ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 11 | November - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

CLINICO-RADIOLOGICAL SEQUELAE OF PULMONARY TUBERCULOSIS: POST TB LUNG DISEASE (PTLD)

Respiratory Medicine

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ABSTRACT

Introduction: India is a highest burden country with prevailing tubercular infection and active TB Case. An early case detection and case holding with regular intake of potent anti TB drug for a prescribed period with preventive protocol are the main stay of management. The recently launched NTEP assure us to achive early detection of TB cases by active surveillance and GeneXpert test and prevention with adopting a modified TB preventive therapy (TPT). The cure rate/ treatment completion rate is most likely to be improved but Somehow, up to half of the TB survivors have symptoms and some form of pulmonary dysfunction like persistent cough, expectoration, shortness of Breath (SOB), chest pain, haemoptysis, recurrent fever or infection etc. even after completion of treatment. These patients needed support for their physical, mental and social and family problems. In our country, so far no authentic survey/ programme were framed up to identify various causes and magnitude of post TB sequelae recently nomenculture as Post TB Lung Disease (PTLD). **Methodology And Objective:** The cured PTB Patients still having persisting chest symptoms were evaluated by clinico-radiological and functional capability (PFT & 6MWT etc) to assess reason and extend of underlying disability due to PTLD. It will be helpful in improving the quality of life. **Discussion:** The problem of post TB sequelae or DPLD is huge one due to accumulation of year after year declared cured cases. Lot of cases of TB who been declared cured/ Treatment completed under RNTCP, of them about >60 % had post TB problem and is even more common with MDR/XDR. Males were predominant in study that too in a productive age group which hampers socio economical status of family. Most common co morbidities associated were DM & COPD. The radiological finding most frequently present were extensive fibrosis (41%,), destroyed one lung with compensatory emphysema (24%), bronchiectasis (24%), fibrocavitory lesion (21%), and COPD (11%). The scar carcinoma (5%) and aspergillosis with a fungus ball (3%) in the cavitory lesions were also observed apart from the healing with calcification (38%) in a quite good number of cases.**Conclusion:** The post tuberculosis sequelae or the Post TB Lung Disease (PTLD) as a new nomenclature has been given a recognition. The permanent disability is reproducible with diagnostic modalities (comparable with post polio or orthopedic beneficiary schemes). The meticulously prepared integrated rehabilitation programme with inbuilt surgical intervention should also be sought out at National level, with a guide line in this regards. A multicentric longitudinal survey may require to identifying this orphan problem.

KEYWORDS

National TB Elimination Programme (NTEP), TB sequelae, Post TB Lung Disease, Corpulmonale, Long term O2 therapy (LTOT), Non-invasive ventilation (NIV)

INTRODUCTION:

India is a highest TB burden country considering the prevailing tubercular infection among the population. The annual risk of TB Infection (ARTI) is around 1.7 with the incidence of new pulmonary TB (PTB) case is > 200/ Lac/ year and mortality rate among them is around 10%. All and above, the MDR-TB is alarming situation with an incidence of >3 % and the prevalence of >12%, among the new and retreatment cases respectively. This scenario required early detection with GeneXpert eg CBNAAT/ TrueNAT & Line Probe Assay, Liquid culture e.g. BACTEC MGIT 960 etc. are all incorporated in the NTEP in recent past to combats further deterioration PTB due to delay in diagnosis.

The well known epidemiological triad in infectious diseases shows that there is interaction and contribution among the three factors, the bacillus, host and environment leading to organ involvement. The pathogenesis of tuberculosis is complex one, and multiple factor play a role i.e. delayed type hypersensitivity (DTH), individual immune competence, virulence of MTB, an early/ or delayed diagnosis, an initial minimal or far advanced lung destruction, and treatment with effective shorter regimen taken without any interruptions ie patient compliance and adherence etc. All these all combine to influence the outcome. The tuberculosis treatment may result in complete resolution, or healing with fibrosis and calcification or even leaving behind persisters which are responsible for endo or exogenous reactivation or remained as dormant bacillus or latent TB. The development of drug resistant tuberculosis (acquired or secondary), relapse after treatment, an opportunistic infection in immune-compromised host, infection with non-tubercular mycobacterium (NTM), and associated preexisting co-morbidity, these all additively contribute to occurrence of post tubercular sequelae of tuberculosis.

The introduction of effective anti-tubercular drugs in the early half of 20th century was a great talking point. It was thought that it will tame this centuries old disease. The TB national program, was launched and later revised to achieve early conversion of sputum with better cure rates (>85%). It was framed up with full efforts towards early diagnosis and case holding to achieve maximum cure or treatment completion/ success rate. However due to increase in undesired treatment defaulters, increased failure rate, intolerance to drugs, relapse after treatment, and emergence of drug resistance, the build-up of confidence soon faded. With occurrence of drug resistance, focus shifted to universal DST & daily fixed dose regimen. In view of WHO's End TB strategy, the national program was again revised and renamed as National Tuberculosis Elimination Program (NTEP), focusing theme was attention to tuberculosis prevention treatment (TPT), survey of house hold contacts, care of vulnerable groups such as HIV and drug-resistance TB. The National TB programme, has worked to reduce the infectious pool of TB in the community, but it remained largely silent regarding care of the patients after treatment completion except, follow-up sputum examination, mere by to detect relapse/ retreatment cases.[2]

Before anti-tubercular treatment era, numerous papers were written about post-tubercular complications, but this topic vanished in the noise of effective anti-TB drugs. Somehow, up to half of the TB survivors have symptoms and some form of persistent pulmonary

dysfunction even after completion of treatment, [1] so these patients needed support for their physical, mental and social problems. [2]

In our country, so far no authentic survey/ programme were framed up to identify various causes and magnitude of post TB sequelae. The symptoms like persistent cough, expectoration, shortness of breath (SOB), chest pain, haemoptysis, recurrent fever or infection etc. remained, even after treatment completion or cure from TB, and the patient is left seeking medical attention. The relapse of tuberculosis could be the cause and patient needs an evaluation but at several occasions it is found that the bacteriological negative patient wrongly diagnosed again as active tuberculosis on the basis of radiology and this is another problem. The symptoms may be due to residual scaring/ distortion/ destruction or reduction of healthy lung parenchyma or pleural involvement with chest wall deformities leading to decreased in functional capability of patients. These are likely to persist/ remain life long as a disability. [2, 3] Although the diagnosis and treatment of tuberculosis is being provided free of cost by the government, despite the most individuals have to bear high out-of-pocket expenditure (on transport, additional medication, nutritional supplementation etc. [2, 3] At another occasion in spite of all pharmacological treatment, recalcitrant patient remained bacteriologic positive, and are a source of infection to the community, these all need to be identified. All the patients having persistent symptoms even after anti TB treatment should be evaluated with the help of patient's history, clinical presentation, pathological, bacteriological and imaging modalities (like chest X-Ray & CT Scan) to understand the various aspects of post tuberculosis ailments, and associated co morbidities for better management and to improve quality of life. Hence we plan to conduct a study in a tertiary care rural Medical College setup.

OBJECTIVE:

This is a prospective observational study to evaluates the clinico-radiological sequelae of a treated cases of pulmonary tuberculosis admitted during the period with effect from January to December 2020 to understand various aspects of post tubercular lung diseases i.e. predisposing factors, underlying lung pathology (transient/ permanent or likely to recurred), extend of radiological evidence and effect of co morbidities to enable us for better management.

Methodology:

- All the willing patient with past history of PTB to be included
- A clinical evaluation of the patients including relevant history and investigations
- A detailed radiological assessment by chest radiograph and CT
- Assessing Functional capability by Spirometry/ 6 MWT
- A Customized management strategy

OBSERVATION AND RESULTS:

Presented In The Table-1

S. No.	Indicators	Observations	Interpretation
1	Total cases in study	N = 66	100%
2	Mean age: (18-85 Yrs)	49.3 Yr	In productive age
3	M:F 43:23	65% : 35%	Almost double in Male
4	Rural : Urban Patients	64% : 36%	Comparable with national scenario
5	Smokers	36 among 43 male	Prevailing 84 % in male
6	Co morbidity	DM 20% HT 18% COPD 12% Other 18%	DM, Cardiovascular including corpulmonale, HIV & COPD further deteriorate the situation
7	Presenting Symptoms	Cough 77% Expectoration 68% Chest Pain 52% Fever 49% SOB /Low SpO2 38% Haemoptysis 15%	Changing pattern in cough/ Expectoration/ or Fever and low SpO2 are alarming. SOB be evaluated with Pulse oxymetery/ ABG
8	General Physical Exam	Hypoxemia(23) 35% Clubbing(10) 15% Pallor(4) 6% Edema(3) 5%	
9	Investigations revealed	Septicemia (31) 47% Anaemia (12) 18% Hyponatremia (8) 12% Hypoalbuminemia (1) 2% Hypokalemia (1) 2%	Out of total 66 Patients, septicemia was present in 47% all were kept in RICU. Inotropes & O_2 therapy
	Radiological Findings (Chest X-Ray/ CT Thorax)	Fibrosis 41% Calcification 38% Compensatory Emphysem 24% Destroyed lung 24% Bronchiectasis 24% Fibrocavitory lesion 21% Pneumothorax 11% Emphysema COPD 11% Carcinoma 5% Aspergillosis 3%	Extensive fibrosis with fibro-cavitary, bronchiectasis and destroyed lung are more prone for recurrent/ persistent symptoms. These all cases had poor lung reserve in accordance with consistent Spirometry & 6MWT findings
11	Wrongly re-diagnosed as TB	07 cases 11%	CXR change or hamoptysis alone does not prove relapse. Bacteriological evidence is required
12	Respiratory Failure	23 cases 35%	Required RICU with O_2 therapy, 7 cases (>30%) of them discharged on long term domestic Oxygen therapy.
13	Spirometry	Conducted in 21 32%	Obstructive…….7 Mixed……4 Restrictive 10
14	6 MWT	Conducted in 21 32%	All Less than 300 meter
15	PAH (Secondary)	6 cases 9%	Corpulmonale & Pulmonary hypetension ECHO done in selected group

DISCUSSION:

The problem of post TB sequelae is huge one. Lot of cases of TB whose been declared cured/ Treatment completed under the national programme of them about >60 % had post TB problem and even more common with MDR/XDR [4, 5] These cases are present clinically with various symptoms including functional deficit etc. and recently (2019) this problem been defined as Post-Tuberculosis Lung Disease, in the **1st International Post-Tubercular symposium** held at Stellenbosch South Africa and abbreviated to PTLD. [6] It is estimated that about 150-200 Million cases cumulatively in past 4 years are present globally who been treated and declared cure or treatment completed but are still suffering from PTLD. [1,5] In our study, out of total 66 cases admitted, we found as usual, almost double the male predominance while mean age was 49 years (productive age group) so most likely to impact socio-economic aspects of patient's family. [1-3] A significant number of male that is 84% remained smokers in our study. The Allwood B W et al. has stress upon smoking cessation and or nicotine replacement therapy in all the patients suffering from tuberculosis. He also mentioned the use of Metformin in the treatment of tuberculosis which results in reduction of cavity formation by reducing the level of Matrix Metaloproteinases (MMP), while he recommended further studies to support his findings. [4] The main symptoms observed in this study were cough in 77%, expectoration 68%, chest pain 52%, fever 49%, SOB 38%, and haemoptysis 15% in order of frequency of presentation, were all most similar to other reported studies. [3, 7-11] An increase or change of cough and expectoration with fever or shortness of breath associated of hypoxemia (35%)/ respiratory failure, required intensive care unit (ICU) management as also happened in our study. The most common co-morbiditis observed in the present study in the decreasing order were the diabetics (20%), Systemic hypertension (18%), COPD (12%), and other miscellaneous 18%. These all have the potential to adverse by impact and cause the worsening of PTLD, which can be alarming and alert us for an adequate and appropriate management. Globally the COPD is enjoying number 3rd status as a killer of mankind. A study of 14050 cases around 18 countries revealed tuberculosis associated with COPD is 2.5 fold more common independent of smoking. [14] The another study covering 5571 cases showed that COPD has higher affinity with pulmonary tuberculosis

(>30%) than without (14%) any ailments. [15] Anti-TB Treatment itself is responsible for some of the side effect i.e. hearing-loss, is often permanent. [2] Out of our 66 patients 7 (11%) were wrongly diagnosed as relapse cases of tuberculosis at peripheral health institutions and put on treatment, hence a district/ tuberculosis-unit level monitoring need to be reinforced.

The radiological evaluation of the underlying PTLD includes the involvement of lung parenchyma, airways, pleura, mediastinum and the chest wall. All these structures are well delineated and reproducible by chest X-ray/ CT thorax as a document. The extend of involvement can also be stratified which helps in the management strategy i.e. medical/ surgical/ or any other including rehabilitation and preventive vaccination [7-9] The most frequent radiological finding in our study were extensive fibrosis (41%), destroyed one lung with compensatory emphysema (24%), bronchiectasis (24%), fibrocavitory lesion (21%), and COPD (11%). We also observed scar carcinoma (5%) and aspergillosis with a fungus ball (3%) in the cavitory lesions, apart from the healing with calcification (38%) in a quite good number of cases. Most of these radiological findings are in combination or super imposed with each other. The Patho-physiological V/Q mismatch especially dead space ventilation in cavitory lesions and loss of alveolar capillary surface in destroyed lung are a few examples leads to hypoxemia apart from bronchospasm and accumulation of secretions in the airways. The pharmacological treatment included, antibiotic, steroids, inotropic support for hemodynamic stability, nebulization therapy, and the patients with respiratory failure were well managed with supplementary Oxygen therapy including NIV and none required ventilator support. The mortality remained zero in the present study and all the seriously ill 23 (35%) cases were managed in RICU and among them 7 cases (30%) were discharged on long term domiciliary oxygen therapy. The electrocardiogram (ECG) and 2 D ECHO are non-invasive modalities enabling us to better understand the cardiac activities, cor-pulmonale and to assess pulmonary arterial hypertension secondary to chronic lung diseases. G S Rajeev et al reported secondary PAH in 46% cases of PTLD (13), while we conducted ECHO in selected group and only in 6 cases (9%) were detected with pulmonary arterial hypertension and or cor-pulmonale. In our study 7 (11%) cases were wrongly diagnosed as relapse of tuberculosis while they were actually bacteriological negative and suffering from PTLD.

In the pre-chemotherapeutic era fresh environmental air, nutritious diet, isolation from community via sanatoria setup, and in some cases surgical intervention was the mainstay of TB Management. The common surgery performed were collapse therapy (including artificial pneumothorax/ pneumoperitonium, thoracoplasty, phrenic nerve palsy etc), broncho-pleural fistula closure and the resection of lung (in the form of wedge/ segmental/ lobar resection or pneumenectomy) are some examples. [10,16] The same dreaded situation is likely to come back because of increasing MDR/XDR cases and very few potent alternative drugs (like Rifampin/ INH and newer Bedaquiline and Delaminid) been discovered. The old wine (repurposed drugs) in new bottle is even served to recalcitrant MDR/XDR cases. The success rate of adjuvant surgery in a series of 5599 cases treated in Russia during a 17-year period, reported an overall mortality rate of 0.1%, with treatment success rates of 93.0% and 92.1% in MDR and XDR-TB, respectively. [10] The overall physical and functional status with 6MWT and spirometry could only be done in 21 (32%) patients which was consistent with the underlying pathology. These tests are also reproducible and serve as documentation of the degree/extend of disability but there could be transient worsening during acute exacerbation.

CONCLUSION:

The post tuberculosis sequelae or the Post TB Lung Disease (PTLD) as a new nomenclature should be given a new reorganization. The individual should be thoroughly evaluated if symptoms or physical disability persist after cure from tuberculosis. The diagnosis of associated co-morbidity and radiology, spirometry, 6MWT are some helpful reproducible modalities to assess the extent of permanent disability (comparable with post polio or orthopedic beneficiary schemes), and this group i.e. PTLD too have physical, mental, socio-economic constraints which are even more prevailing among drug resistant patient. The meticulously prepared integrated rehabilitation programme with surgical intervention should also be sought out for better management of PTLD, and in this regards a national level sample survey to assess magnitude of problem be considered.

REFERENCES:

1. S RaviMohan et al " Tuberculosis and lung damage: from epidemiology to pathophysiology", Eur Respir Rev 2018; 27: 170077
2. Blessina Amulya Kumar, Rehabilitation of treated TB patients: Social, psychological and economic aspects; Int J Mycobacteriol. 2016 Dec;5 Suppl 1:S129-S130. doi: 10.1016 /j.ijmyco.2016.11.021. Epub 2016 Nov 27.
3. Maryam Gohar Ali et al; Post tuberculosis sequelae in patients treated for tuberculosis: An observational study at a tertiary care center of a high TB burden country; European Respiratory Journal 2018 52: PA2745.
4. Allwood BW, van der Zalm MM, Amaral AFS, et al. Post-tuberculosis lung health: perspectives from the First International Symposium. Int J Tuberc Lung Dis2020; **24:** 820–28.
5. Migliori GB, Marx FM, Ambrosino N, et al. Clinical standards for the assessment, management and rehabilitation of post-TB lung disease. *Int J Tuberc Lung Dis* 2021; **25:** 797–813.
6. The 1st Internationl Post-Tuberculosis Symposium, Life after TB 22-23 July 2019 STIAS Institute, Stellenbosch South Africa.
7. Aymen Ayari et al, Management of pulmonary tuberculosis sequelae; European Respiratory Journal 2015 46: PA; DOI: 10.1183/13993003. congress-2015.PA2762.
8. Rupak Singla, et al., Sequelae of pulmonary multidrug-resistant tuberculosis at the completion of treatment; Lung India. 2018 Jan-Feb; 35(1): 4–8.
9. Nishant Aggarwal1, et al.; Post-tuberculosis sequelae and their correlation with quality of life: An observational study at a tertiary care center of north India, https://doi.org/10.1101/2021.10.04.21264524; this version posted October 5, 2021 .
10. Simon Tibe1ri et al; Managing severe tuberculosis and its sequelae: from intensive care to surgery and rehabilitation;J Bras Pneumol. 2019; 45(2):e20180324.
11. Musafiri S et al.; The Aftermath of Pulmonary Tuberculosis: Predictors of Severe Pulmonary Sequelae and Quality of Life of Patients Visiting a Tertiary Level of Care in Rwanda, East Africa; Austin J Pulm Respir Med 2015; 2(2): 1027.
12. Hyae Young Kim, MD,Koun-Sik Song, MD, Jin Mo Goo, MD Jin Seong Lee, MD, Kyoung Soo Lee, MD,Tae-Hwan Lim, MD; Thoracic Sequelae and Complications of Tuberculosis,
13. G.S. Rajeev, Pulmonary Hypertension In Post Tuberculosis Pulmonary Sequelae: Attention Needed. DOI:https://doi.org/10.1016/j.chest.2020.05.454.
14. Amaral AF, Coton S, Kato B, et al. Tuberculosis associates with both airflow obstruction and low lung function: BOLD results. Eur Respir J 2015; 46: 1104–1112.
15. Menezes AM, Hallal PC, Perez-Padilla R, et al. Tuberculosis and airflow obstruction: evidence from the PLATINO study in Latin America. Eur Respir J 2007; 30: 1180–1185
16. Marrone MT, Venkataramanan V, Goodman M, Hill AC, Jereb JA, Mase SR. Surgical interventions for drug-resistant tuberculosis: a systematic review and meta-analysis. Int J Tuberc Lung Dis. 2013;17(1):6-16. https://doi.org/10.5588/ijtld.12.0198.