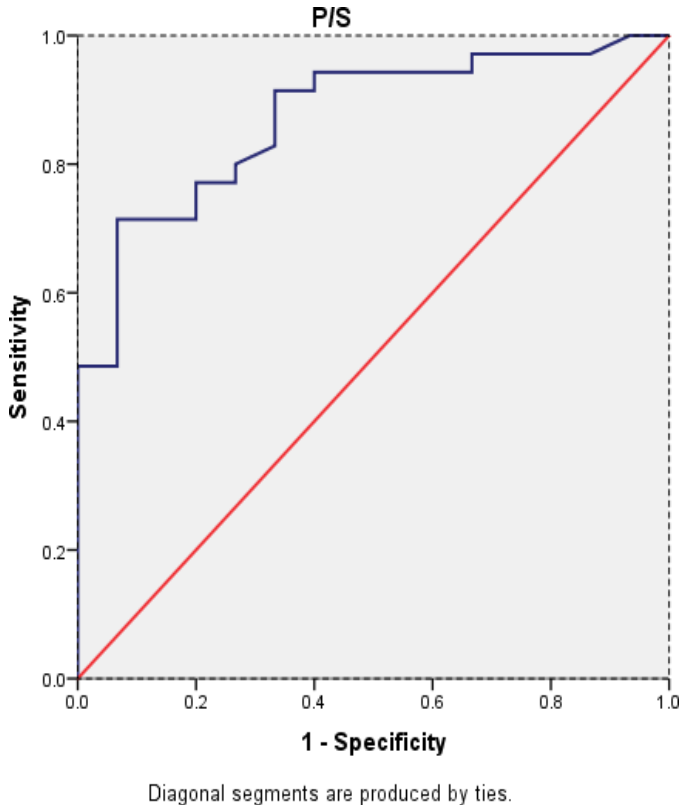

Fig-2: Roc of Pleural Fluid Alkaline Phosphatase

CONCLUSION

The results in our study suggest that integration of pleural fluid alkaline phosphatase and P/S Alkaline phosphatase ratio in clinical work up provides a more comprehensive assessment in patients with tuberculous pleural effusion and will help in reaching more accurate diagnosis. Applying the cut off values obtained from ROC curve analysis P/S ALP ratio of more than ≥0.49 had a sensitivity of 83.3%, a specificity of 87.5%, Whereas P ALP of more than

≥75.8 had a sensitivity of 83.7%, a specificity of 69.2% [Table 8]. Given that selection bias is slightly inherent in our study group, these findings should be validated in larger and more representative population.

REFERENCES

1. Global Tuberculosis report 2018. Geneva WHO, 2108. Available online http://www.who.int/tb/publications/global_report/en/
2. Kiroshka VS, Zhurzha LE, Tudos TP. A method of differentiating transudate and exudate. Problemy tuberkuleza. 1990(8):62-3.
3. Tahaoglu K, Kizkin Ö, El R. Alkaline phosphatase: distinguishing between pleural exudates and transudates. Chest. 1994 Jun 1;105(6):1912-3.
4. Metintaş M, Alataş Ö, Alataş F, Çolak Ö, Özdemir N, Erginel S. Comparative analysis of biochemical parameters for differentiation of pleural exudates from transudates: Light's criteria, cholesterol, bilirubin, albumin gradient, alkaline phosphatase, creatine kinase, and uric acid. Clinica Chimica Acta. 1997 Aug 29;264(2):149-62.
5. Gazquez I, Porcel JM, Vives M, de Vera MV, Rudio M. Pleural alkaline phosphatase in seperation of transudative and exudative pleural effusions. Chest. 1997 Aug 1;112(2):569.
6. Lone MA, Wahid A, Saleem SM, Koul P, Dhobi GN, Shahnawaz A. Alkaline phosphatase in pleural effusions. Indian journal of chest diseases and allied sciences. 2003 Jul 18;45(3):161-4.
7. Syabbalo NC. Use of pleural alkaline phosphatase content to diagnose tuberculous effusions. Chest. 1991 Feb 1;99(2):522-4.