

Original Article

Demography, Clinico-Pathological Features and Outcome of Extrapulmonary Tuberculosis: 2 Years Prospective Study

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Introduction

Tuberculosis (TB) is an infectious disease that primarily affects lungs followed by other organs. Extrapulmonary TB can present with non-specific symptoms such as unintentional weight loss (more than 1.5 kg in a month), night sweats and fever for more than 2 weeks. Other symptoms depend on the site or organ affected.

Aims and Objectives; *To study the demographic, clinico-pathological features and outcome of extrapulmonary tuberculosis patients at a tertiary care hospital of Kashmir valley.*

Materials and Methods: *A prospective study with regard to demography and clinic-pathological features and outcome, of extra-pulmonary tuberculosis patients above 18 years was conducted over two years which was recorded interpreted and analyzed.*

Results and Observation: *In our study of 148 patients of extra-pulmonary tuberculosis we found 106 of them below age of 45 years with mean age of 45 yrs±11.22. Males predominated being 91 (61.4%), labourers and students comprised 40 each (27%). 116(78.3%) were from rural areas. 2 patients were found to be HIV Positive. 36 (24.3%) were smokers and a total of 93 (62.8%) were married. Mean Hb was 10.8±2.30 g/dl, TLC count was 7.73±2.80 mm³, platelet count was 232.23±100 mm³. Erythrocyte sedimentation rate was 46.2±11.3mmhr. Fever, Weight loss and anorexia were most common symptoms. 144 (97.2%) got cured, 4 patients died not because of tuberculosis, but of underlying diseases. 24 (16.2%) patients had ATT induced Hepatitis, 11 (7.4%) had Hyperurecemia, 9(6.08%) had Gastritis, 6(4.05%) had Nausea/Vomiting, 2 (1.35%) had Neuropsychiatric manifestation.*

Conclusion: *Tuberculosis most commonly occurs in younger patients, especially from rural area. The disease is most often seen in those who work in overcrowded and unhygienic places. Due to low prevalence of HIV in Kashmir association with HIV was low. Most patients had good response to daily regimen and most common drug related side effect was hepatitis. Genetic aspect could be the possible factor for drug response and toxicity.*

Keywords: *Demography ;Extra-pulmonary tuberculosis; outcome.*

Introduction

Tuberculosis (TB) is a chronic disease that primarily affects lungs followed by other organs.

Most infections do not have symptoms, known as latent tuberculosis. About 10% of latent infections progress to active disease which, if left

untreated, kills about half of those infected. The classic symptoms of active pulmonary TB are a chronic cough with bloodcontaining sputum, fever, night sweats, and weight loss. One-third of the world's population is thought to be infected with TB.^[1] In 2014, there were 9.6 million cases of active TB which resulted in 1.5 million deaths. More than 95% of deaths occurred in developing countries. The number of new cases each year has decreased since 2000¹ In healthy people, infection with Mycobacterium Tuberculosis often causes no symptoms, since the person's immune system acts to "wall off" the bacteria. New infections occur in about 1% of the population each year². It is a disease of poverty affecting mostly young adults in their most productive years. The vast majority of TB deaths are in the developing world.

5-10% of people who are infected with TB bacilli (but who are not infected with HIV) become sick or infectious at some time during their life. People with HIV and TB infection are much more likely to develop TB. The risk for developing TB disease is also higher in persons with diabetes, other chronic debilitating disease leading to immune-compromise, poor living conditions, tobacco smokers etc³.

Extra-pulmonary TB can present with non-specific symptoms such as unintentional weight loss (more than 1.5 kg in a month), night sweats and fever for more than 2 weeks. Other symptoms depend on the site or organ affected. The most common types of extra-pulmonary tuberculosis are:

- Tubercular lymphadenitis
- Tuberculous pleural effusion (usually single-sided)
- tuberculosis of the bones and joints
- Tuberculous pericardial effusion
- Tubercular meningitis
- Disseminated / miliary tuberculosis
- Tubercular empyema
- Abdominal tuberculosis

Disseminated tuberculosis and tuberculosis meningitis are acute, severe forms of TB, often occurring soon after primary infection. They occur

most commonly in children and young adults. These acute forms of TB are often fatal. When this form of disease is suspected, treatment should be commenced immediately without waiting for bacteriological proof of diagnosis in the form of culture, provided we have clinical and laboratory evidence especially cells, sugar, protein and ADA in favour of tuberculosis. HIV positive patients particularly those with low CD4 counts may present with extra pulmonary disease. The presentation of extra-pulmonary TB is generally no different between HIV positive and HIV-negative patients, however, differences do occur. Six months treatment is as effective in extra-pulmonary as in pulmonary disease. In some instances of severe or complicated disease (meningitis, TB bones/joints, miliary TB) treatment may need to be extended to nine months.

Aims and Objectives

To study the demographic, clinic- pathological features and clinical outcome of extra- pulmonary tuberculosis patients at SKIMS a tertiary care hospital of Kashmir valley.

Materials and Methods

All patients > 18 years of age of extra-pulmonary tuberculosis. A prospective study of tuberculosis patients was conducted in the infectious disease department, division of Internal Medicine, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar from June 2013 to May 2015. Tuberculosis patients who visited infectious disease clinic on OPD basis and patients who were admitted in General Medicine ward were taken up in this study. For each patient clinical presentation, socio demographic profile and outcome of treatment was recorded interpreted and analyzed.

Investigations

All patients was subjected to following investigations:

- CBC
- Complete biochemistry

- Urine examination
- Chest x-ray
- ECG
- USG Abdomen
- HIV

Other investigations were done according to a case of tuberculosis

- Sputum for AFB
- Sputum culture for AFB
- MRI chest/abdomen
- CT chest/abdomen
- FNAC/biopsy
- Urine for AFB and culture.
- Urine for PCR MTB

Results and Observation

In our study of 148 patients of extra-pulmonary tuberculosis we found 106 of them below age of 45 years with mean age of 45 yrs±11.22. Males predominated being 91 (61.4%), labourers and students comprised 40 each (27%). 116(78.3%) were from rural areas 32(21.62%) from urban areas. 2 patients were found to be HIV Positive.36 (24.3%) were smokers and a total of 93 (62.8%) were married. (table 1)

Type of tuberculosis

In our study of 148 patients different organs/tissues involved were as ; Pleural tuberculosis 35(23.6%),TB Lymphadenitis overall 40(27%), {includes cervical 33 (22.2%), Abdominal LAP 5 (3.3%), Axillary 2(1.2%) of patients}, followed by Abdominal tuberculosis 35(23.6%), GUTB 11(7.4%),Disseminated 11(7.4%), CNS 8 (5.4%),cardiac 6(4.0%), breast 2(1.35%) as shown in (table 2)

Clinical Presentation

In TB Lymphadenitis: Fever was found in 20 (57.1%) , Cough in 9 (25.7%) , Weight loss in 1(2.9%), Cervical LAP in 26(74.3%), Decreased Appetite in 7(20.0%),Pain abdomen in 3(8.6%) patients.

In pleural TB: Fever was found in 29(82.9%) , Cough in 20(57.1%), Hemoptysis in 2(5.7%), Weight loss in 3 (8.6%), Nausea/Vomiting in 5(14.3%), Chest pain in 10(28.6%),

Breathlessness in 16(45.7%), Decreased Appetite in 1(2.9%), Pain abdomen in 1(2.9%) patient.

In abdominal TB: Fever was seen in 15(45.5%), Cough in 8(24.2%), Hemoptysis in 1(3.0%), Weight loss in 9 (27.3%), Nausea/Vomiting in 3(9.1%), Cervical swelling in 1(3.0%), Decreased Apetitein 11(33.3%), Pain abdomen in 21(63.6%) of patients,

In CNS TB: Fever was seen in 6(75.0%), Cough in 1(12.5%) , Weight loss in 1(12.5%), Decreased Apetite in 2(12.5%) ,Pain abdomen in 1(12.5%), Headache in 2(25.0%) of patients.

In GUTB: Fever was seen in 6(54.5%), Coughin 2(18.2%), Nausea/Vomiting in 1(9.1%), BLN 1(9.1%), Pain abdomen 5(50.0%) of patients.

In disseminated, cardiac and breast tuberculosis, Fever was seen in 8(72.7%), 3(50.0%),1(50.0%) of patients respectively. Cough was seen in 5 (45.5%), 3(50.0%),0(0.0%) of patients respectively, Weight loss in 2(18.2%), 0(0.0%), 0(0.0%) of patients, Nausea/Vomiting 1(9.1%),2(33.3%), 0(0.0%) of patients respectively .

Diagnostic procedures and histological features;

In our study 62 patients under went different invasive procedures. These procedures where done in those where base line investigations, fluid analysis and noninvasive investigations were inconclusive. Of these, 35(23.5%) underwent FNAC, 15 (10%) underwent Excisional biopsy, 6(4.0%) underwent diagnostic Laparatomy, 1(0.6%) underwent open biopsy, 2(1.2%) underwent pleural biopsy,1(0.6%) underwent pleuroscopy, 2(1.2%) underwent Peritoneoscopy. The results on histopathological examination of different procedures which were done during evaluation of these patients were as :

In FNAC; Caseous necrosis was found in 16(45.7%) of cases, chronic Granulomatous inflammation was found in 14(40%) of cases, Langerhans type giant cells in 5(14.2%) of cases.

In Diagnostic Laparatomy, Caseous necrosis was found in 3(50%) of cases, Granulomatous disease in 3(50%) of cases, Langerhans type giant cells in 4(66.6%) of cases and non caseating granulomas in 2(33.3%) of cases.

In Excisional biopsy, caseous necrosis was found in 7(46.6%) of cases, Granulomatous lymphadenitis in 5(33.3%) of cases and Langerhans type giant cells in 3(20%) of cases.

In pleural biopsy chronic Granulomatous disease with Langerhans type giant cells with caseating granulomas was seen. In pleuroscopy the biopsy revealed chronic inflammatory infiltrate with few epithelioid cells. Peritoneoscopic biopsy revealed chronic Granulomatous disease with Langerhans type giant cells, non caseating granulomas. (table3)

The treatment outcome of the patients in our study was excellent ; 144 (97.2%) were cured , 4 patients died not because of tuberculosis , but of underlying diseases. 8 patients were treated as defaulters (Cat II WHO) rest were treated as Cat I WHO with daily regime of ATT. In our study there was no relapse and there were no defaulters as shown in {Table 4}

In our study, the treatment related complications were seen and included ATT induced Hepatitis in 24 (16.2%) patients, Hyperurecemia in 11 (7.4%), had Gastritis in 9(6.08%), Nausea/ Vomiting in 6(4.05%) Neuropsychiatric manifest-ation in 2 (1.35%).{Table 5}

All the patients, underwent baseline investigations, the results were as; Hb was 10.8±2.30 g/dl, TLC count was 7.73±2.80 mm³, platelet count was 232.23±100 mm³. Erythrocyte sedimentation rate was 46.2±11.3mmhr. KFT/LFT were as per (Table 6)

In our study, 74 (37%) patients had underlying comorbidity, 23(11.5%) had Hypertension, 17(8.5%) had Diabetes, 2(1.0%) had Rheumatoid arthritis, 3(1.5%) had Chronic Renal Failure, 6(3.0% had Hypothyroidism, 14(7.0%) had COPD,2(1.0%) had SLE as shown in table 7

Table 1 ; Demography of patients

Age		Sex		Residence		Smoking		Married		HIV Status		Alcohol /other addiction	
<45	>45	Male	female	Rural	Urban	yes	No	Yes	No	Positive	Negative	Absent	Present
106	42	91	57	116	32	36	112	93	55	2	146	138	8

Table 2; Types of tuberculosis

Type of tuberculosis (TB)	NO of patients	Percentage(%)	
Pleural	35	23.6%	
Abdominal	35	23.6%	
Lymphadenitis	Cervical	33	22.2%
	Abdominal	5	3.3%
	Axillary	2	1.35%
Genitourinary tuberculosis(GUTB)	11	7.4%	
Disseminated	11	5.5%	
CNS	8	5.4%	
Cardiac	6	4.0%	
Breast	2	1.35%	

Table 3; Diagnostic procedures and histo-pathological findings

Procedure	Histo-pathological diagnosis			
	Caseousnecrosis(%)	Chronic granulomatous lymphadenitis(%)	Langerhans type gaint cells(%)	Non caseating granulomas(%)
FNAC(n=35)	16(45.7%)	14(40%)	5(14.2%)	0%
Diagnostic laproscopy(n=6)	3(50%)	3(50%)	4(66.6%)	2(33.3%)
Excisional biopsy (n=15)	7(46.6%)	5(33.3%)	3(20%)	0%
Open biopsy(n=1)	1(100%)	1(100%)	0%	0%
Pleural biopsy(n=2)	2(100%)	2(100%)	0%	0%
Pleuroscopy(n=1)	0%	1(100%)	1(100%)	0%
Peritonoscopy(n=2)	0%	1(100%)	1(100%)	1(100%)

Table 4; Treatment outcome

Outcome	No. of patients(N=148)	Percentage
Cured	144	97.25%
Default	0	0%
Relapse	0	0%
Died	4	02.75%
Total	148	100%

Table 5; Treatment related complications

Treatment Related Complications	No. of patients	Percentage(%)
ATT Induced Hepatitis	24	16.2%
Hyperurecemia	11	7.4%
Gastritis	9	6.08%
Nausea/ Vomitting	6	4.05%
Neuropsychitric Complications	2	1.350%
Total	52	35.08%

Table 6 ; Baseline characteristics

Baseline Investigations	Minimum	Maximum	Mean	StandardDeviation
Hb	2.30g/dl	15.9g/dl	10.8	2.48
TLC	4.3×10 ³ /ul	18.74×10 ³ /ul	7.73	2.96
ESR mm/hr	13	75	46.2	12.55
Neutrophils	42.00%	98.00%	71.11	11.63
Lymphocytes	2.00%	58.00%	19.98	10.71
PLT	14×10 ³ /ul	520×10 ³ /ul	232.23	100.0
Urea (mg/dl)	11	240	34.31	30.3
Creatinine (mg/dl)	0.02	11.60	0.96	1.23
Bilirubin(mg/dl)	0.02	1.33	.56	0.35
AST (U/L)	5	112	32.98	16.64
ALT(U/L)	10	111	35.29	15.9
ALP	51	233	112.26	37.88
Protein(g/dl)	3.5	8.73	6.61	.868
Albumin(g/dl)	2.1	5.7	4.14	.735
LDH(U/L)	67	322	215.63	51.97
Glucose(mg//dl)	65	232	104.33	19.3

Table 7; Underlying comorbidities in our patients

Comorbidities	No of patients	Percentage
Hypertention	23	11.5%
Diabetes	17	8.5%
Rheumatoid Arthritis	2	1.0%
Chronic renal disease	3	1.5%
Hypothyroidism	6	3.0%
COPD	14	7.0%
SLE	2	1.0%
CML	1	0.5%
Coronary artery disease	4	2.0%
Lung Ca.	2	1.0%

Discussion

In our study of extra-pulmonary tuberculosis 106 patients were in the age group of 20-45 years. Our study is consistent with the study done by Ogboi s. j. et al (2010) in Nigeria⁴ and with a study done by Gebretsadikberhe et al (2012) in northern Ethiopia⁵

In our study 116 patients (78.3%) were from rural area, which was consistent with the results seen by Mengistuendris et al (2014) in his study in Ethiopia⁶

In our study 36 (24.3%) were smokers. In a study conducted by Jianmingwang et al (2009)⁷, the proportion of cigarette smoking was 54.6%. I. Burnet et al (2011) in south Africa conducted a study where they have seen 56 and 60% of patients with active and latent TB infection were smokers⁸.

In our study, 2 (1.5%) were HIV positive. The seroprevalence of HIV among TB patients in a study conducted by Bahl R; Singh B et al (2007) in Jammu and Kashmir was 1.6%¹⁰. A study conducted by Mubarik et al (2010)¹¹ found that out of 1141 patients tested, 26 proved to have HIV infection. However a study conducted by D Acharyal (2007)¹² found that out of 250 cases of TB admitted, 25 cases (10%) were diagnosed as HIV positive.

In our study 80 (54%) of cases were Labourers and students. The results were comparable with a study conducted by Gebretsadikberhe et al (2012).⁵

In our study the most common presentation on admission were as :

In Tubercular lymphadenitis: Cervical swelling Decreased Appetite which was consistent with a study conducted by M. Fatih Garca et al (2013)¹³

In Pleural TB: Fever, chest pain, breathlessness, and decreased Appetite in concordance with a study conducted by Arun Gopi et al (2007) and by Mbata Godwin c et al (2015).^{14,15}

In Abdominal TB: Fever, weight loss, decreased appetite and pain abdomen in concordance with a study carried by others^{16,17}.

In CNS TB: Headache was seen in 2 consistent with a study done by N.E. Anderson et al (2010)¹⁸

In Disseminated TB: Fever, Cough, Weight loss were predominant symptoms. These features were in close concordance with the study conducted by J. Ayatollahi (2004)¹⁹.

In our study the baseline Haematological changes associated with tuberculosis have been investigated. The minimum HB in our study was 2.7g/dl and a maximum was 18.6g/dl with a mean of 10.8 ± 2.30 , TLC minimum of $4.0 \times 10^3/\text{ul}$ and a maximum of $16.74 \times 10^3/\text{ul}$ with a mean of 7.73 ± 2.80 , Platelets were minimum of 15,000 and a maximum of 4,90,000 with a mean of 232.23 ± 100.0 , the minimum neutrophil count was 42.00% and the maximum was 96.00% with a mean of 70.33 ± 11.58 . While as minimum lymphocyte count was 4.00% and the maximum was 58.00%. ESR with a minimum value of 16mm/hr and a maximum value of 77mm/hr with a mean of 46.2 ± 11.3 . Our results are comparable with a study conducted by Singh KJ, Ahluwalia G et al (2001)²⁰ and with a study conducted by Olaniyi JA et al (2003)²¹ in Nigeria.

In our study the drug related side effects were noted in 52 of cases (35.1%). ATT induced hepatitis was seen in 24 (16.2%) of the cases, Hyperurecemia in 9 (6.08%). Gastritis in 6 (4.05%), Nausea/Vomiting 2 (1.35%), Neuropsychiatric 2 (1.35%) (table 16). Our study is consistent with a study conducted by Omar kherad et al (2009)⁴ who found drug related side effects in 75 (30%) of cases, and was in concordance with other studies conducted by Xia YY et al (2007) in china.²² The treatment outcome of our study was slightly better than that conducted by Mengistu Endris et al (2014)²³. (97.2%) of cases were cured as compared to 94.8% in the above mentioned study. Genetic aspects and sample size may be the attributing factors for the difference in results.

Conclusion

Our study revealed that tuberculosis haunts younger working productive age group. Most of the patients were from rural areas where poverty, ignorance and lack of adequate health facility still prevail. Males were more commonly affected than

females so were labourers and students as compared to other professions. These results again point to development of disease in those individuals who work in crowded and unhygienic places. Due to low prevalence of HIV in Kashmir association with HIV is low. Symptoms vary as per the organ system involved. Most patients had good response and most common drug related side effect was hepatitis and that too with a high prevalence which further needs to be assessed in larger studies especially with regard to genetic aspects.

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