

CHAPTER II

LITERATURE REVIEW

The researcher has divided the literature review into the 3 sections: 1) relationship between TB and HIV, 2) relevant scientific findings in characteristics of HIV/TB co-infection, and 3) WHO guidelines on management of TB/HIV.

2.1 Relationship between TB and HIV

Aderaye et al. (2004) studied the relationship between HIV status and pulmonary tuberculosis in Addis Ababa. A total of 168 patients with diagnosis of pulmonary AFB culture- positive tuberculosis had their chest X-rays in 2002. Their medical records were reviewed for site, pattern, and extent of disease. The study found that mycobacterial colony count reduced in TB patients with HIV compared to HIV-negative patients ($p=0.002$).

Mohammad and Naing (2004) studied characteristics of HIV-infected tuberculosis patients in Kota Bharu Hospital, Kelant, Malaysia. A descriptive study was carried out on 149 HIV-infected TB patients during 1998 and 2001. The study found that among HIV-infected TB patients 45% (67 patients) of them presented with cough and only 51% of them (76 patients) had a positive sputum smear while sputum smear is positive is 65% to 80% in TB patient without HIV.

Zhang et al. (1995) in 1994 studied a relationship between mycobacterium tuberculosis and human immunodeficiency virus-1 replication in New York University Medical Center, New York, United States. Specimens (blood and sputum) of the 3 HIV infected TB patients were tested with in-dept microbiology, immunology and molecular laboratory method. The studies found that synergistic interaction between HIV and TB organisms increased P24 (HIV antigen) level. That means TB and its components may activate HIV replication. Stimulation of HIV-1 replication by TB can exacerbate dysfunction of the host immune response in dually infected individual.

Day et al. (2004) in 2003 tried to answer a question “Does Tuberculosis increase HIV load?”. An observational cohort study was designed to study 80 HIV infected patients in South Africa. Of these, 30 of them were TB patients and 50 were in the control group. The study found that HIV viral load was higher in TB group than the non-TB group (4.73 vs. 4.24 \log_{10} copies/ml, $p=0.003$).

Juffermans et al. (2001) in 2000 studied patients with active Tuberculosis and HIV coreceptors CXCR4 and CCR5 on CD⁺T cells. A case-control study was designed in hospitals, centers in Amsterdam, Netherlands. Blood specimens of 8 healthy persons in control group and 8 TB patients in the case group were tested using microbacterial and molecular laboratory methods. The study found elevated expression of HIV coreceptors (CXCR4 and CCR5) that progress HIV infection. This study supports the idea that blocking these coreceptors may slow progression of HIV infection during co- infection.

In summary, HIV caused AFB count reduction that made AFB positive sputum smear lower in HIV-infected patients compared with the level in non HIV-TB patients. In contrast, TB may enhance HIV replication that showed higher HIV viral load in TB than non TB group. In addition, TB can speed up HIV progress by elevating of HIV coreceptors.

2.2 Relevant scientific findings in characteristics of HIV/TB co-infection

Quy et al. (2006) from 1998 to 2000 studied drug resistant among smear-positive tuberculosis patients in Ho Chi Minh City, Vietnam. A random sample of patients diagnosed TB by the national TB program (NTP) was offered HIV testing and submitted sputum for mycobacterium tuberculosis drug sensitivity testing. This study examined the prevalence of HIV infection and anti-TB drug resistance and the relationship between these factors and TB treatment outcomes in 2196 TB patients. This study found that mortality was associated with HIV-infection (adjusted odd ratio [aOR] 30.9, 95% CI 13.7-69.8). The risk of treatment failure was associated with drug resistant but not with HIV status. However, it only examined outcomes for a small number of HIV patients (51 HIV patients only) and did not analyze factors associated with poor treatment outcomes in HIV-infected TB patients.

Mohammad & Naing (2004) from 1998 to 2001 studied characteristics of HIV-infected tuberculosis patients in Kota Bharu Hospital, Kelant, Malaysia. A descriptive study was carried out on 149 HIV-infected TB patients. The studied found that majority of patients were male (94.6%), single (45%) and an average age was 34

years. The most common HIV transmission category was through injection drug users (73%).

Diez Ruiz-Navarro et al. (2005) from 1996 to 1997 studied effects of HIV status and other factors on outcome of tuberculosis treatment in Spain. A retrospective cohort study was designed to study 4899 new tuberculosis cases. The study found that 64% of patients were male, and IDU was not a common HIV transmission category (only 8%). Satisfactory outcome was 43% in HIV-infected patients vs. 71% in non HIV patients, mortality rate was 21% vs. 6%, and unsatisfactory outcomes were 35% vs. 23% ($p < 0.05$). Mortality rate increased in drug use group (non intravenous group) (aOR=1.97; 95%CI 1.01-3.99) while unsatisfactory outcomes (failure and transferred out) increase in IDU (aOR = 1.71; 95%CI 1.06-2.75), and increase in women (aOR= 2.05; 95% CI=1.19-3.54).

Anunnatsiri et al. (2005) in 2004 studied factors associated with treatment outcomes in pulmonary tuberculosis in the Northeastern Thailand. Factors related to treatment outcomes in smear-positive pulmonary tuberculosis were evaluated in 226 adult patients. The studied found that old age (cutting point was not available) was associated with treatment failure/dead (OR 44.1; 95%CI 2.0-983.7), HIV co-infection (OR 27.5; 95%CI 1.3-560), and previously treated tuberculosis (OR 9.7; 95%CI 1.6-59)

Connolly et al. (1998) from 1991 to 1995 studied impact of the human immunodeficiency virus epidemic on mortality among adults with tuberculosis in

rural South Africa. Data was extracted from control program database to examine the impact of the HIV epidemic on mortality among adults with tuberculosis from 1991 to 1995. This study found that mortality rate in HIV-infected TB patients was 45% and risk factor for high mortality rate was older age (cutting point was not available) ($p < 0.001$), HIV infection (OR 3.5; 95%CI 2.3-5.4) and smear negative (OR 2.5; 95%CI 1.8-3.5).

Atomiya et al. (2002) from 1996 to 1997 carried out an evaluation of disease patterns, treatment and prognosis of tuberculosis in AIDS patients. The medical records of the 100 HIV infected TB patients were evaluated retrospectively. Of these, 76% were male, an average age was 36 years old. HIV transmission route was sexual transmission (68%). Mortality was 12% and success treatment was 74%. Fever was found on 83% of all patients, cough was found on 65% and weight lost was accounted for 51%. AFB smear was positive on 50% of pulmonary TB patients.

Wobeser et al. (1999) from 1992 to 1993 studied outcome of pulmonary tuberculosis treatment in the tertiary care setting-Toronto 1992/1993. Consecutive cases of culture proven pulmonary TB were obtained on 145 patients. Median age was 41 in all patients and there were 32 in HIV-infected TB patients. Prevalence of drug use category was 18 % in HIV-infected TB patients. Nine percent of them had previous TB treatment. Seventy seven percent presented with HIV related symptoms. This study found that completed treatment was 27% vs. 58% and mortality was 23% vs. 17% in HIV infected TB and non-HIV patients, respectively. Factors of treatment failure were injection drug use (aOR 5.7; 95%CI 1.5-22), HIV infection (aOR 2.9;

95%CI 1.4-14.7), and adverse drug reaction (aOR 2.9; 95%CI 3.9-66.4). An increased risk of death was associated with age greater than 50 years old (aOR 16.7, 95% 2.6-1.5.1) and having HIV infection (aOR 16.1, 95%CI 3.9-66.4).

Lawn and Acheampong (1999) in 1998 studied factors associated with pulmonary tuberculosis mortality in adults at Ghanaian Teaching hospital. The medical records and chest radiographs of 160 TB patients were retrospectively reviewed, of these 80 died and 80 were cured during the same period. This study found that mortality was also associated with increased age (cutting point was not provided) ($p<0.001$), residence in a rural area ($p<0.05$), and sputum smear-negative disease ($p<0.01$). In addition, patients who died were 2.1 times more likely to have a history of previous TB treatment ($p<0.01$).

Witor et al. (1999) from 1995 to 1998 studied efficacy of trimethoprim-sulphamethoxazole (co-trimoxazole) prophylaxis and morbidity and mortality in HIV-infected patients with tuberculosis in Abidja, Cote d'Ivoire. A randomized controlled trial was conducted on 771 HIV-infected TB patients. This study found that 61% of patients were male and median age was 33. Daily co-trimoxazole prophylaxis was well tolerated and significantly decreased mortality (decreased risk 46%; 95%CI 23%-62%, $p<0.01$) and hospital admission (decreased risk 43%; 95%CI 10%-64%, $p=0.02$).

Mwaungulu et al.(2004) from 1999 and 2000 studied Co-trimoxazole which can prophylactic reduce mortality in human immunodeficiency virus-positive

tuberculosis patients in Karogra District, Malawi. A cohort study with a historical comparison group was conducted in 717 TB patients, 70% of them were HIV-positive. Co-trimoxazole was offered to HIV-infected patients in addition to routine care. The study found that overall TB mortality rate reduced from 37% to 29%. Although TB mortality rate was unchanged between 2 years in HIV-negative patients, it reduced from 43% to 24% in HIV-infected patients. This study concluded that Co-trimoxazole prophylaxis should therefore be added to the routine care of HIV-infected TB patients.

Dean et al. (2002) from 1996 to 1999 studied treatment of tuberculosis in HIV infected persons in the era of highly active antiretroviral therapy (HAART). Medical records of 188 HIV infected TB patients were reviewed retrospectively in London, UK. The study found that HAART significantly associated reduction in viral load, mortality and AIDS defining illness. Three and a half percent of cases in HAART had AIDS defining illness compared with 24.5% of cases without HAART (RR=0.14).

Girardi et al. (2001) from 1995-1998 studied changing clinical presentation and survival in HIV-associated tuberculosis after highly active antiretroviral therapy (HAART) in Roma, Italy. Clinical charts of 67 HIV-infected TB patients in 1995-1996 and 51 HIV-infected TB patients in 1997-1998 were reviewed. Decreased risk of dying was observed in patients starting HAART after TB diagnoses (aOR=0.14; 95%CI 0.03-0.57). The study concluded that HAART is a major factor in prolonging life in the HIV-infected TB patients.

TB treatment outcome in Vietnam (WHO, 2002; 2003; 2004): treatment outcome in all new sputum smear (+) nationwide from 2000-2002 was quite stable. The cure rates were 89.9% in 2000 and 90.5% in 2002. Death rates were increasing slightly as it was 3.1% in 2000 and 3.4% in 2002 as shown in Table 1.

Table 1 TB treatment outcomes of AFB (+) patients in the national reports

Year	Total # of treated patients	Treatment outcomes					
		Cure rate (%)	TC rate* (%)	Death rate (%)	Failure rate (%)	Default rate (%)	TO rate** (%)
2000	53,158	89.9	2.2	3.1	1.0	1.8	1.9
2001	54,178	91.0	1.6	3.1	1.0	1.8	1.9
2002	56,150	90.5	1.9	3.4	0.8	1.5	2.0

* *Treatment completed rate* ** *Transfer out rate*

TB treatment outcome in An Giang (An Giang report on TB, 2004): treatment outcomes in all new sputum smear (+) in An Giang province was high. The cure rates were 92.2% in 2000, 93.1% in 2001 and 93.0% in 2002. Death rates were increased slightly with 3.9% in 2000 and 2001 then to 4.1 in 2002 as shown in Table 2.

Table 2 TB treatment outcomes of AFB (+) patients in An Giang provincial reports

Year	Total # of treated patients	Treatment outcomes						
		Cure rate (%)	TC rate (%)	Death (%)	rate	Failure rate (%)	Default rate (%)	TO rate (%)
2000	3420	92.2	0.1	3.9		2.6	0.8	0.3
2001	3868	93.1	0.1	3.9		1.6	0.8	0.4
2002	4566	93.0	1.1	4.1		1.0	0.7	0.1

In summary, HIV-infected TB patients were more male and young. In most studies the transmission route was injection drug use. HIV-infection increased risk of death. Cure rate of TB treatment was much lower and death rate was much higher in TB patients with HIV-infection. Many studies found that mortality rate in HIV-infected TB patients associated with older age, female, drug users, adverse event, rural residence, and Cotrimoxazole prophylaxis. Lastly, ARV improved TB treatment outcomes significantly in HIV-infected TB patients.

2.3 WHO guidelines on management of TB/HIV (WHO, 2006)

A. Establish mechanisms for collaboration

- 1 Set up a coordinating body for TB/HIV activities at all levels
- 2 Conduct surveillance of HIV prevalence among tuberculosis patients
- 3 Carry out joint TB/HIV planning
- 4 Conduct monitoring and evaluation

B. Decrease the burden of tuberculosis in people living with HIV/AIDS

5. Establish intensified tuberculosis case-finding
6. Introduce isoniazid preventive therapy
7. Ensure tuberculosis infection control in health care and congregate settings

C. Decrease the burden of HIV in tuberculosis patients

8. Provide HIV testing and counselling
9. Introduce HIV prevention methods
10. Introduce co-trimoxazole preventive therapy
11. Ensure HIV/AIDS care and support
12. Introduce antiretroviral therapy