Original Research Article

Clinical outcome of tubercular pleural effusion in patients treated under revised national tuberculosis control programme

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ABSTRACT

Background: Although it is curable, tuberculosis remains one of the most frequent causes of pleural effusions on a global scale, especially in developing countries. Tuberculous pleural effusion (TPE) is one of the most common forms of extrapulmonary tuberculosis. The recommended treatment for TPE was regimen developed by revised national tuberculosis control programme- directly observed treatment-short course (RNTCP-DOTS).

Methods: The present study was conducted at Sri Siddhartha medical college hospital and research centre, Tumkur (Tumakuru), Karnataka, India for one and half year during the period of October 2010 to April 2012. 50 patients were included in the study after meeting inclusion criteria. Detailed history and clinical examination of patients were done including chest X-ray. Treatment was given with RNTCP-DOTS regimen. After complete treatment the recovery of patients was evaluated by chest X-ray.

Results: A total of 50 patients were included in the study. The mean age group was 41 years. Male (62%) preponderance was seen compared to females (38%). Chest pain and fever are the common clinical symptoms observed in all the patients. Moderate amount of pleural fluid accumulation was seen in 41 (82%) cases. Presence of lymphocytes was noted in all the samples. Out of 50 patients, 4 (8%) of them are detected as HIV positive and 6 (12%) are noticed as diabetic. 48 (96%) patients were having pleural fluid protein value more than 2.9 g/dl and 49 (98%) patients had pleural fluid sugar more than 60 mg/dl.   14 (43%) were reported of having ADA (elaborate the abbreviation- Adenosine deaminase) in the ranges 100-150 U/L. 30 (60%) patients were reported of having >10 g/dl of hemoglobin, 36 (72%) with total leucocyte count 4000-11000 cells/cumm and 45 (90%) with ESR >20 mm/hr. After completion of treatment out of 50, 40 patients were analyzed with chest X-ray and the outcome observed was normal appearance.

Conclusions: Early detection of tuberculosis was done by pleural fluid analysis and chest X-ray. After complete treatment with RNTCP-DOTS regimen all TPE cases produced significant cure rate when examined by chest X-ray.

Keywords: DOTS, RNTCP, Tubercular pleural effusion

INTRODUCTION

Tuberculosis (TB), which is one of the oldest diseases known to affect humans and is likely to have existed in prehominids, is a major cause of death both developing and developed countries. According to the World Health Organization, there were an estimated 9.6 million incident cases of tuberculosis globally in 2014. 5.4 million among men, 3.2 million among women and 1.0 million among children.[1] In India, more than 40% of adult population is infected with TB and about 1.9 million people develop TB disease every year. The prevalence 299 and the mortality 28 per 1,00,000 population, respectively. The HIV infected population in

India was estimated to be about 1.8 to 2.9 million in 2007, almost half of whom are also infected with TB and, thus, are at greater risk of breaking down with TB disease.[2] Tuberculosis is always the leading etiology of pleural effusions in the developing countries.[3] Tuberculous pleural effusion (TPE) results from *Mycobacterium tuberculosis* infection of the pleura and is characterized by an intense chronic accumulation of fluid and inflammatory cells in pleural space.[4]

Early approaches to treatment of tuberculosis include adequate rest, good food, good climate and use of a variety of agents such as cod liver oil, antimony, alkaline mineral water and gold. The national tuberculosis control programme (NTCP) was introduced by Government of India in 1962 and its backbone was the district tuberculosis programme. It was integrated with and implemented through the general public health services.[5] Based on an appraisal of the NTCP, the revised national tuberculosis control programme (RNTCP) was introduced in India in 1993 guided by WHO and supported by World Bank.[6] The RNTCP introduced directly observed treatment-short course (DOTS) for treating cases and has been recognised as the best cost-effective approach to TB control. It is composed of five distinct elements

- Political commitment
- Microscopy services
- Drug supplies
- Surveillance and monitoring systems and use of highly efficacious regimens and
- Direct observation of treatment.[7]

DOTS has two principles; to ensure that the patient with tuberculosis completes therapy to cure and to prevent drug resistance from developing in the community.[7]

Only a few numbers of studies were carried on clinical outcome of TPE under the programme RNTCP in the region of Karnataka. Hence the present study aimed to assess its outcome in patients treated under RNTCP-DOTS programme, and its success rate in Tumakuru district, Karnataka, India.

METHODS

The present study was conducted at Sri Siddhartha medical college hospital and research centre, Tumkur (Tumakuru), Karnataka, India for one and half year during the period of October 2010 to April 2012. A total 50 patients residing in Karnataka state and with exudative pleural effusion with predominant lymphocytosis that is supported by raised pleural ADA levels were included in the study. Patients with transudate and exudative pleural effusion due to other causes like malignancy and empyema were excluded from the study.

The patients included were diagnosed completely by collecting their detailed history, clinical examination, routine blood investigations, sputum examination, chest X-rays, ultrasound of thorax and pleural fluid analysis. The pleural fluid was analyzed for cell count, cell type, protein and sugar content. The pleural fluid adenosine deaminase (no need) (ADA) was estimated in doubtful cases of pleural effusion and considered exudative if the levels of pleural fluid protein was > 2.9 g/dl. The diagnosis of tuberculosis is further supported by predominant lymphocytosis in pleural fluid analysis and pleural fluid ADA levels. All patients diagnosed were treated under RNTCP regimen appropriately as given in Table 1. Data collected from the study were analyzed and presented in number and percentages. Percentages were calculated by using Microsoft office excel 2010 version.

Table 1: RNTCP regimen.

Treatment groups	Type of patient	Regimen	
		Intensive phase	Continuous phase
New group (category I)	New sputum smear positive	2H3R3Z3E3	4H3R3
	New sputum smear negative		
	New extra pulmonaary		
	Others		
Previously treated (category II)	Sputum smear-positive relapse	2H3R3Z3E3S3 + 1H3R3Z3E3	5H3R3E3
	Sputum smear-positive failure		
	Sputum smear-positive treatment after default		
	Others		

RESULTS

Table 2 shows the demographic and clinical profile of the patients included (50) in the study. The age of the

patients involved in the study ranges from 18-above 70 years. The mean age group was 41 years. Maximum number (30%) of patients was under the age group of 21-30 years. Male (62%) preponderance was seen compared

to females (38%). Chest pain and fever are the common clinical symptoms observed in all the patients. Cough was seen in 41 (82%) patients followed by breathlessness in 21 (42%) patients. Signs of TB along with TPE were observed in 12 (24%) cases.

Table 2: Demographic and clinical profile of the patients.

Characteristics	Number of patients (%)
Age (in years)	
18-20	2 (4%)
21-30	15 (30%)
31-40	10 (20%)
41-50	10 (20%)
51-60	5 (10%)
61-70	6 (12%)
>70	2 (4%)
Sex	
Male	31 (62%)
Female	19 (38%)
Clinical symptoms	
Fever	50 (100%)
Cough	41 (82%)
Hemoptysis	4 (8%)
Chest pain	50 (100%)
Breathless ness	21 (42%)
Loss of weight	4 (8%)
Signs along with tubercular pleural effusion	
Nil	38 (76%)
Present	12 (24%)
Tubercular consolidation	5 (10%)
Tubercular fibrosis	7 (14%)
Chest x-ray	
Left pleural effusion	26 (52%)
Right pleural effusion	24 (48%)
Amount Of Effusion	
Minimum	9 (18%)
Moderate	41 (82%)
Gross appearance of effusion fluid	
Hemmorhagic appearance (spelling)	1 (2%)
Straw coloured	49 (98%)
Cell type of patients studied- all lymphocytes	
60-70	2 (4%)
70-80	7 (14%)
80-90	8 (16%)
>90	33 (66%)
Human immunodeficiency virus	
Reactive	4 (8%)
Non-reactive	46 (92%)

Tubercular consolidation in 5 (10%) and fibrosis in 7 (14%) patients was observed. Left pleural effusion was seen in 26 (52%) and right pleural effusion in 24 (48%) cases. Moderate amount of pleural fluid accumulation was seen in 41 (82%) cases.

On investigation straw coloured pleural fluid was noticed in 49 (98%) and 1 (2%) with hemorrhagic appearance. On cytology of pleural fluid, presence of lymphocytes were detected in all the samples. 33 (66%) patients samples were reported of having lymphocytes >90. Out of 50 patients, 4 (8%) of them are detected as HIV positive and 6 (12%) are noticed as diabetic.

Table 3: Pleural fluid analysis among patients.

Analysis	Number of patients (%)	Mean±SD
Pleural fluid protein (g/dl)		
<4	13 (26%)	4.54±0.96
4-6	36 (72%)	
>6	1 (2%)	
Pleural fluid sugar (mg/dl)		
<100	22 (44%)	107.98±40.94
100-200	26 (52%)	
>200	2 (2%)	
Adenosine deaminase values (U/L)		
<50	6 (18.7%)	95.12±38.30
50-100	10 (31.2%)	
100-150	14 (43.7%)	
>150	2 (6.3%)	
Random blood sugar (mg/dl)		
<100	21 (42%)	120.26±46.04
100-200	23 (46%)	
>200	6 (12%)	

The pleural fluid was analysed for presence of proteins, sugars and ADA. On estimation of pleural fluid protein and glucose in all the samples, 48 (96%) patients were having pleural fluid protein value more than 2.9 g/dl and 49 (98%) patients had pleural fluid sugar more than 60 mg/dl. Out 50, ADA levels were estimated only in 32 patients. Among them, 14 (43%) were reported of having ADA in the ranges 100-150 U/L. The blood glucose levels were also estimated for all the patients to assess diabetes mellitus. And the results were presented in Table 3. Liver function tests were also done in all the patients to assess the presence of hepatitis. Out of 50, 3 (6%) patients were noted of having drug induced hepatitis as given in Table 4.

Table 5 gives the hematological estimation among all the patients involved in the study. 30 (60%) patients were reported of having >10 g/dl of hemoglobin, 36 (72%) with total leucocyte count (TLC) 4000-11000 cells/cumm and 45 (90%) with >20 erythrocyte sedimentation rate (ESR).

Table 6 gives the outcomes of the treatment. After completion of treatment out of 50, 40 patients were analyzed with chest X-ray and the outcome observed was normal appearance. In case of remaining 10 patients, 1 patient died during course of treatment, 4 were default from treatment and 5 did not attend for X-ray.

Table 4: Liver function tests.

Variables	Initial	Month 2	Month 4	Month 6	% change
Normal	50 (100.0%)	47 (94.0%)	47 (94.0%)	47 (94.0%)	-6.0%
Raised	-	3 (6.0%)	3 (6.0%)	3 (6.0%)	+6.0%
Total	**50 (100.0%)**	**50 (100.0%)**	**50 (100.0%)**	**50 (100.0%)**	

Table 5: Hematological parameters of patients studied.

Hematological parameters	Number of patients (%)	Mean±SD
Hemoglobin (g/dl)		
<6.0	1 (2%)	
6-8	8 (16%)	
8-10	11 (22%)	10.87±2.77
>10	**30 (60%)**	
Total leucocyte count (cells/cumm)		
<4000	4 (8%)	
4000-11000	36 (72%)	9739.46±3519.9
>11000	10 (20%)	
Erythrocyte sedimentation rate (mm/hr)		
<12	1 (2%)	
12-20	4 (8%)	45.04±19.27
>20	45 (90%)	

Table 6: Chest X-ray after treatment.

Chest x-ray after treatment	Initial (n = 50)	Final (n = 40)	% change
Normal	0	40 (100%)	+100.0
Abnormal	50 (100%)	0	-100.0
Not done	-	5	-
Default from treatment	-	4	-
Death	-	1	-

All the patients have improved significantly (P <0.001**) after treatment.

DISCUSSION

The prevalence rate of TB is increasing throughout the world with susceptibility for extrapulmonary involvement.[8,9] There are significant ethnic, age and sex differences for various sites of extra pulmonary TB.[10-12] Villegas et al also found pleural TB as second only after TB lymphadenitis.[13] In the present study, 62% were males and 38% were females , 30% of the patients were in the age group of 21-30 years. This demographic status present in our study was similar to the study conducted by Reechaipichitkul et al on 132 patients.[14] The increased incidence of the disease in males as compared to females is possibly due to the fact that both tuberculosis and diabetes are more common in males. In our study, the predominant presenting symptoms noted were pleuritic chest pain (100%), fever (100%), dry cough (82%) in all age groups. This was in accordance with the result given by Ray et al. He reported the clinical symptoms like fever and pleuritic chest pain were common in patients with exudative pleural effusions (81.35% and 62.5% respectively).[15]

In the present study 38% of patients were found to be anaemic. In a study done by Reddy 31.5% were found to be anaemic.[16] 90% of patients in this study group showed an ESR between >20 mm/hr and 8% had values between 12-20 mm/hr. Single determination of the value is of no significance and repeated tests have some practical value. The test also has some practical value in the prognosis of chronic pulmonary tuberculosis cases under treatment.[17] 72% patients showed TLC as 4000-11000 cells/cumm and 20% with >11000. Few patients who had far advanced tuberculosis showed a normal blood count, and certain others with mild to moderately advanced tuberculosis had a higher white cell count.

So there was no correlation noticed between the severity of tuberculosis and total white cell count. Previous studies have proved that leukocyte picture is of no help in diagnosis of tuberculosis and our study also shows the same.In the present study, 96% patients had pleural fluid protein value more than 2.9 g/dl, 98% patients had pleural fluid sugar more than 60 mg/dl, 60% of the patients had elevated ADA levels. These values of pleural fluid analysis were in accordance with the studies of Ray et al.[15] The relation between DM and TB is more prominent in younger people who are receiving insulin.[18] Overall, the risk of tuberculosis attributed to diabetes is 25%.[19] At an individual level, HIV is a more potent risk factor for TB in comparison to DM, but due to the high frequency of DM, its effect on the TB burden is equal or even greater than HIV. 20 8% of the patients had reported HIV with tubercular pleural effusion. In the present study the random blood sugar observed was >200 mg/dl in12% of the patients with TPE. In a study done by Sachdeva et al and others, it was showed that high incidence of pulmonary tuberculosis was associated with severe hyperglycemia.[21] According to Halprashanth, the cure rate was 74.6% and the default rate was 14.5%.The failure rate was 9.1% and death rate was 1.8%, as outcome in sputum positive pulmonary tuberculosis treated with RNTCP-DOTS.[22] In another study conducted by Reddy, the cure rate was 78.6% and the default rate was 8.6% and death rate was 12.9%.[16] In our study, after treatment with RNTCP-DOTS the cure rate was 90%, default rate was 8% and 2% of the patients died during the course of the treatment.

CONCLUSION

Pleural effusion is a commonly encountered in medical practice and the commonest cause is tuberculosis, as is evidenced from the present study. In this study only the initial step in evaluating cases of pleural effusion was established and determined the cause of pleural effusion by a detailed history, clinical examination and investigations like a chest radiology and pleural fluid analysis. By using the advanced diagnostic approaches, detailed clinical history and examination of the patient of the patient has to be made. All suspected cases of pleural effusion should undergo sonography of the thorax along with routine chest x-ray. Fluid cytology should be done to confirm tuberculosis or to rule out malignancy, which guides the physician for further evaluation of the patient if required.

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