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Abstract

Background: Nearly one third of the global population i.e. two billion people are infected with mycobacteria tuberculosis and are at risk of developing the disease. Pleural effusion is one of the common complications of pulmonary tuberculosis. In this study, the clinical features, the positivity rate of microbiological procedures and blind pleural biopsies, radiological manifestations, biochemical and hematological profiles of serum and pleural fluid were analyzed.

Objectives: To report our experience of 108 patients with tuberculous pleural effusion and discuss the clinical features, radiological findings, biochemical, cytological and microbiological analysis of pleural fluid, hematological and biochemical profiles of serum and positivity rate of microbiological procedures and blind pleural biopsies in these patients.

Methods: This study was a hospital based descriptive cross sectional study performed at Chest Medical Ward, Yangon General Hospital, Myanmar, of study period from January 2004 through January 2005. A total of 108 patients were included. Thorough history taking and physical examinations, radiological findings, hematological and serum biochemical profiles were recorded. Pleural aspiration and biopsy were also performed. At least two pieces of pleural tissue were taken and one piece of each sample of pleural tissue was cultured for mycobacteria and the rest was sent for histological examination. Macroscopic findings, cytological, microbiological and biochemical analysis of pleural fluid were analyzed.

Results: A total of 108 patients, 74 males and 34 females were included. Their mean age was 42.60 ± 16.34 (range 12-81 years). Common presentations were breathlessness (82.4%), cough (81.5%), fever (80.6%), and night sweat (78.7%), loss of appetite (74.1%), significant weight loss (72.2%) and chest pain (67.6%). Only 39.3% of TB patients produced sputum in their history. Haemoptysis was present in only 7.4% of the patients. Regarding the physical signs, 53.7% of them had fever during admission, 15.7% were cachexic, cervical lymph nodes were palpable in 14.8% and had clubbing of fingers in 5.6%. They also had respiratory physical signs other than pleural effusion which include crepitation (31.5 %), collapse (15.7

%), pleural rub (13.0 %) and signs of consolidation (11.1 %). Only one patient (0.9%) had positive AFB smear in pleural fluid. Culture of pleural effusion and pleural biopsy reports for AFB were positive in 5.6% and 1.9% respectively. 91 patients (84.3 %) were diagnosed on first biopsy procedure and 15 (13.8%) and 2 (1.9 %) of patients needed second and third session of procedures respectively. Only 2 patients (1.9%) had bilateral pleural involvement. Associated radiological pulmonary parenchymal lesions were noted in 28 patients (25.9 %). 7 patients revealed blood stained pleural fluid (6.48%). The rest had straw color aspirates. Mean Pleural fluid and serum protein ratio was 0.69 ± 0.17. Pleural fluid LDH was high in most cases with a mean ± SD was 726.24 ± 383.64. Serum LDH also was high (507.39 ± 170.76). The mean ratio of pleural fluid and serum LDH was 1.56 ± 1.16. The main WBC subset was lymphocytes (mean 91.96% of total WBC population) and polymorph was detected only 6.86 ± 15.88 % (mean ± SD). Total and differential white cell counts of peripheral blood film were within normal limits. Mean ESR was high 77.4 mm/1st hour.

Conclusion: Analysis of pleural fluid can have an important contribution for investigation of patients with pleural effusion. Although highly specific, percentage positivity of microbiological examinations on pleural fluid does not reach the degree required for a single diagnostic investigation for tuberculosis. The Light's criteria are fulfilled in all cases. Pleural biopsy will be useful as an ultimate procedure in cases with diagnostic problem as it is a procedure which can give a definitive tissue diagnosis.

Key Words: Tuberculosis, Pleural effusion, Pleural biopsy, Light's criteria

Introduction

Nearly one third of the global population i.e. two billion people are infected with Mycobacteria tuberculosis and at risk of developing the disease. More than eight million people develop active TB and about two million die every year. More than 90% of global TB cases and deaths occur in the developing world mainly Asia and Africa.

In Myanmar(Formerly Burma), it is one of the major public health problems and recent estimates suggest that 1.66% of the population become infected with tuberculosis every year, out of which about 80000 people progress to develop tuberculosis. According to the "Annual Hospital Statistical Report, Ministry of Health", it is the 8th single leading cause of morbidity by trend, 1998 - 2003 and the 2nd single leading cause of mortality by sex treated in hospitals, 2003 (Ministry of Health, 2003).

Tuberculosis is a disease with protean manifestations. The clinical presentation of TB can mimic several diseases and can be a diagnostic problem even in endemic areas. Virulence and load of the infecting mycobacterium, the immune status of the host, the organ system involved, all influences the clinical manifestations of tuberculosis. Pleural effusion is one of the common complications of primary tuberculosis or in conjunction with pulmonary infiltrate typical of post primary tuberculosis (Seibert, Haynes, Middleton, & Bass, 1991). Ferrer JS et al (1996) pointed out that 28.7% of pleural effusions (113 patients out of 394 patients) are due to tuberculosis among Spanish patients.

The inner surface of the chest wall and the surface of the lungs are covered by the parietal and visceral pleural, respectively, with a potential space of 10-24 μm between the 2 pleural surfaces. This space is normally filled with approximately 1 ml of fluid, representing the balance between (1) hydrostatic and oncotic forces in the visceral and parietal pleural vessels and (2) extensive lymphatic drainage. Pleural effusions result from disruption of this balance. Large amounts of fluid can accumulate in the pleural space under pathologic conditions. The parietal pleura have sensory innervation and small apertures that aid in the absorption of particles and fluid.

The diagnosis of tuberculosis pleural effusion (TPE) can be difficult to make because of the low positivity of the various diagnostic tests. Lymphocytic exudates seen in TB pleural effusion also can occur in other disease such as malignancy, collagen vascular disease and lymphoma. A definitive diagnosis of TPE requires the presence of granulomas in pleural tissue or a stained AFB or positive culture from the pleural tissue or pleural fluid.

The physical signs of the presence of pleural effusions may identify patients who require further diagnostic procedures. A met analysis addressed the diagnostic accuracy of the physical examination for pleural effusion using CXR or computed tomography (CT) scan as the reference standard (Wong, Holroyd-Leduc, & Straus, 2009). To achieve this objective, the authors identified 310 potential studies, totaling 934 patients, met the inclusion criteria. Of the 8 physical examination maneuvers evaluated in the included studies, the presence of dullness to conventional percussion (summary positive likelihood ratio-LR-8.7) and asymmetric chest expansion (positive LR 8.1) argued convincingly for the diagnosis of pleural effusion. In contrast, the absence of reduce tactile vocal fremitus reduced the

probability of pleural effusion (negative LR 0.21). These signs should guide performance of the clinical examination for detecting pleural effusion (Ocak, 2010).

Many patients are asymptomatic on the discovery of a pleural effusion. Pleuritic chest pain indicates inflammation of the parietal pleura (because the visceral pleura are not innervated and thus not sensitive to pain). Other symptoms include dry, nonproductive cough and dyspnea. Constitutional symptoms are almost always present. Physical examination findings that can reveal the presence of an effusion are reduced tactile fremitus, stony dull note on percussion, and diminished or absent breath sounds on auscultation. TB pleural effusion is usually unilateral and is small to moderate in size although massive effusion can also occur. Bilateral effusion is rare. The pleural fluid is exudative and lymphocyte rich.

T-cell interferon-gamma release assays (IGRAs) have emerged as attractive for the diagnosis of latent tuberculosis. One prospective study has recently compared the diagnostic performance of four different IGRAs using pleural fluid mononuclear cells with that of unstimulated IFN-γ concentrations in pleural fluid, in 63 patients from a high TB/HIV burden setting (Dheda et al., 2009). All IGRAs, performed poorly because, at best, they missed 15% of TB cases and incorrectly diagnosed a further 20%. In contrast, unstimulated IFN-γ levels >0.31 IU/mL had 97% sensitivity and 100% specifi city for identifying TB pleuritis. Currently, there is little convincing evidence to support the use of IGRAs against other available markers of TB such as IFN-γ or adenosine deaminase (Ocak, 2010).

Few studies have examined the role of positron-emission tomography (using 18-fl uorodeoxyglucose) combined with CT (PET-CT) in the investigation of pleural diseases. In one series, 83 patients with undiagnosed effusions and/or pleural thickening after routine clinical investigations (including blind pleural biopsy) underwent a PET-CT scan before a thoracoscopic or open surgical biopsy (Orki et al., 2009). The final histopathological diagnoses were malignant disease in 44 patients (including 25 mesotheliomas) and benign pleural conditions in the remaining 39 patients (30 chronic pleuritis and 9 tuberculosis). The operating characteristics of PET-CT for identifying malignant pleurisy were: sensitivity 100%, specificity 94%, positive LR 19.5 and negative LR 0.01.

Evaluation of exudative pleural effusion usually includes thorough history, complete clinical examination, appropriate blood tests, radiographs, studies of pleural fluid and needle biopsy of pleura using Abram's pleural biopsy needle or Cope's biopsy needle. However following these procedures some patients still have undiagnosed condition and the clinical management of these cases is controversial. The initial step of the investigation is the distinction between transudates and exudates, as this gives an indication of the pathophysiologic mechanisms, the differential diagnosis and the need for further investigations.

Because of their high sensitivity in identifying exudates, the criteria proposed by Light et al (1972) have become the standard method for making the distinction. The classic work of Light and colleagues demonstrated that 99% of pleural effusions could be classified into two general categories: transudative or exudative .A basic difference is that transudates, in general, reflect a systemic perturbation, whereas exudates usually signify underlying local (pleuropulmonary) disease. The 'Light' criteria include a pleural fluid to serum protein ratio greater than 0.5, a pleural fluid to serum LDH ratio greater than 0.6 and a pleural LDH

concentration more than two thirds normal upper limit for serum. If any one of these critical values is exceeded, the effusion is exudates. The original study of Light and colleagues had a diagnostic sensitivity of 99% and specificity of 98% for exudates.

In this study we report our experience with 108 patients with confirmed diagnosis of TPE and discuss the clinical features, radiological findings, biochemical, cytological and microbiological analysis of pleural fluid, hematological and biochemical profiles of serum and positivity rates of microbiological procedure and blind pleural biopsy in these patients. We also analyzed the likelihood ratios of some of the important presenting features in this study.

Patients and methods

Patients: This study was a hospital based descriptive cross sectional study performed at the Department of Respiratory Medicine, Rangoon General Hospital (RGH), Myanmar (Formerly Burma) from January 2004 through January 2005. We did not perform any sampling procedure. All patients with pleural effusion, having positive AFB in pleural fluid (smear or culture) or positive histology of tuberculosis in pleural biopsy were included except those with following exclusion criteria.

Exclusion criteria

1. Renal insufficiency and/or liver insufficiency: Patients may present faulty high values of pleural fluid Adenosine deaminase level.

2. Multiple pathology of pleural effusion: Patients with more than one etiology of pleural effusion.

3. Patient's refusal

Written informed consent was obtained from patient. Before requesting consent, the individual was explained in an understandable language about the aims of the study, the methods of conduct, expected duration of subject participation, benefits, foreseeable rights or discomfort, the extent of confidentiality, extent of investigators responsibility, provision of medical services, the right to refuse to participate and withdraw from the study without affecting further medical care.

Detailed history, thorough physical examination, radiological findings, haematological and biochemical findings were recorded in the proforma. Pleural aspiration and biopsy was performed on all patients after obtaining the written consent. At least two pieces of pleural tissue were taken and one piece of each sample of pleural tissue was cultured for mycobacteria and the rest was sent for histological examination. Macroscopic findings, cytological, microbiological and biochemical analysis of pleural fluid were performed in all patients.

History taking: Patients name, age, sex, race, ID number, marital status, occupation, body weight, address, date of admission and discharge were recorded. Symptoms such as the history of fever, cough, sputum, haemoptysis, dyspnoea, chest pain, weight loss, loss of appetite and night sweats were recorded and analyzed. The past history of TB, TB contact, diabetes mellitus, hypertension and frequent chest infection were also enquired. Personal and social history such as history of drinking, smoking and income were recorded. Family history also was noted.

Physical examinations: Patient's general conditions such as cachexia, body weight, breathlessness, and fever were noted. Physical signs such as cervical or scalene lymph node enlargement, clubbing, erythema nodosum, phlyctanugular conjunctivitis, SVC obstruction were also recorded. Thorough respiratory system examination was done to find out features of collapse, consolidation and pleural effusion.

Radiological examinations: CXR (PA) view was taken in every patient and lateral view was taken, if necessary. The amount of fluid, the side involved, hilar and/or mediastinum lymphadenopathy, parenchymal involvement, cavitation and any other radiographic abnormalities were noted.

Serum haematological profiles: Full blood count and ESR were done in every patient.

Serum biochemical profiles: Plasma total and differential protein and LDH were taken in every patient to calculate the ratio fulfilling 'light' criteria.

Pleural fluid aspiration

Macroscopic appearance of pleural fluid: Macroscopic appearance of pleural aspirates was recorded.

Cytology, cell types and cell counts: Differential white cell counts of pleural fluid were recorded and calculated as percentage. The actual number of cells was not counted.

Microbiology of pleural fluid: Ziehl-Neelsen staining and AFB culture were done. AFB culture was performed on Lowenstein Jensen medium in all patients. Gram stain, aerobic and an aerobic culture of pleural fluid were performed only on patients suspected of pneumonia.

Biochemistry of pleural fluid: Determination of pleural fluid total protein concentration (g/l), LDH(U/L), total cholesterol (mmol/l) and sugar (mmol/l) were performed . 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 measures by Giusti and Galanti method.

Pleural biopsy: All patients were subjected to thoracentesis and closed pleural biopsy using Abram's needle after obtaining a written consent. At least two samples were taken, one was

sent for histological examination the other was for tissue AFB culture. If no definite tissue diagnosis was obtained after 3rd pleural biopsy, he or she was classified as undiagnosed and excluded from the study unless pleural fluid AFB was detected. Biopsy procedure was usually done at 8th or 9th ICS at posterior axillary line.

Statistical Analysis: All the background clinical data were recorded in standardized proforma. Record files were constructed in the Microsoft Excel software. The final data file in the form of record file in Microsoft Excel was exported as data base file and it was opened in the SPSS 16.0 for Windows software. Descriptive statistics including mean with SD, median, minimum and maximum values were calculated. Correlations of regression Coefficients (finding of r value) and P- value were calculated among pleural fluid biochemical finding were tabulated. The correlation matrix of multiple regressions among independent variables of pleural fluid all TB patients were created as multiple small scattered diagrams with regression line.

Results

A total of 108 patients, 74 males and 34 females were included in this research. Their mean age was 42.60 ± 16.34 (range 12-81 years). The commonest one was age between thirty one and forty.

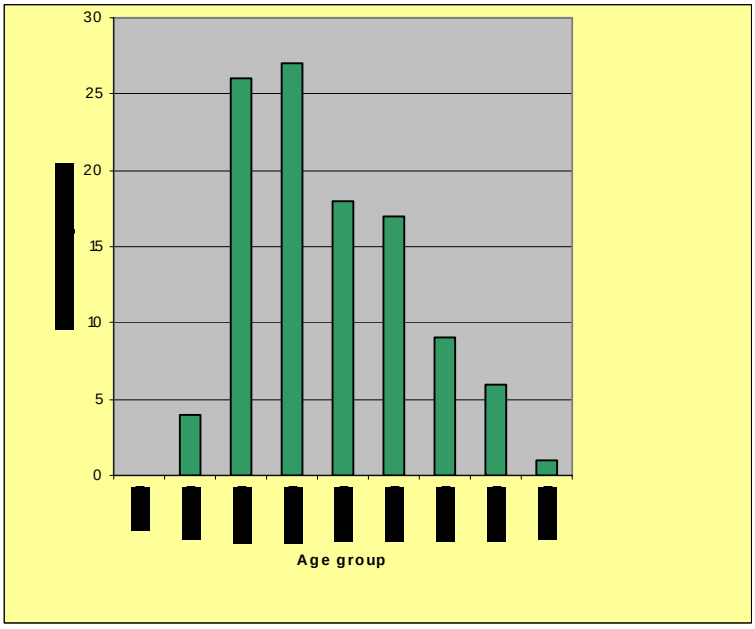

Figure 1: Patients' distribution by age group in tuberculous pleural effusion

The positivity of microbiological procedures is shown in table 1.

Table 1: Percentage positivity of microbiological procedures among 108 patients

	Procedure	N	%
1	ZN Stain of pleural fluid	1	0.93
2	Culture of pleural fluid in LJ medium	6	5.65
3	Culture of biopsy tissue in LJ medium	2	1.86

All patients had positive histology of granulomas in pleural biopsy tissue examination. Ninety one patients (84.3 %) of TPE were diagnosed as TB by histology on first biopsy procedure. Fifteen (13.8) and two (1.9 %) of patients needed second and third session of procedures respectively.

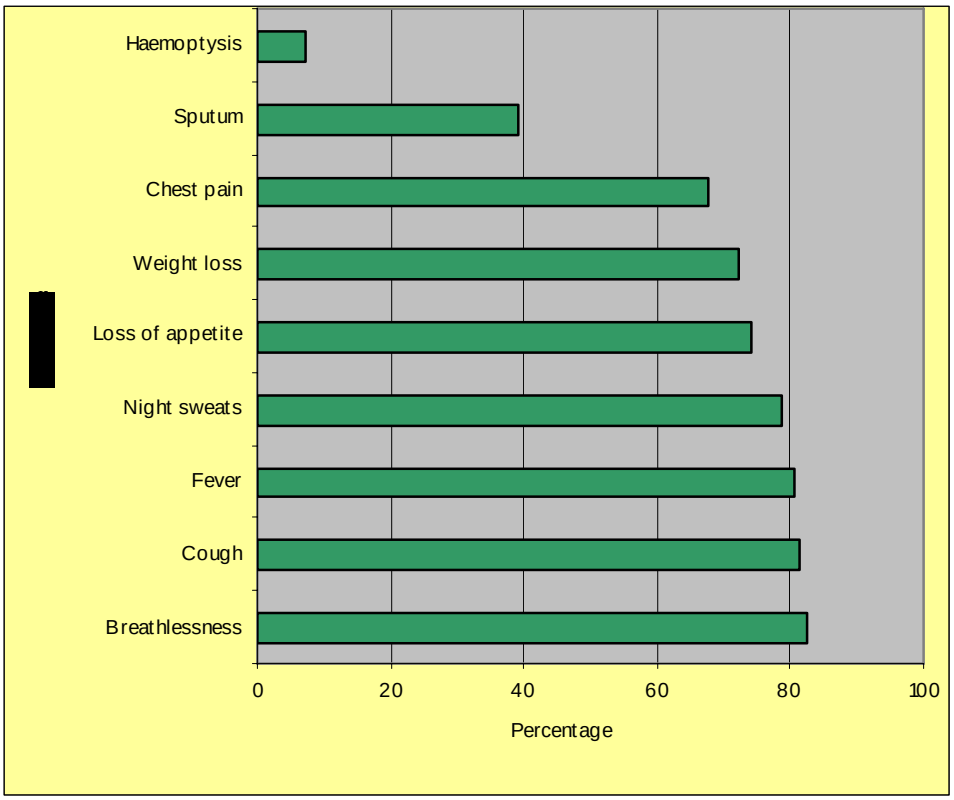

Figure 2: Percentage of patients with various symptoms

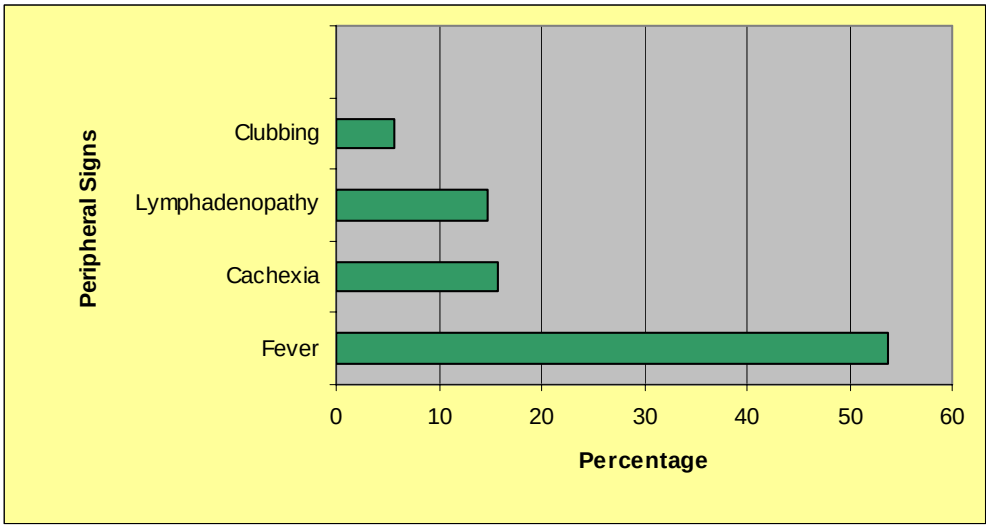

Figure 3: Percentage of patients with peripheral physical signs

Figure 2 and 3 and 4 show the clinical symptoms and signs of patients with TPE. Haemoptysis was present in only 7.4% and all had associated pulmonary parenchymal lesions on CXR.

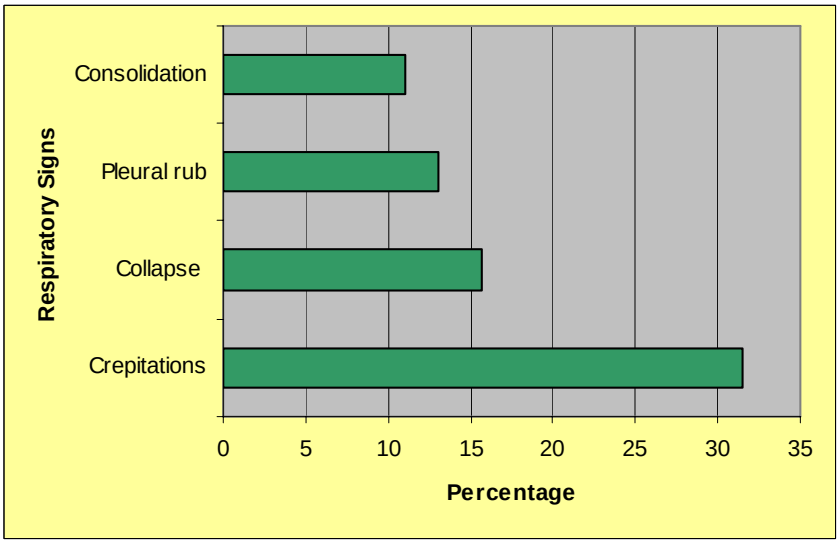

Figure 4: Percentage of patients with additional respiratory physical signs of TPE (other than signs of pleural effusion)

Table 2 shows sides of chest involved in patients with TB pleural effusion.

Table 2: Side of chest involved in patients with TB pleural effusion

Side	**Frequency**	**Percent**
Right side	63	58.3
Left side	43	39.8
Both side	2	1.9
Total	108	100

Associated radiological pulmonary parenchymal lesions were noted in twenty eight patients (25.9 %). Out of 108 patients with TPE, seven patients revealed blood stained pleural fluid (6.48%). The rest had straw color aspirates.

Table 4 shows the biochemical and hematological profiles of serum and pleural fluid in all patients.

Besides, Table 5 and figure 6 represent the correlation among independent biochemical variables. Linear correlation is noted between age and pleural fluid glucose level (P=.01), pleural fluid protein and serum protein (P=.005), pleural fluid LDH and serum LDH (P=.000) and pleural fluid glucose and pleural fluid cholesterol (P.002).There are no associations among other biochemical profiles of TPE.

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Table 4: Biochemical and hematological levels of serum and pleural fluid in patients with tuberculous pleural effusion

VARIABLES (unit)	**Valid No. of patients 'n'**	**Mean**	**Median**	**Minimum**	**Maximum**	**Standard deviaton**
AGE (years)	108	42.6019	39.5000	12.0000	81.000	16.3427
BIOCHEMICAL LEVELS						
Pleural fluid ADA(U/L)	108	73.9074	64.0000	22.0000	186.000	33.9567
Pleural fluid (PF) Protein (g/L)	108	49.1481	45.5000	24.0000	100.000	12.2060
Serum (S) Protein (g/L)	108	71.0000	71.0000	52.0000	96.000	8.7531
(PF:S)Protein	108	.6969	.6688	.3288	1.471	.1698
Pleural fluid(PF) LDH (U/L)	108	726.2407	673.5000	126.0000	2614.000	383.6402
Serum (S) LDH (U/L)	108	507.3889	491.5000	101.0000	1278.000	170.7601
(PF:S) LDH	108	1.5584	1.3295	.3818	9.740	1.1698
Pleural fluid Glucose (mMol/L)	108	4.4972	4.2500	1.3000	15.600	1.8652
Pleural fluid Cholesterol (mMol/L)	108	2.2741	2.1000	1.1000	5.000	.6442
PLEURAL FLUID LEUCOCYTE SUBSETS (%Total wbc)						
Lymphocytes	108	91.9630	98.0000	2.0000	100.000	17.5344
Neutrophils	108	6.8611	2.0000	0.0000	70.000	15.8818
Histiocytes	108	.9630	0.0000	0.0000	18.000	2.5170
PERIPHERAL BLOOD HAEMATOLOGICAL LEVELS						
Haemoglobin (Gm%)	108	11.0481	10.9000	6.4000	15.400	1.6467
Polymorphs (% Total wbc)	108	65.6296	65.0000	43.0000	85.000	7.6288
Lymphocytes (% Total wbc)	108	26.8426	28.0000	8.0000	45.000	6.3056
Monocytes (% Total wbc)	108	4.2222	4.0000	0.0000	19.000	2.6060
Eosinophils (% Total wbc)	108	2.7593	3.0000	0.0000	10.000	1.8336
Basophils (% Total wbc)	108	.4630	0.0000	0.0000	5.000	.8364
ESR (mm/1st hour)	108	77.4074	80.0000	15.0000	140.000	32.2018

Table 5: Correlation between independent biochemical variables of TPE

		Age	ADA	Protein	Serum Protein	PFProtein:SProtein	LDH	Serum LDH	PFLDH : SLDH	GLU	Chol
Age	Pearson Correlation	1	-.167	.124	.039	.127	.147	-.071	.187	.247**	.078
	Sig. (2-tailed)		.085	.199	.692	.189	.129	.466	.053	.010	.422
ADA	Pearson Correlation	-.167	1	-.113	.144	-.188	-.054	-.132	-.059	.003	.062
	Sig. (2-tailed)	.085		.243	.137	.051	.578	.173	.542	.973	.526
Protein	Pearson Correlation	.124	-.113	1	.269**	.873**	.098	.067	-.017	.119	.058
	Sig. (2-tailed)	.199	.243		.005	.000	.311	.488	.862	.221	.552
Serum Protein	Pearson Correlation	.039	.144	.269**	1	-.223*	-.107	-.087	-.064	.146	.044
	Sig. (2-tailed)	.692	.137	.005		.020	.272	.371	.509	.130	.653
PFProtein:SProtein	Pearson Correlation	.127	-.188	.873**	-.223*	1	.186	.131	.026	.069	.050
	Sig. (2-tailed)	.189	.051	.000	.020		.053	.176	.789	.481	.609
LDH	Pearson Correlation	.147	-.054	.098	-.107	.186	1	.349**	.628**	-.007	.160
	Sig. (2-tailed)	.129	.578	.311	.272	.053		.000	.000	.942	.097
Serum LDH	Pearson Correlation	-.071	-.132	.067	-.087	.131	.349**	1	-.326**	-.081	.001
	Sig. (2-tailed)	.466	.173	.488	.371	.176	.000		.001	.405	.995
PFLDH: SLDH	Pearson Correlation	.187	-.059	-.017	-.064	.026	.628**	-.326**	1	.065	.129
	Sig. (2-tailed)	.053	.542	.862	.509	.789	.000	.001		.506	.185
GLU	Pearson Correlation	.247**	.003	.119	.146	.069	-.007	-.081	.065	1	.297**
	Sig. (2-tailed)	.010	.973	.221	.130	.481	.942	.405	.506		.002
Chol	Pearson Correlation	.078	.062	.058	.044	.050	.160	.001	.129	.297**	1
	Sig. (2-tailed)	.422	.526	.552	.653	.609	.097	.995	.185	.002	

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

PF=Pleural fluid, S= Serum

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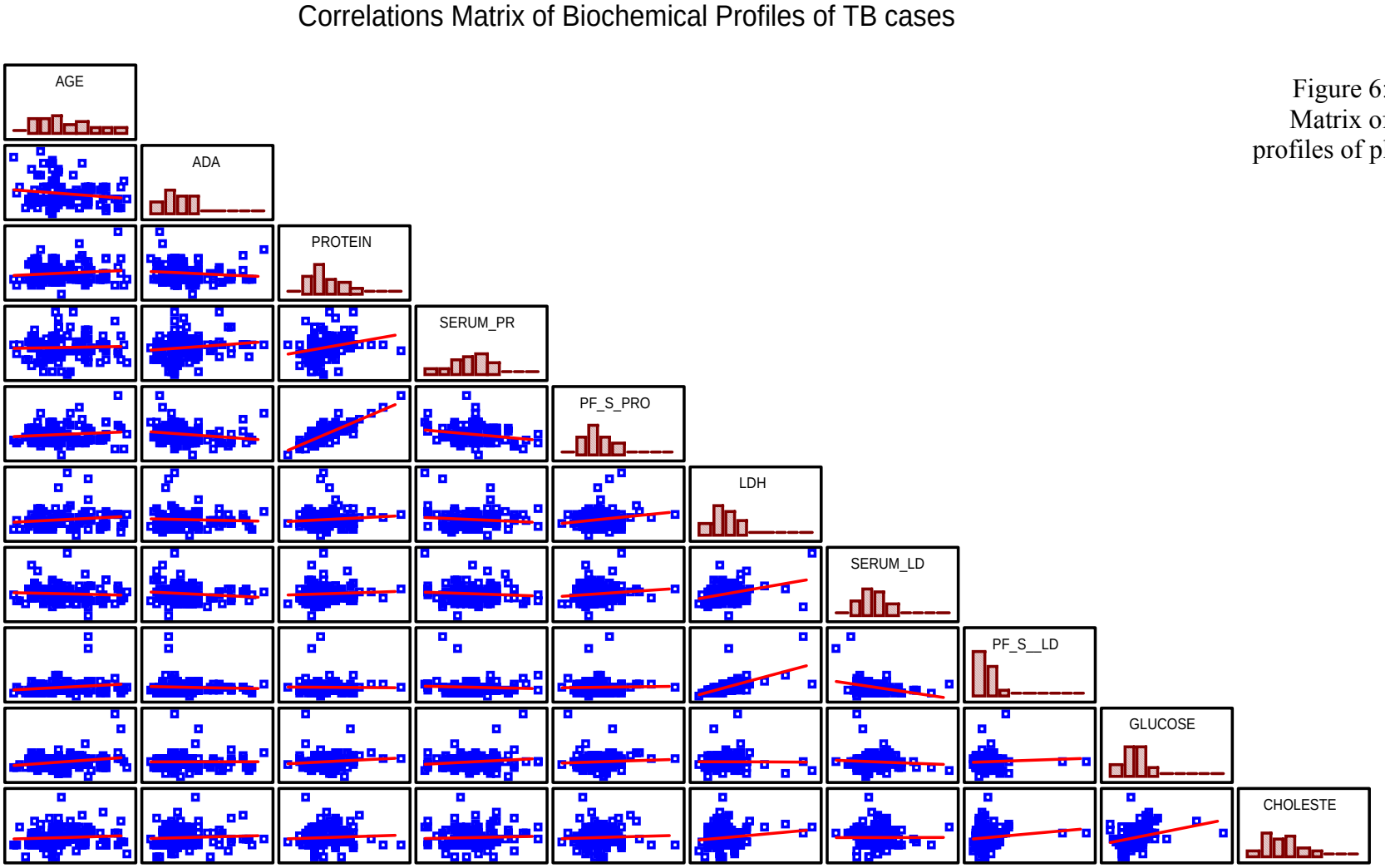

Figure 6: Correlations Matrix of biochemical profiles of pleural fluid in TB patients

The likelihood ratio (LR) of some of the presenting symptoms and signs were calculated. The presence of pleural rub (positive likelihood ratio LR 3.9) and breathlessness (positive likelihood ratio LR 0.9) for blood stained pleural fluid were noted. Clubbing of the fingers for pulmonary crackles and for cervical lymphadenopathy were (negative LR 1.02) and (negative LR 1.0) respectively. The LR of chest pain for pleural rub was 1.3. The LR of breathlessness (positive LR 0.95) and pulmonary crackles (positive LR 2.08) for haemoptysis were also calculated.

Discussion & Conclusion

Common presentation of tuberculous pleural effusion were fever, breathlessness, cough, night sweat, loss of appetite, weight loss and chest pain. Cough was mainly unproductive. Haemoptysis was rare and if present, was associated with parenchymal lesion. Generally clinical symptoms and physical signs do not positively help for definitive diagnosis of TPE.

According to the likelihood ratio calculation, pleural rub is the important physical signs for blood stained pleural fluid and pulmonary crackles is valuable for haemoptysis. These signs should guide in clinical teaching.

Diagnostic pleural aspiration and pleural biopsy could be performed by a single session of procedure. Results of cytological and microbiological examination as well as pleural biopsy could be obtained within 3 to 5 days but AFB culture took one months to produce results and it did not influence the diagnosis as well as treatment of the patient in this study. In patients with non informative pleural fluid and pleural biopsy examinations, the procedure needed to be repeated.

Smear examination of pleural fluid using Ziehl-Neelson stain had a very low positivity rate i.e. 0.9 % of cases in this study and so was the positive culture of AFB from the fluid i.e. 5.6 % of patients. Mycobacteria can be cultured from pleural tissue but the time required and the positivity rate was still unsatisfactory to be of value in routine clinical management. Pleural biopsy culture was positive in 1.9 % in the present study. This may reflect the paucibacillary status of pleural fluid which results at least partly from immunologic mechanism.

The positivity rate of microbiological tests in this study was consistent with another study from 105 patients in which pleural fluid AFB staining, pleural fluid AFB culture and pleural biopsy AFB culture were positive in 0 %, 5 % and 2 % respectively (Mihmanli & Ozseker, 2004). But the positivity rate was higher in the study by Valdes L et al (1998) which showed a positive smear of pleural fluid was 5.5 % and positive culture was 36.6 % of patients. Pleural biopsy tissue culture also was high at 56.4 %. The low positivity rate in the present study supports that the basic mechanism of TPE is immunologic.

The positivity rate of first session of pleural biopsy was 84.3 % of TPE in this study. The second and third biopsy sessions were needed in fifteen patients and two patients respectively. Repeat performance of pleural biopsy is obviously an inconvenience to the patients and also consumes a certain amount of medical resources. Closed pleural biopsy is a

fairly blind procedure rendering it into a diagnostic procedure with less than desired positivity rate. However pleural biopsy will be useful as an ultimate procedure in cases with diagnostic problem as it is a procedure which can give a definitive tissue diagnosis. Pleuroscopy resolves the diagnostic problem but the procedure requires more material resources and expertise.

Although a number of tests have been proposed to differentiate pleural fluid transudates from exudates, the tests first proposed by Light et al have become the criterion standards. The fluid is considered exudates if any of the following apply:

- Ratio of pleural fluid to serum protein greater than 0.5
- Ratio of pleural fluid to serum lactate dehydrogenase (LDH) greater than 0.6
- Pleural fluid LDH greater than two thirds of the upper limits of normal serum value

In our study, the nature of TPE was that of an exudates which is easily demonstrable by measuring protein and LDH in serum and pleural fluid, applying the Light criteria. According to a meta-analysis by Heffner J, Brown L, Barbieri C et al (1997), exudative pleural effusions meet at least one of the following criteria:

- Pleural fluid protein >2.9 g/dL (29 g/L)
- Pleural fluid cholesterol >45 mg/dL (1.16 mmol/L)
- Pleural fluid LDH >60 percent of upper limit for serum

In our study mean pleural fluid protein +/- SD was 49.15 +/- 12.2 and mean pleural fluid cholesterol +/- SD was 2.27 +/- 0.64 which is consistent with the meta- analysis data to support exudates. Mean pleural fluid LDH was 726.7 which is above 60% of the upper limit for serum and also consistent with the data of meta-analysis. The normal value for serum LDH is 70-250 IU/L.

Leers MP, Kleinveld HA and Scharnhorst V (2007) stated that pleural fluid cholesterol concentration for correct classification of more pleural effusions than achieved by the use of Light criteria. They also pointed out that combination of cholesterol and LDH had the highest discriminatory potential and the added advantage that no patient plasma is needed for correct classification. In our study, these findings as well as Light criteria are supported.

Light RW et al (2002) also found that pleural fluid glucose level below 60 mg/dl (3.3 mmol.l) suggests malignant effusion, TPE or lupus pleuritis. In our study mean pleural fluid glucose concentration was 4.49 mmol/l which is not very low compared to the finding of Light et al (2002).

Main type of pleural fluid leucocyte in tuberculous pleural effusion was lymphocyte. Neutrophil count in pleural fluid of tuberculous effusion was low. In a study by Burgess LJ et al (1995), pleural fluid lymphocyte / neutrophil ratio 0.75 or greater was used as a combined parameter for diagnostic confirmation, the sensitivity, the specificity; positive predictive value (PPV), negative predictive value (NPV) and efficiency for the identification of TB were increased. In our study lymphocyte counts were significantly higher than other studies to such an extent that many cases reached infinity in ratio (e.g. 100 polymorph: 0 neutrophil). Statistically it is inapplicable to include them in calculating sensitivity and specificity. Cell counting in pleural fluid depends on the method of counting and needs a standardization to be of use in calculating such important measures as sensitivity and specificity. Cell counting in the present study was done manually and counting by machine is more reliable to get accurate result. There was no significant change of peripheral blood differential white cell count. ESR which reflects inflammatory state in general was raised in most cases. It has no diagnostic value for any specific disease.

In this study the best cutoff level of ADA activity was tested at 42.5 IU/L when sensitivity was 87% and specificity was 89%. Several studies have suggested that an elevated pleural fluid ADA level predict TPE with sensitivity of 90 to100 % and specificity of 89 to 100% when the Giusti method is used (Roth, 1999).

We noticed that there were significant linear correlation between age and pleural fluid glucose level, pleural fluid protein and serum protein, pleural fluid LDH and serum LDH and pleural fluid glucose and pleural fluid cholesterol. There are no associations among other biochemical profiles of TPE. It is suggested that pleural fluid levels of protein and LDH are partially depends on their plasma values and need measuring the plasma levels at the same time to get more accurate result. The reason of significant correlation between pleural fluid glucose level and age and pleural fluid glucose level and pleural fluid cholesterol is unclear.

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