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EFFICACY OF C-REACTIVE PROTEIN (CRP) LEVELS IN ETIOLOGIC DIAGNOSIS OF PLEURAL EFFUSION

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ABSTRACT

Objective: The diagnosis of tubercular pleural effusion is difficult as tubercle bacilli are rarely found from thoracocentesis and pleural lavage and other noninvasive traditional tools of diagnosis have low sensitivity and specificity. CRP levels have been found to be higher in exudates when compare to transudates. It is therefore worthwhile to study the value of C-reactive protein in diagnosis of transudative and exudative pleural effusion. **Methods:** Study was carried out at Government Medical College Kannouj during December 2013 to August 2014 which comprised of fifty two patients of pleural effusion. **Results:** In this study, 38 were male and 14 were female pleural effusion was studied in which 46.15% cases of tubercular pleural effusion were present. Pleural fluid C-reactive protein maximally raised in exudative pleural effusion i.e. 3.54 + 2.14 mg/dl and transudative pleural effusion pleural fluid C - reactive protein was 0.80 + 0.42 mg/dl. **Conclusion:** Tubercular pleural effusion had high CRP levels when compare to transudative and malignant pleural effusions.

Key words: TB Pleural Effusion, C-reactive protein, biochemical marker, transudative and exudative pleural effusion

INTRODUCTION

Pleural effusion is the abnormal accumulation of fluid in the pleural space and it is a common problem in clinical practice which is always abnormal and indicates the presence of an underlying disease. The leading causes of pleural effusion are bacterial pneumonia, cirrhosis, malignancy, left ventricular failure, viral infections and pulmonary embolism. **(1, 2)** However, Tubercular pleurisy is the major cause of pleural effusion in India (3). Analysis of pleural fluid (PF) is an important tool in correctly diagnosing the etiology of pleural effusion. Conservative methods of diagnosis may not be able to ascertain the cause of pleural effusion or give an early diagnosis. The diagnosis of tubercular pleural effusion is difficult as tubercle bacilli are rarely found from thoracocentesis and pleural lavage and other noninvasive traditional tools of diagnosis have low sensitivity and specificity.**(4)**

Adenosine deaminase (ADA), an enzyme of purine salvage and catabolic pathway, is involved in the proliferation and differentiation of T lymphocytes. Tubercular pleurisy is a result of delayed hypersensitivity reaction in response to mycobacterium antigen. Measurement of

ADA in pleural fluid has been widely used in the differential diagnosis of lymphocytic exudative pleural effusion as high values have been found in tubercular pleural effusion.**(5)**

C-reactive protein (CRP) is an acute phase protein synthesized by hepatocytes and used as marker of inflammation and tissue injury. **(6)** CRP is contemplation to help out in complement binding to foreign and damaged cells and enhance the phagocytosis by macrophages. It plays an important role in innate immunity against infection. **(7)** In many studies, CRP levels have been found to be higher in exudates when analysed with to transudates. In exudates higher levels have been found in parapneumonic pleural effusions and tubercular pleural effusion.**(8,9)** It is therefore worthwhile to study the value of C-reactive protein in diagnosis of transudative and exudative pleural effusion. Here Exudative pleural effusion means tubercular, malignant and parapneumonic cause.

MATERIAL AND METHODS

This study was carried out in patients admitted in ward and outdoor clinics of Government Medical College, Kannouj during December 2013 to August 2014 which comprised of fifty two patients of pleural effusion those patients that age more than 14 years and had Clinical and Radiological evidence of Pleural Effusion. Present study excluded that patient who's had age more than 65 years, not given consent and pleural effusion due to trauma. Study also collected the detailed history, thorough physical examination, radiological findings, haematological, biochemical and plural aspiration findings. Macroscopic findings, cytological, microbiological and biochemical analysis of pleural fluid were performed in all patients including C-reactive protein levels. To differentiate transudate from exudate, the ratio of pleural fluid and serum protein; the ratio of pleural fluid and serum LDH were calculated. Pleural fluid Adenosine deaminase level was measured by Giusti and Galanti method and C-reactive protein in pleural fluid were measured by immune-turbidimetric method by using kit.

After a detailed history, clinical examination and investigations, the 52 cases of pleural effusion were divided into 4 groups in which Group 1 had 24 cases of Tubercular pleural effusion, Group 2 had 13 cases of Transudative pleural effusion, 8 cases of malignant pleural effusion in Group 3 and 7 cases of Parapneumonicpleural effusion in Group 4.

RESULTS

In this study, 38 were male and 14 were female pleural effusion were studied in which 24 cases (46.15%) of tubercular pleural effusion, 13 cases (25%) of transudative pleural effusion, 8 cases (15.38%) of malignant pleural effusion and 7 cases (13.46%) of parapneumonic pleural effusion were present. Figure 2 showed that pleural effusion were more common in male than female and Tubercular pleural effusion was also more common in male than female.

In our study pleural effusion were more common in age group of 26 – 35 years of age (28.84%) and in 36 – 45 years age group (21.15%) and in age group of 46 – 55 were 19.23% .Thus maximum preponderance of pleural effusion occurred in 26 – 55 years of age group. Pleural effusion was more common in age group of 26-55 years. (Table 1)

TABLE –1: AGE AND SEX DISTIRBUTION OF PLEURAL EFFUSION

Age (yrs)	No. of cases		Percentage
	Male	Female	
15-25	8	3	21.15
26-35	10	5	28.84
36-45	9	2	21.15
46-55	8	2	19.23
56-65	3	2	9.61
Total	38	14	100

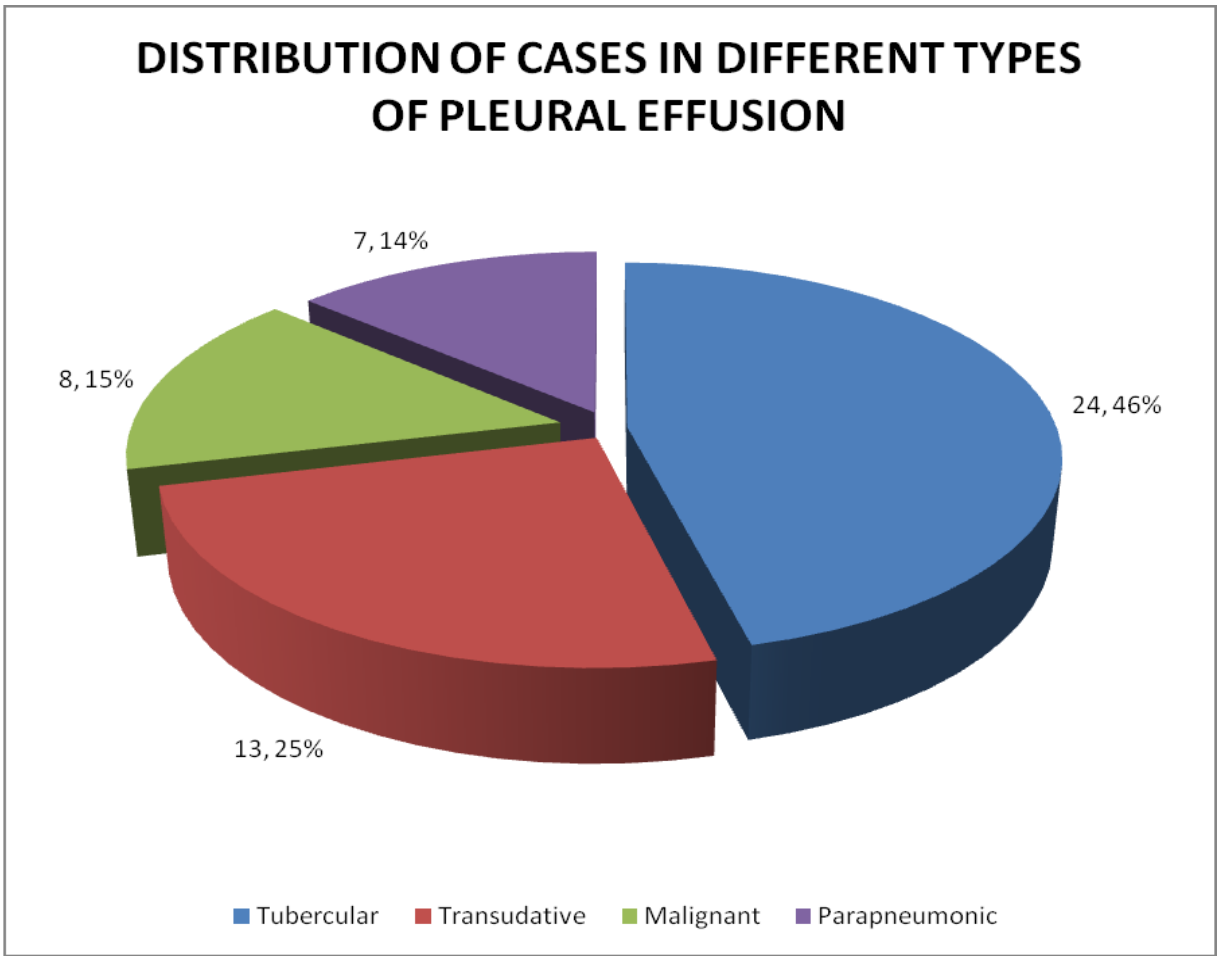

Figure 1: distribution of cases in different types of pleural effusion

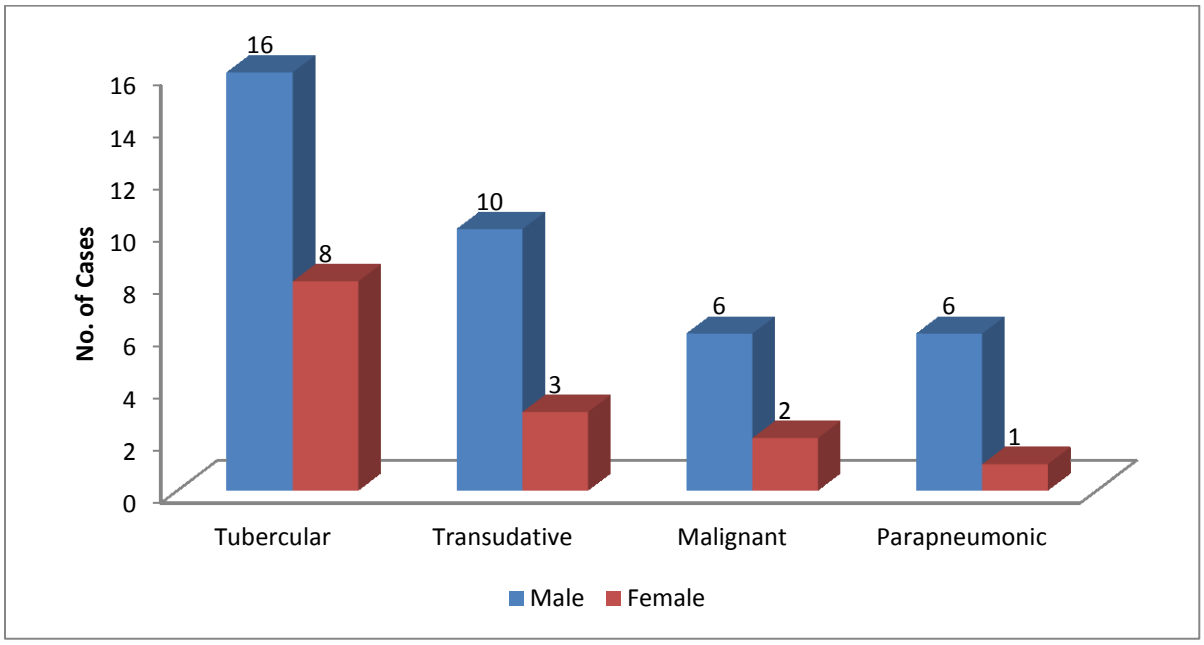

FIGURE 2: **Sex distribution of pleural effusion**

TABLE – 2 : Pleura effusion Hb, Total Count and ESR

Type of Effusion	Hb (gram %) Mean ± SD	Total Count	ESR
Tubercular	9.61 ± 0.817	7800 ± 900	68 ± 13.09
Transudative	8.61 ± 1.49	7000 ± 1500	15.7 ± 5.68
Malignant	8.41 ± 0.95	8000 ± 1300	45 ± 13.16
PPE	11.76 ± 0.97	12500 ± 1500	41.6 ± 10.8

The patients of tubercular of pleural effusion had Hb% (mean ± S.D.) = 9.61 ± 0.817. Transudative pleural effusion patients had Hb (8.61 ± 1.49) gm%, malignant pleural effusion patients had Hb (8.41 ± 0.95) gm%, Parapenumonic pleural effusion had Hb (11.76 ± 0.97) gm%. Thus patients of parapneumonic pleural effusion had higher haemoglobin. Patients with parapneumonic pleural effusion had higher total leucocyte count. (12,500 ± 1500). Patients with tubercular pleural effusion had higher Erythrocyte sedimentation rate (ESR) (68.00 ± 13.09).(Table 2)

In current study, parapneumonic pleural effusion patients had higher pleural fluid protein (5.1 ± 0.79) gm% followed by tubercular pleural effusion (4.9 ± 0.92) gm% pleural fluid protein. Patients with malignant pleural effusion had lowest pleural fluid sugar level (44.3 ± 11.26) mg% followed by parapneumonic pleural effusion that had (48.0 ± 7.83) mg%. Patients with malignant pleural effusion had highest LDH level i.e. (253 ± 139.7) U/L and lowest in transudative pleural effusion i.e. (85.5 ± 27.9) U/L. (Table 3)

TABLE – 3: PLEURAL FLUID PROTEIN, SUGAR AND LDH LEVEL

Type of Pleural effusion	Protein (gm%) Mean ± SD	Sugar (mg%) Mean ± SD	LDH (U/L) Mean ± SD
Tubercular	4.9 ± 0.92	59.1 ± 11.24	139 ± 51.6
Transudative	2.1 ± 0.39	67.8 ± 13.41	85.5± 27.9
Malignant	4.7 ± 0.41	44.3 ± 11.26	253.5 ± 139.7
PPE	5.1 ± 0.79	48.0 ± 7.83	180 ± 78.2

TABLE – 4 : PLEURAL FLUID C REACTIVE PROTEIN LEVEL

Type of Pleural effusion	C-reactive protein (mg/dl) Mean ± SD	'p' value
Tubercular	3.21 ± 0.81	0.001
Transudative	0.80 ± 0.42	0.001
Malignant	1.21 ± 1.05	0.001
PPE	7.32 ± 0.98	0.001

In our study parapneumonic pleural effusion patients had 7.32 ± 0.98 mg/dl. C- reactive protein in pleural fluid followed by tubercular pleural effusion patients who had C- reactive protein 3.21 + 0.81 mg/dl. Thus C - reactive protein in pleural fluid was maximally raised in parapneumonic pleural effusion followed by tubercular pleural effusion. Malignant pleural effusion patients had 1.21 ± 1.05 mg/dl C - reactive protein in pleural fluid. Transudative pleural effusion patients had 0.80 + 0.42 mg/dl C - reactive protein in pleural fluid.(Table 4)

In present study, pleural fluid C-reactive protein maximally raised in exudative pleural effusion i.e. 3.54 ± 2.14 mg/dl and transudative pleural effusion pleural fluid C - reactive protein was 0.80 ± 0.42 mg/dl.

DISCUSSION

Pleural effusion occur secondary to either systemic causes or disease of pleura. Conventional non-invasive diagnostic methods are not always accurate in establishing the diagnosis of pleural effusion. Analysis of pleural fluid yields significant information in early differential diagnosis of pleural effusion. Standard workup analysis of pleural fluid includes differentiating whether pleural fluid is transudative or exudative. For many years the most accepted criteria for discriminating transudative from exudative pleural effusion is **Light's criteria**. However Light's criteria may differentiate certain transudative effusion as exudative effusion.**(10)**

The most important cause of transudative pleural effusion is cardiac failure. TB is the leading cause of preventable morbidity and mortality from an infective agent and tubercular effusion is important treatable cause of exudative pleural effusion. Other common etiological causes of exudative effusions are pleural effusions, malignancy, parapneumonic fungal infections, connective tissue disorders, etc. Various biological markers have been investigated in the diagnosis of pleural effusion. Among these pleural fluids CRP, ADA, cytokines, interferon γ, tumour markers, interleukins, vascular endothelial growth factor have been found to be of value in the differential diagnosis of pleural effusion.**(11)** Nevertheless many of these

markers have some degree of value, either because of low specificity & or sensitivity along with high cost value.

The diagnosis of tubercular pleural effusion is difficult because of low specificity and sensitivity of various non-invasive procedures which are commonly used in Indian context are acid fast bacilli staining, culture of pleural tap and tuberculin skin testing. Diagnosis increases to 96.2% with pleural biopsy but the disadvantage of its invasiveness.

In our study a patient diagnosed as mesothelioma had CRP level was 0.8mg%. While **E Garcia Pachon et al**, study report showed that a patient with mesothelioma had elevated CRP level was 8.9mg/L.**(12)**

C - reactive protein is another sensitive marker in distinguishing the diagnosis of pleural effusion. It is widely used as a maker of inflammation and tissue injury. CRP levels have been found higher in benign than malignant pleural effusion. High pleural fluid CRP levels have been reported in tubercular pleural effusion and parapneumonic pleural effusion.**(13)**

In our study CRP levels were lowest in transudative effusion when report anlysed with exudative effusion which was highly significant ($p<0.001$). A elevated level was seen in inflammatory pleural effusion (tubercular effusion and PPE) when report anlysed with non inflammatory effusion (transudative and malignant effusion) ($p<0.001$). Tubercular pleural effusion had high CRP levels when report anlysed with transudative and malignant pleural effusions which were highly significant ($p<0.001$). But the highest values were found in PPE ($p<0.001$) which was highly significant when report with transudative effusion, tubercular effusion and malignant effusion ($p<0.001$).

Yilmaz UT et al, reported in their study that high levels of CRP in exudates when report anlysed with transudates and elevated levels in parapneumonic pleural effusions when report anlysed with other types of exudative pleural effusions and also reported high sensitivity (93.7%), specificity (76.5%) and PPV of 98.4% at a cutoff value of 30mg/L.(**9**) A similar report was also reported by **Castano- Vidrialesa JL et al**, and they reported good sensitivity (82%), specificity (87.5%) and PPV (95.5%) in diagnosis of exudative pleural effusion.(**8**)

Daniil ZD et al, high level of multiple biomarkers in discerning pleural effusion (**14**). They concluded the combination of ADA and CRP levels might be sufficient in discriminating the three different groups of pleural effusion, tubercular, malignant and PPE which were same as our study.

CONCLUSION

Current study showed that C - reactive protein is important biomarker in discriminating pleural effusion. CRP levels were lowest in transudative effusion when analysed with to exudative effusion which was highly significant ($p<0.001$). Tubercular pleural effusion had high CRP levels when analysed with transudative and malignant pleural effusions.

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REFERENCES

1. Hassan T, Al-Alawi M, Chotirmall SH, McElvaney NG. Pleural fluid analysis: Stand still or awork in progress? Pulmonary medicine 2012; 2012:10-20.
2. Light RW. Disorders of Pleura and Mediastinum. Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J. Harrison's Principles of Internal Medicine 18th ed. McGraw-Hill. Medical publishing division USA; 2012: 2178-80.
3. Motoki S, Kimihiko M, Akira H, Yuzo S, Hikotaro K. Pleural effusion adenosine deaminase(ADA) level and occult tuberculous pleurisy. Ann Thoraccardiovascsurg 2009; 15(5):294-6.
4. Bharth KG, Vinay B,Debapriya B. Role of Adenosine deaminase estimation in differentiation of tuberculous and non-tuberculous exudative pleural effusions. J Clin Mede Res 2010; 2(2): 79-84.
5. Arun G, Sethu MM, Surendra KS, Steven AS. Diagnosis and treatment of tuberculous pleural effusion in 2006. Chest 2007; 131(3): 880-9.
6. Rafael LL. Adenosine deaminase in the diagnosis of tuberculous pleural effusion: Is it really an ideal test? A word of caution. Chest 2005; 127(2): 417-18.
7. Hoda- Abu-Yousef, Sherif A, Hassan A, Essam O. Value of C-reactive protein in etiologic diagnosis of pleural effusion. Egyptian Journal of bronchology 2010; 4(2): 124-30.
8. Castano VJL, Amores AC. Use of pleural fluid C-Reactive protein in laboratory diagnosis of pleural effusions. Eur J Med 1992; 1(4): 201-7.
9. Yilmaz T, Yildrim Z, Turkoz Y, Biber C, Erdogan Y, Keyf AI, et al. Use of pleural fluid Creactiveprotein in diagnosis of pleural effusions. Respir Med 2000; 94(5): 432-5.
10. LightRW, MacGregor MI, Luchsinger PC, et al. Pleural effusions: the diagnostic separation of transudates and exudates Ann Intern Med 1972; 77:507-513.
11. Emmet E. McGrath,and Paul B. Anderson. Diagnosis of Pleural Effusion: A Systematic Approach.Am J Crit Care March 2011 vol. 20 no. 2 119-128
12. Garcia EP, Pallida IN, Shum C. Mesothelioma, adenosine deaminase and C-reactive protein. Arch Bronconeumol 2005; 41(3): 175.
13. Yilmaz Turay U, Yildirim Z, Türköz Y, Biber C, Erdoğan Y, Keyf AI, Uğurman F, Ayaz A, Ergün P, Harputluoğlu M.Use of pleural fluid C-reactive protein in diagnosis of pleural effusions. 10. Respir Med. 2000 May;94(5):432-5.
14. Daniil ZD, Zintzaras E, Kiropoulas T, Papaioannou AI, Koustsokera A, Kastanis A, et al.Discrimination of exudative pleural effusions based on multiple biological parameters. EurRespir J 2007; 30(5): 957-64.