

**COHORT STUDY OF HIV POSITIVE
AND HIV NEGATIVE TUBERCULOSIS
in PENANG HOSPITAL:
COMPARISON OF CLINICAL
MANIFESTATIONS**

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INTRODUCTION (1)

- The incidence of tuberculosis (TB) is currently increasing in HIV infected patients in many parts of the world. This has led to renewed interest in this ancient disease.
- The risk of developing TB after an infectious contact has been estimated to be 5-15%/year in HIV infected patients (compared to 5-10% during life time of non HIV infected patients).*

* Raviglione M, Harries A et al. TB and HIV: Current status in African. *AIDS* 1997;11 (suppl. B).

INTRODUCTION (2)

- HIV induced immuno-suppression modifies the clinical presentation of TB. The treatment of TB is also more complex and difficult in HIV infected patients.

OBJECTIVES

- To look at the differences in clinical presentation of TB based on their **HIV status**.
- To look at the differences in **clinical presentation** of HIV and TB co-infection based on their **CD4 counts**.

METHODOLOGY (1)

- Retrospective Study
- All cases of adult active TB treated in the Respiratory Unit, Penang Hospital from January 2004 to December 2005.
- The information was obtained from patient's medical report, TB booklet, HIV clinic record and in-patient record (if they were admitted before).
- Demographic characteristics, clinical presentation, method of diagnosis, CD4 count and HIV status were recorded and analyzed.

METHODOLOGY (2)

- Diagnosis of TB were based on clinical impression and relevant investigations including a chest radiograph, sputum examination, tissue / blood culture for *Mycobacterium Tuberculosis* and biopsy when deemed necessary by the physician.

METHODOLOGY (3)

- HIV serological testing was performed using ELISA method and confirmed by Western Blot. Absolute CD4 lymphocyte numbers were quantified.
- HIV serological testing was done routinely for all newly diagnosed adult TB cases.
- Severely immuno-compromised patient was defined as CD4 count < 200 cell/mm³.

METHODOLOGY (4)

Inclusion criteria:

- Diagnosis of TB according to the WHO criteria and the Malaysian Clinical Practice Guideline for the control and management of TB
- Adult TB patient (>12 years old)

METHODOLOGY (5)

Exclusion criteria:

- Diagnosis of active symptomatic bacterial infection (other than TB) or fungal or protozoal infection

Statistical analysis:

- Using Chi-square test (SPSS Version 13.0)

RESULTS

- Total of **820** patients treated for TB
- **103** patients are HIV infected patients (**12.6%**)
- CD4 count (mean): **108.67**

**CHARACTERISTICS OF PATIENTS TREATED FOR TB IN RESPIRATORY UNIT,
PENANG HOSPITAL 2004-2005**

	N	%
Total of Pt (REGISTERED)	969	
Total of Pt (STUDY)	820	
SEX		
▪ MALE	594	72.4
▪ FEMALE	226	27.6
AGE		
▪ 13-34 yrs	220	26.8
▪ 35-59 yrs	419	51.1
▪ > 60 yrs	181	22.1
ETHNIC		
▪ MALAY	259	31.6
▪ CHINESE	403	49.1
▪ INDIAN	121	14.8
▪ OTHERS	37	4.5
TYPE OF TB		
▪ PTB	633	77.2
▪ EXTRA-TB	102	12.4
▪ COMBINATION	85	10.4
ANTI-TB REGIMEN		
▪ EHRZ	442	53.9
▪ SHRZ	242	29.5
▪ HRZ	44	5.4
▪ OTHERS	92	11.2
COMPLICATION		
▪ CADR	47	5.7
▪ DIH	35	4.3
▪ OTHERS	11	1.3
HIV STATUS		
▪ +VE	103	12.6
▪ -VE	717	87.4

CHARACTERISTICS OF HIV AND TB COINFECTED PATIENTS IN RESPIRATORY UNIT, PENANG HOSPITAL 2004-2005

	N	%
Total HIV-TB co-infection	103	12.6
SEX		
▪ MALE	90	87.4
▪ FEMALE	13	12.6
AGE		
▪ 13-34 yrs	26	25.2
▪ 35-59 yrs	71	68.9
▪ > 60 yrs	6	5.9
ETHNIC		
▪ MALAY	27	26.2
▪ CHINESE	57	55.3
▪ INDIAN	14	13.6
▪ OTHERS	5	4.9
HIV STATUS		
▪ KNOWN CASE	38	36.9
▪ NEWLY DIAGNOSED	65	63.1
TYPE OF TB		
▪ PTB	49	47.6
▪ EXTRA-TB	19	18.4
▪ COMBINATION	35	34.0
METHOD OF DIAGNOSIS		
▪ CLINICAL	17	16.4
▪ AFB CULTURE	26	25.2
▪ AFB SMEAR	66	64.1
▪ TISSUE HPE	25	24.3
CD4 COUNT (cell/mm³) AT PRESENTATION		
▪ ≥ 500	2	1.9
▪ > 200	18	17.5
▪ ≤ 200	83	80.6

COMMON CLINICAL PRESENTATION OBSERVED IN HIV ASSOCIATED TB

CLINICAL PRESENTATION	TOTAL / PERCENTAGE
Weight loss	100 (97.1%)
Prolonged fever	92 (89.3%)
Night sweat	90 (87.4%)
Cough	73 (70.9%)
Lymph node enlargement	35 (34.0%)
Dyspnoea	31 (30.1%)
Haemoptysis	14 (13.6%)
Diarrhoea	4 (3.9%)
Per-rectal bleeding	3 (2.9%)
Meningitis	3 (2.9%)
Pleuritic chest pain	3 (2.9%)
Backache	2 (1.9%)
Intestinal obstruction	1 (1.0%)
Scrotal swelling	1 (1.0%)
Asymptomatic	1 (1.0%)

TYPE OF TUBERCULOSIS OBSERVED IN HIV +VE AND HIV -VE POPULATION

	HIV +VE	HIV -VE	P VALUE
PULMONARY TB*	49 (47.6%)	584 (81.4%)	P < 0.01
EXTRAPULMONARY TB**	19 (18.4%)	83 (11.6%)	P < 0.05
COMBINATION TB	35 (34.0%)	50 (7.0%)	NS

TYPE OF TUBERCULOSIS OBSERVED IN HIV ASSOCIATED TB AS A FUNCTION OF IMMUNE STATUS

	CD4 COUNT > 200	CD4 COUNT ≤ 200
PULMONARY TB [*]	12 (24.5%)	37 (75.5%)
EXTRAPULMONARY TB ^{**}	4 (21.1%)	15 (78.9%)

* P value: 0.842; ** P value: 0.215

NS

NS

CHEST RADIOGRAPHIC FINDING OBSERVED IN HIV +VE AND HIV -VE POPULATION

CHEST RADIOGRAPH	HIV +VE	HIV -VE	P VALUE
Normal	12 (11.7%)	48 (6.7%)	NS
Abnormal	91 (88.3%)	669 (93.3%)	
▪ Cavitating lesion	14 (15.4%)	381 (57.0%)	P < 0.01
▪ Site			
▪ UL	36 (39.6%)	562 (84.0%)	P < 0.01
▪ ML + LL	55 (60.4%)	107 (16.0%)	P < 0.01

CHEST RADIOGRAPHIC FINDING OBSERVED IN HIV ASSOCIATED TB AS A FUNCTION OF IMMUNE STATUS

CHEST RADIOGRAPH	CD4 COUNT > 200	CD4 COUNT ≤ 200
Normal*	3 (15.0%)	9 (10.8%)
Abnormal	17 (85.0%)	74 (89.2%)
▪ Cavitating lesion**	3 (15.0%)	8 (9.6%)
▪ Site		
▪ UL***	13 (76.5%)	26 (35.1%)
▪ ML + LL****	4 (23.5%)	48 (64.9%)

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* P value: 0.603; ** P value: 0.017; *** P value: 0.003; **** P value: 0.009

MANTOUX TEST RESULTS OBSERVED IN HIV +VE AND HIV -VE POPULATION

	HIV +VE	HIV -VE	P VALUE
Mantoux test			P < 0.01
▪ Positive (> 10mm)	28 (27.2%)	378 (52.7%)	
▪ Negative (< 10mm)	75 (72.8%)	181 (25.2%)	
▪ Not done	0 (0.0%)	158 (22.1%)	

**BACTERIOLOGICAL RESULTS
OBSERVED IN HIV ASSOCIATED TB AS
A FUNCTION OF IMMUNE STATUS**

	CD4 COUNT > 200	CD4 COUNT ≤ 200	
Mantoux test*			
▪ Positive (> 10mm)	16 (80.0%)	12 (14.5%)	S
▪ Negative (< 10mm)	4 (20.0%)	71 (85.5%)	
Acid fast bacilli on smear**	15 (75.0%)	51 (61.4%)	NS
Acid fast bacilli culture***	3 (15.0%)	21 (25.3%)	NS
▪ Sensitive	3 (15.0%)	16 (19.3%)	
▪ Drug resistance	0 (0.0%)	5 (6.0%)	
▪ MDR	0 (0.0%)	0 (0.0%)	

* P value: 0.0001; ** P value: 0.257; *** P value: 0.240

**BACTERIOLOGICAL RESULTS
OBSERVED IN HIV ASSOCIATED TB AS
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	CD4 COUNT > 200	CD4 COUNT ≤ 200	
Mantoux test*			
▪ Positive (> 10mm)	16 (80.0%)	12 (14.5%)	S
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Acid fast bacilli on smear**	15 (75.0%)	51 (61.4%)	NS
Acid fast bacilli culture***	3 (15.0%)	21 (25.3%)	NS
▪ Sensitive	3 (15.0%)	16 (19.3%)	
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* P value: 0.0001; ** P value: 0.257; *** P value: 0.240

**THE CLINICAL PICTURE OF TB
DEPENDS ON THE STAGE OF
HIV INFECTION & ASSOCIATED
DEGREE OF IMMUNODEFICIENCY**

DISCUSSION

Tuberculosis has become of interest due to increased prevalence in many countries. The HIV pandemic has changed TB, from an endemic disease to worldwide epidemic.

TB-HIV COINFECTION

- In early HIV infection, the features are characteristic for post primary TB and resemble those seen in the pre-HIV era.
- More advanced immunodeficiency is usually associated with an increased frequency of disease resembling primary pulmonary TB and extra-pulmonary disease.

Perronne C et al. Tuberculosis in patients infected with the HIV. *Presse Med* 1998.

Jones BE et al. Relationship of the Manifestations of TB to CD4 counts in patients with human immunodeficiency virus infection. *Am Rev Respir Dis* 1993; 148: 1292-1297.

L. Aaron et al. TB in HIV infected patients: A comprehensive review. *Euro Society of Clin Microbio and Infect Dis* 2004.

CLINICAL MANIFESTATION

- Prolonged insidious symptoms found in majority of patients consisting of weight loss, prolonged low grade fever and nocturnal sweat may delay the diagnosis.
- The classical picture of pulmonary TB is seen mainly in less immuno-compromised patients (CD4 count > 200 cells/mm³).

L. Aaron et al. TB in HIV infected patients: A comprehensive review. *Euro Society of Clin Microbio and Infect Dis* 2004.

CLINICAL MANIFESTATION

- All varieties of extra-pulmonary TB have been described in HIV infected patients. Isolated extra-pulmonary localizations are described in 53-63% of HIV associated TB cases.*

(In our series, only 18.4% are isolated extra-pulmonary)

Perronne C et al. Tuberculosis in patients infected with the HIV. *Presse Med* 1998.

Jones BE et al. Relationship of the Manifestations of TB to CD4 counts in patients with human immunodeficiency virus infection. *Am Rev Respir Dis* 1993; 148: 1292-1297

MANTOUX TEST

- The contribution of skin test / Mantoux test for TB diagnosis depends on the immune status.
- During active TB, the Mantoux test is positive in 30% of HIV infected patients with a CD4 count $< 200/\text{mm}^3$ and in 50% of those with CD4 count $> 200/\text{mm}^3$.

(In our series, it is 14.5% and 80.0% respectively)

Jones BE et al. Relationship of the Manifestations of TB to CD4 counts in patients with human immunodeficiency virus infection. *Am Rev Respir Dis* 1993; 148: 1292-1297

CHEST RADIOGRAPH

- Atypical features like lower lobe involvement with diffuse infiltrations are more commonly seen than cavitation.
- Cavitating lesions are rarely seen in patients with a CD4 count $< 200/\text{mm}^3$.
- Chest radiograph is normal in 8-20% despite the presence of smear positive sputum.*
(In our series, it is 11.7%)

Perlman DC et al. Variation of chest radiographic patterns in pulmonary tuberculosis by degree of HIV related immunosuppression. CPCRA. *Clin Infect Dis* 1997.

Perronne C et al. Tuberculosis in patients infected with the HIV. *Presse Med* 1998; 17: 1479-1483

CONCLUSION

- Worldwide incidence of TB is **increasing**, particularly in areas where HIV is prevalent.
- The CD4 count **does not** predict the occurrence of TB.
- Majority of HIV co-infected patients presented with **prolonged, insidious and non specific symptoms** like weight loss, fever and night sweats.

CONCLUSION

- HIV and TB co-infected patients with CD4 count ≤ 200 are more likely to have **atypical chest radiographs**.
- Mantoux test is **not helpful** to diagnose TB in those with late HIV disease.
- Therefore to diagnose TB in severely immunocompromised HIV patients, we need to have **high index of suspicion**.

THANK YOU