

## CHAPTER I

### INTRODUCTION

#### 1.1 Background and Significant of the problem

Human immunodeficiency virus and Tuberculosis (HIV/TB) co-infection is a serious public health issue in countries that have high TB burden. HIV fuels TB epidemic in several ways. Up to 50% of people living with HIV and acquired immunodeficiency syndrome (AIDS) develop TB during their lifetime, compare to 5%-10% of HIV negative persons (World Health Organization [WHO], 2004). HIV infected patients have reduced mycobacterial colony count compare to HIV-negative patients (Aderaye et al., 2004). As high as 55% of pulmonary tuberculosis in HIV infected patients present with negative sputum smear that will be predisposal them to poor treatment outcome as it may cause delay of tuberculosis diagnosis and initiation of anti TB therapy (Trinh et al., 2006). Treatment outcome on TB cases with HIV is also worse than those with HIV negative. A study in Atlanta, USA, from 1995 to 2001 showed that risk of death increased 3 times in patients who were HIV positive (Romo-Garcia et al., 2004). In South Africa, HIV positive status patients had an increased risk of TB treatment failure 2 times and mortality up to 7 times (Rustomje et al., 2004). Another study between Royal Foundation of TB Elimination (KNCV) and Pham Ngoc Thach hospital found that the cure rate of TB treatment reduced 1.8 times in HIV infected (Quy et al., 2006). Moreover, direct observation treatment sort course (DOTS) strategy just relies on passive TB case finding that healthcare workers wait

for patients to come in when they have developed suspected TB symptoms. This practice can cause delay in diagnosis as 45% of HIV patients presented with cough symptoms while only 51% had positive sputum smear (Mohamad & Naing, 2004)

### *TB epidemic in Vietnam*

Vietnam is located in Southeast Asia that borders with China in the north, Cambodia and Lao in the west and it has a long coast in the east side (See Figure 1). Vietnam covers an area of 331,114km<sup>2</sup> and its population is 82,069 million (United Nation Development Program [UNDP], 2005). The country has 64 administrative cities and provinces. About 70% of the population earn a living from farming. The GDP per capita is 553 USD in 2005.

Vietnam ranked 13<sup>th</sup> out of 22 countries with high TB burden in the world in 2005 (WHO report, 2005). This is a country with high TB burden, and prevalence of all TB forms was 240/100,000 population in 2004 (Huong et al., 2005). The National TB Control Program (NTP) has gained a great achievement for the prevention and control of TB that leads this country to meet 100% DOTS coverage since 2002. Vietnam is one of the first of 22 countries to reach WHO target for successful DOTS implementation, including more than 70% case detection and more than 85 % cure for new, smear-positive TB cases since 2000 (Huong et al., 2005). Nevertheless, Vietnam has seen stable or rising case notification, and HIV may be an important cause of this. KNCV experts predict that every year 10% of the HIV infected people in Vietnam will be infected with TB and 50% of them will develop active TB (KNCV, 2004).



Figure 1 Map of Vietnam (The World Factbook, 2006)

### *HIV epidemic in Vietnam*

The first HIV infected case in Vietnam was identified in 1990 (Vietnam Ministry of Health, 2003). By the end of May 2006, the reported number of cumulative HIV infected cases was 108,789. Of these, 18,421 had developed AIDS

and 10,717 had died. HIV epidemic is still at the concentration stage that seriously fueled by injection drug use and prostitution. UNAIDS estimated that there were 220,000 HIV infected people in Vietnam by the end of 2003 (UNAIDS, 2004) (see Figure A1 in Appendix A). The sentinel surveillance showed that proportion of HIV infection in TB cases increased from 1.82% in 2000 to 4.7% in 2004 (Vietnam Ministry of Health, 2003) (see Figure A2 in Appendix A). This proportion is at alarm level in some provinces and cities that HIV prevalence is high. In addition, TB prevalence among HIV patients was from 25%-38% in various studies (Le et al., 2001; Louie et al, 2004; An Giang report on HIV, 2005) (see Figure A3 in appendix A)

#### *TB and HIV in Angiang*

An Giang is a province on the South West of Vietnam that borders with Cambodia. There are one city, one township and 9 districts with 145 communes in this province (see Figure 2). Its population is 2,152,736 (An Giang report on HIV, 2005). Agriculture, construction industry and trade service have contributed to the development of this city 38%, 13% and 48%, respectively in 2004. The GDP per capita was \$387 in 2004.

An Giang ranked first out of 64 provinces in Vietnam in TB prevalence that was 252/100,000 in 2004 (National TB program report, 2005). This province has implemented a program of routine HIV testing for all TB patients since 1996. Patients are offered brief pre-test counseling, followed by more extensive post-test counseling based on HIV test results. In 2004, there were 5,463 patients diagnosed

with TB who then all enrolled in treatment. Of these, 5,376 (98%) were HIV-tested, and 192 (3.6% of 5,376) were HIV-positive.

An Giang ranked 5th in HIV prevalence in Vietnam that was 199/100,000 in 2004 (Vietnam Ministry of Health, 2004). HIV tests have been carried on persons presenting with AIDS symptoms, clients of voluntary counseling and testing (VCT) services and individuals from the sentinel surveillance groups that consists of injection drug users (IDU), commercial sex workers (CSW), military recruit, sexual transmission diseases (STD) patients, TB patients, and blood donors. In order to provide good HIV care and prevention to TB patients, all TB patients have been screened with HIV since 1996. The Preventive Medicine Center (PMC) in An Giang province has started providing leadership and funding for annual chest x-ray (CXR) screening on all people living with HIV/AIDS (PHA) in the province in 1999. Regular data collection within this program did not begin until 2001. The rationale for this program was that there were high rates of HIV in this province, and TB was noted as the most common opportunistic infection (OI) among those individuals.

As TB/HIV is a significant public health issue and there is limited study to address this issue in Vietnam. Therefore, I proposed a retrospective cohort study to evaluate characteristics and factors associated with unsuccessful treatment outcomes of the HIV-infected TB patients in An Giang province, Vietnam.



Figure 2 Map of An Giang Province where study is implemented (An Giang statistic data, 2004)

## **1.2 Research objectives**

The objectives of this study are:

1. To describe characteristics of HIV-infected TB patients in An Giang from 2001 to 2004
2. To describe TB treatment outcomes of HIV-infected TB patients in An Giang from 2001 to 2004
3. To determine possible factors associated with unsuccessful TB treatment outcome among HIV-infected TB patients

## **1.3 Research questions**

1. What are characteristics of HIV-infected TB patients in An Giang province from 2001 to 2004?
2. What are TB treatment outcomes of HIV-infected TB patients?
3. What are factors (for example, demographic, behavior, economic, education, and clinical factors) that associate with treatment outcomes on HIV-infected TB patients in An Giang province?

## **1.4 Research hypotheses**

HIV-infected TB patients are young, have low income jobs, and have low education. They get HIV infected through both injection drug use (IDU) and sexual route.

1. TB treatment outcomes of HIV-infected TB patients are worse than ones of TB non HIV patients.

2. Factors associated with unsuccessful treatment outcome are younger age-group, female, low education, from rural areas, IDU, re-treatment patients, having adverse events during TB treatment, and having HIV care and treatment.

### 1.5 Variables to be studied

The following variables will be studied in this research:

- *Socio-demographic data:* location (urban/rural area), date of birth, gender, education level, ethnicity, religion, marital status, occupation, time of HIV diagnoses, risk behavior group (IDU or CSW),
- *Clinical data:* - HIV symptoms at time of diagnoses, getting co-trimoxazole prophylaxis therapy (to prevent opportunistic infections among HIV-infected patients), getting ART treatment,
  - TB data: having chest x-ray screening for TB diagnoses, CXR results, history of TB treatment, symptoms of TB, acid fast bacilli (AFB) status, registration status (see section 1.7), TB initial treatment regiment, 2<sup>nd</sup> TB treatment regiment, reasons for change TB treatment, final treatment outcomes, hospitalize at time of TB diagnoses.

### 1.6 Definition

#### A. Definitions of tuberculosis cases (WHO, 2006)

- *Case of tuberculosis:* A patient in whom tuberculosis has been confirmed by bacteriology or diagnosed by a clinician.



- *Definite case*: A patient with positive culture for the *Mycobacterium tuberculosis* complex. In countries where culture is not routinely available, a patient with 2 sputum smears positive for acid-fast bacilli (AFB+) is also considered a definite case.
- *Pulmonary case*: A patient with TB disease involving the lung parenchyma.
  - *Smear-positive pulmonary case*: A patient with at least 2 initial sputum smear examinations (direct smear microscopy) AFB+; or one sputum examination AFB+ and radiographic abnormalities consistent with active pulmonary tuberculosis as determined by a clinician; or one sputum specimen AFB+ and culture positive for *M. tuberculosis*.
  - *Smear-negative pulmonary case*: A patient with pulmonary tuberculosis not meeting the above criteria for smear-positive disease.
  - Diagnostic criteria should include at least 3 sputum smear examinations negative for AFB; and radiographic abnormalities consistent with active pulmonary TB; and no response to a course of broad-spectrum antibiotics; and decision by a clinician to treat with a full course of anti-TB therapy; or positive culture but negative AFB sputum examinations.
- *Extrapulmonary case*: A patient with tuberculosis of organs other than the lungs (e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges). Diagnosis should be based on one culture-positive

specimen, or histological or strong clinical evidence consistent with active extrapulmonary disease, followed by a decision by a clinician to treat with a full course of anti-TB chemotherapy. Note that a patient diagnosed with both pulmonary and extrapulmonary tuberculosis should be classified as a pulmonary case.

- *New case*: A patient who has never had treatment for tuberculosis or who has taken anti-TB drugs for less than 1 month.
- *Relapse case*: A patient previously declared cured but with a new episode of bacteriologically positive (sputum smear or culture) tuberculosis.
- *Re-treatment case*: A patient previously treated for tuberculosis, undergoing treatment for a new episode of bacteriologically-positive tuberculosis.

#### **B. Definitions of treatment outcomes (WHO, 2006)**

- *Cured*: An initially smear-positive patient who was smear-negative in the last month of treatment and on at least one previous occasion.
- *Completed treatment*: A patient who completed treatment but did not meet the criteria for cure or failure.
- *Died*: A patient who died from any cause during treatment.
- *Failed*: A smear-positive patient who remained smear-positive at month 5 or later during treatment.
- *Defaulted*: A patient whose treatment was interrupted for 2 consecutive months or more.

- *Transferred out:* A patient who transferred to another reporting unit and whose treatment outcome is not known.
- *Successfully treated:* A patient who was cured and who completed treatment.