

Clinical Manifestations and Outcome among Acquired Immune Deficiency Syndrome (AIDS) Patients with Mycobacterium Tuberculosis

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Introduction: The most explosive HIV-AIDS pandemic areas in Asia and the world are India and Thailand while the common opportunistic infection in most developing countries is Tuberculosis (TB). The risk of tuberculosis disease progression is about 100 times greater in HIV sero-positive than in sero-negative people, and the mortality rate is about four times greater in HIV positive people with tuberculosis than in HIV negative people with tuberculosis.

Objectives: The objective of this study was to determine the clinical manifestations and outcome among AIDS patients with Mycobacterium tuberculosis infections.

Methods: This retrospective study was conducted at Bamrasnaradura infectious disease hospital Thailand, in which patients were identified for a period of six months and then followed up for the next six months. Adults from both sexes 16 years old and above diagnosed as AIDS-TB included in study. All the data collected by questionnaire was recorded, keyed, edited and analyzed by using Epi info 6 software and data is presented by: median and range for quantitative variables, frequency and percentage for qualitative variable.

Discussion: A series of studies have been conducted in Thailand regarding tuberculosis with AIDS. Most studies showed tuberculosis as either the first or second most common opportunistic infection among AIDS patients. A high mortality of about 30% seen among AIDS patients with tuberculosis was reported in one study. Sixteen months is reported as the mean survival time among these cases.

Results: In this study the most common clinical features observed were fever, loss of weight, and loss of appetite, cough, and enlarged lymph nodes. Oral candidiasis is most frequently occurring opportunistic infection. PPE was a very common cutaneous manifestation. Streptomycin found to be the most frequent resistant drug.

Conclusion: The majority of cases belong to the age group, which is socially and sexually active. Involvement of this group leaves a major impact on social and economical well being of the country as well as they play an important role in transmission of TB and AIDS. Lost of follow-up rate is very high and majority lost follow-up with in first month, an important factor in occurrence of drug resistance.

Key words: Tuberculosis; Acquired Immune Deficiency Syndrome (AIDS); Multi Drug Resistance (NDR).

Introduction

About 2 billion people, or one third of the world's population, are infected with Mycobacterium tuberculosis (WHO).¹ It is the leading cause of premature death among adults in less industrialized

countries. An estimated eight million new cases of tuberculosis occur each year, mostly in developing countries.² In 1993, the WHO declared tuberculosis as a global emergency and launched a worldwide surveillance, prevention and treatment programs.³ Despite these ongoing efforts and the availability of effective chemotherapy and the Bacilli Calmette-Guérin (BCG) vaccine, the tubercle bacillus continues to claim more lives each year than any other single infectious agent.⁴

The tuberculosis and HIV pandemics are closely intertwined, and when the paths of these two

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diseases cross, the results are disastrous. The risk of tuberculosis disease progression is about 100 times greater in HIV seropositive than in HIV seronegative people, and the mortality rate is about four times greater in HIV positive people with tuberculosis than in HIV negative people with tuberculosis.³⁻⁵ Most studies of tuberculosis and HIV co-infection have stressed the impact of HIV on the natural progression of tuberculosis, but mounting immunologic and virologic evidence suggests that the host immune response to tuberculosis bacillus may enhance HIV replication and accelerate the progression of HIV infection.⁶

Specific objectives of the study were, to describe the clinical manifestations of Mycobacterium tuberculosis among AIDS patients and to determine the outcome of AIDS patients with tuberculosis.

Patients and Methods

This Retrospective descriptive study was conducted at Bamrasnaradura infectious disease hospital of Thailand and data was collected from November 13, 2000 to January 8, 2001. In this study patients were identified for a period of six months and then followed up to next six months.

Inclusion Criteria two hundred patients identified from April 1st, 1999 to September 30th, 1999 at the microbiology lab of Bamrasnaradura hospital as having positive AFB test confirmed by culture and sensitivity test in the central chest hospital and being HIV positive during the study period.

130 patients included in the study on the basis of inclusion criteria and availability of files from record room. Both sexes, adults 16 years old and above, diagnosed as AIDS with TB were included.

Demographic, clinical and laboratory data were collected by reviewing medical charts.

Diagnosis of AIDS was based on AIDS classification in Thailand

Diagnosis of TB was based on TB classification in Thailand

All the data collected by questionnaire were analyzed by using EPI-INFO-6 software and data were presented by, median and range for quantitative variable, frequency and percentage for qualitative variable. The results were presented by frequency distribution, tables

Results

Among 130 patients, 96 were males (73.8%)

and 34 female (26.2%). Single were 57(46.7%) and married 55 (45.1%), separated, widowed and divorced were 2(1.5%), 4(3.3%), and 4(3.3%) respectively. Single and married patients were in majority. Similarly 21 to 30 years and 31 to 40 years age groups were in majority, 51(39.2%) and 49 (37.7%) respectively. Details of demographic data are shown in table 1.

Table 1: Demographic Characteristics among AIDS Patients with Tuberculosis, N = 130

Characteristics	No. of Cases	%
Sex		
Male	96	73.8
Female	34	26.2
Age (years)		
<21	6	4.6
21-30	51	39.2
31-40	49	37.7
41-50	16	12.3
51-60	6	4.6
>60	2	1.5
Marital status		
Single	57	46.7
Married	55	45.1
Widowed	4	3.3
Divorced	4	3.3
Separated	2	1.5

The details of clinical features are given in the table 2.

Opportunistic infections were observed any time during study period in 73(56.2%) patients; the most common infection was oral candidiasis. Opportunistic infections were divided into three groups according to the number of infections present in patient: presence of one infection was observed in 59(45.4%) cases, two infections in 10(7.8%) cases and

three infections in 2(1.5%) cases. Cryptococcal infection was second highest, others were Cytomegalo virus, Pneumocystis carinii pneumonia (PCP) Histplasmosis, Toxoplasmosis, etc; details are given in table 4.

Most of the patients 100(76.9%) were prescribed with routine treatment, i.e., 2 months INH,

Table 2: Clinical Features among AIDS Patients with Tuberculosis N = 130		
Clinical Features	Frequency	%
Fever	105	80.8
Loss of weight	84	64.6
Loss of appetite	72	55.4
Cough	72	55.4
Enlarged lymph nodes	45	36.4
Abdominal pain	20	15.4
Diarrhea	17	13.1
Weakness	13	10.0
Headache	11	8.5
Pallor	9	6.9
Shortness of breath	7	5.4
Vomiting	7	5.4
Chest pain	6	4.6
Drowsiness	6	4.6
Hemoptysis	3	2.3
Neck stiffness	2	1.5
Nausea	2	1.5
Abdominal distension	2	1.5

Table 3: Type of Tuberculosis among AIDS Patients with Tuberculosis, N = 130		
Type of Tuberculosis	Frequency	%
Pulmonary tuberculosis	57	43.8
Disseminated	42	32.3

Table 4: Opportunistic infections observed any time during study period among AIDS patients with tuberculosis, N = 73		
Infections	Frequency	%
tuberculosis		
Extra pulmonary tuberculosis	31	23.8
One infection	59	45.4
Oral candidiasis	38	29.2
Cryptococcal meningitis	6	4.6
Pneumocystis cranii pneumonia	5	3.8
Histoplasmosis	2	1.5
Herpes simplex	2	1.5
Toxoplasmosis	1	.8
Superficial fungal infection	1	.8
Oesophageal candidiasis	1	.8
Herpes zoster	1	.8
Chicken pox	1	.8
Cytomegalo virus	1	.8
Two infections	10	7.8
Cryptococcal meningitis + OC	3	2.3
Cryptococcal meningitis + CMV	2	1.5
Cryptococcal meningitis + HZ	1	.8
Cryptococcal meningitis + PCP	1	.8
OC + CMV	1	.8
OC + HS	1	.8
OC + Toxoplasmosis	1	.8
Three infections	2	1.5
Cryptococcal meningitis + OC + PCP	1	.8

OC + CMV + PCP	1	.8
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CMV = Cytomegalo virus

HZ = Herpes zoster

OC = Oral candidiasis

PCP= Pneumocystis carinii pneumonia

HS = Herpes simplex

Rifampin, Pyrizinamide and ethambutol followed by 4 months INH and Rifampin (2HRZE/4HR). Three (2.3%) patients received 2HRES/4HR, 7 (5.4%) patients were given HRZE (4 drugs) for long time depending upon their AFB status and clinical improvement as most of them had drug resistance, 8 (6.2%) patients received two or three first line drugs plus quinilone and / or Kanamycin as they were having multidrug resistance, 2(1.5%) received HEZS; both of them were resistant to rifampicin. One patient received HRZE 6 months/RZE 6 months, he had resistance to INH and streptomycin.

Nine (6.9%) patients did not receive anti tuberculous treatment, 4 of them died after diagnosis during hospitalization, 2 lost follow-up after diagnosis, 1 transferred to another hospital, 1 patient developed sulpha drug eruption (Bactrim given for PCP) during diagnosis and then lost follow-up and for 1 patient reason is not known.

Most of the patients were receiving Bactrim as prophylactic for Pneumocystis carinii pneumonia. Prior history of tuberculosis was noticed in 20 (15.38%).

As regards specimen used for diagnostic culture sensitivity, most frequent was Lymph node aspirate (36.2%) and biopsy (8.5%), followed by total (45.2%), sputum (40.8%), hemoculture 7 (5.4%), stool (3.8%) trans-tracheal aspirate (1.5%), pus from the lesions (1.5%), pleural fluid (1.5%) and cerebrospinal fluid (.8%) case.

As shown in table 5 positive specimens were placed in four categories according to the presence of organism (AFB) per field. 62 (47.7%) were 1+, 25 (19.2%) 2+, 42 (32.3%) 3+ and 1 (.8%) specimen was 4+.

Table 5: Frequency of Acid Fast Bacilli (AFB) Grading on Culture-positivity Examination among AIDS Patients with Tuberculosis, N = 130

AFB Grading	Frequency	%
1+ (1-9 AFB/100 fields)	62	47.7
2+ (1-9AFB/10 fields)	25	19.2
3+ (1-9AFB/field)	42	32.3
4+ (>9 AFB/field)	1	.8

Table 6 shows that resistance to anti-tuberculous treatment was observed in 46(35.3%) cases, 24(18.5%) were resistant to single drug, 22 (16.8%) had multi drug resistance.

Table 6: Frequency of Antituberculosis Resistant Drugs on Culture Sensitivity, N = 46		
Resistant Drugs	Frequency	%
* Single drug resistance		
Streptomycin	14	10.8
Rifampicin	6	4.6
INH	3	2.3
Ethambutol	1	.8
Total	24	18.5
* Multidrug resistance		
INH + Rifampicin	5	3.8
INH + Rifampicin + Ethambutol	2	1.5
INH + Rifampicin + Streptomycin	6	4.6
INH + Rifampicin + Ethambutol Streptomycin	5	3.8
Total	18	13.7
* Multiple drug resistance		
Rifampicin + Ethambutol	2	1.5
INH + Streptomycin	1	.8
INH + Ethambutol	1	.8
Total	4	3.1

*Single drug resistance defined as resistant to only one anti-tuberculous agent

*MDR defined as resistance to at least Isoniazid and Rifampicin.

*Multiple drug resistance defined as resistance to more than one first line anti tuberculous drugs but not the combination of Isoniazid and Rifampicin.¹⁵

Other diagnostic procedures performed were X-ray chest PA view, CT scan brain, and endoscopy and ultrasonography abdomen. X-ray chest findings were observed in 96 (73.8%) cases; in 86 (63.8%) cases findings were consistent with tuberculosis, 7 (5.4%) were non-specific and 6 (4.6%) were normal. Details of x-ray chest findings are given in table 7.

CD4 count was recorded from 11 (8.4%) sheets. CD4 count and other lab data are described in table 8.

Pleural effusion	3	2.3
Non-specific	7	5.4
Normal	6	4.6

The patients were followed up during the specified time for the hospital visits, treatment compliance and survival. Twenty five (19.2%) lost follow up within first month after diagnosis, 15 (11.5%) lost follow up with in three months, 19 (14.6%) lost follow-up with in six months, 17 (13.1%) lost follow-up with in 9 months, 2 (1.5%) lost follow-up with in 12 months, 30 (23.1%) completed the treatment for one year. Nine (6.9%) were treatment defaulters and 13(10%) died during the specified time of study. Outcome data was compiled and observed that, 30 (23.1%) completed treatment, follow-up and survived during the specified time, 13 (10%) died during this time and 86 (66.2%) lost follow-up.

Table 7: Details of X-ray Chest Finding, N = 96

X-ray Findings	Frequency	%
Reticulo nodular infiltrate	16	12.3
Patchy reticular infiltrate	12	9.2
Reticular infiltrate	8	6.2
Diffuse reticular infiltrate	7	5.4
Localized upper lobe infiltrate	8	6.2
Mixed infiltrate	5	3.8
Localized infiltrate lower lobe	1	.8
Reticular shadow	3	2.3
Diffuse interstitial infiltrate	3	2.3
Hilar/Mediastinal/Para tracheal Lymphadenopathy	4	3.1
Thickening of interstitial Lung marking	3	2.3
Haziness upper and lower lobe	6	4.6
Cavity	3	2.3
Disseminated miliary infiltrate	1	.8

Discussion

Human immunodeficiency virus induced immunosuppression is an important contributor to the TB epidemic and probably accounts for a minimum of 30% of excess TB cases during the period from 1985 through 1990.⁸

Bamrasnaradura hospital, a 600 beds hospital located in Nonthburi province, providing health care to the people of Nonthburi, Bangkok, and central area of Thailand. It was established in 1960 as an infectious disease hospital, later upgraded as tertiary care center. At present this hospital is internationally recognized as training, research and management center for HIV/AIDS. This hospital is well equipped to provide special diagnostic facilities and therapeutic management to the HIV/AIDS patients.

In this study male to female ratio was nearly 3:1, this figure is similar to two separate studies, one carried out at Montefiore Medical center New York and other carried out at Italy.^{9, 10} But it differs from previous studies of tuberculosis and AIDS infection in Thailand.^{11, 12} This controversy suggests that either in our pool females were more as compared to previous studies or the incidence of disease has risen among females.

The predominant age group was 21 to 40 years, (76.9%), and similarly single (46.7%) and married (45.1%) were in majority. The figures in these

two groups are nearly the same as mentioned in a previous study at Bamrasnaradura Hospital.¹² This similarity suggests that disease is more prevalent among socially and sexually active population.

Resistance to anti tuberculous treatment was observed in 35.5%; 18.5% were resistant to single drug, 13.7% had multidrug resistance and 3.1% had multiple

drug resistance. Among the single drug resistance the streptomycin was the most frequent drug (10.8%) and among multi drug resistant drugs combination of INH and Rifampin was frequent. Our findings are supported by a study carried out in Baku Azerbaijan.¹⁴ Single drug resistance is defined as resistance to only

Table 8: Laboratory Findings among AIDS Patients with Tuberculosis. N = 130

Variable	Frequency	Missing	Median	Minimum	Maximum
CD 4 count	11	119	46	3	360
Creatinin	62	68	0.8	0.5	11
Blood urea	119	11	69	0.7	100
ALT	64	66	28	9	111
AST	62	68	49.5	20	270
Billirubin total	57	73	0.9	0.2	12.7
ALP	46	84	130	53	883
WBC	86	44	6995	2070	27000
Haemoglobin	76	54	8.54	3	15
Haemetocrit	76	54	26	11	45
Platelet count	75	55	223000	23000	392000

one antituberculous agent. Multidrug resistant tuberculosis was defined as resistance to at least Isoniazid and Rifampicin. Multiple drug resistance is defined as resistance to more than one first line anti tuberculous drugs but not the combination of Isoniazid and Rifampicin.¹⁵

Our study showed reticulonodular infiltrate and patchy reticular infiltrate in 12.3% and 9.2% of cases respectively, while cavity and pleural effusion were least common findings. In a previous study hilar or mediastinal lymphadenopathy and diffuse interstitial infiltrate were frequent findings in X-ray chest.¹² In support of our findings one study had mentioned" higher percentage for nodular infiltrate for tuberculosis cases and interstitial or diffuse infiltrate for PCP.¹⁶

Conclusion

In our study the most common clinical

features observed were fever, loss of weight, loss of appetite, cough, and enlarged lymph nodes. These clinical features are almost consistent with previous studies.

Oral candidiasis is most frequently occurring opportunistic infection. Pruritic Papular Eruption (PPE) was a very common cutaneous manifestation. Streptomycin was found to be the most frequent resistant drug in contrast to the previous study carried out at Bamrasnaradura Hospital. Among the patients who died, disseminated tuberculosis was the most frequent diagnosis.

The majority of cases belonged to the age group, which is socially and sexually active. Involvement of this group leaves a major impact on social and economical well being of the country as well as they play an important role in transmission of tuberculosis and AIDS.

Lost of follow-up rate is very high and majority lost follow-up with in first month. This is the

main problem in controlling tuberculosis and an important factor in occurrence of drug resistance.

Patient compliance should be improved by direct counseling and through media on mass level. More over prompt diagnosis and aggressive treatment of tuberculosis are important for improving survival. DOT should be implemented wherever possible especially among the AIDS patients with tuberculosis.

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