



High Incidence and Poor Outcome in Smear Positive Elderly Pulmonary Tuberculosis: Surin Hospital, Thailand

P Sueyanyongsiri*, N Sumpansirikul and S Sueyanyongsiri

Surin Hospital, Affiliated Institutes of Suranaree University of Technology, Thailand

*Corresponding Author: P Sueyanyongsiri, Surin Hospital, Affiliated Institutes of Suranaree University of Technology, Thailand.

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Abstract

Background: Age-related factors not only increase the risk of TB reactivation but also enhance susceptibility to TB infection, abetting outbreaks, high co-morbidity and high mortality. This study aim to evaluated incidence and prognostic factors that effected mortality in elderly smear positive pulmonary tuberculosis.

Methods: A five years retrospective cohort study of smear positive pulmonary tuberculosis patients from January 2013 to December 2018. This study was conducted at Surin hospital, a secondary-care referral center in Thailand. The inclusion criteria were age 15 years, smear positive. The identified patients were divided into two groups. Patients: age 15-69 years and age higher than 69 year. All of the general data and medical records for the enrolled patients were reviewed. Patients who had diabetes, acquired immunodeficiency syndrome (HIV disease), chronic kidney disease, cirrhosis or age more than 69 years were defined as immune-compromised host. Relative risk was used. Significance testing by chi-square, Fisher's exact test and time-to-event curves were generated by the Kaplan-Meier method and compared using the log-rank test. Cox proportional hazards regression analysis was performed to identify prognostic factors for 40-day survival after admission.

Results: In 5844 patients of tuberculosis from 2013 to 2018 have 675 patients identified that smear positive pulmonary tuberculosis, 401 were in control group and 134 were in the elderly group, 140 patients died and 535 patients survived. In the elderly age group, female was higher than male. The elderly group had statistically significant difference higher in acute respiratory failure and chronic kidney disease, but lower in HIV disease. The mortality rate increased continuously with age, risk difference 6.5% per 20 years. In elderly group are increase mortality rate, relative risk 1.55 times. There had statistically significant difference between two groups in mortality by univariable Cox's regression analysis (hazards ratio=1.56; 95%confidence interval=1.10-2.20; P=0.012) and by multivariable Cox's regression analysis (hazards ratio=1.76; 95% confidence interval=1.23-2.54; P=0.002) were associated with 40 days survival. The medial survival was 17 and 35 days in elderly and control group, significant in log rank test (P<0.010).

Conclusion: In the elderly age group, female was higher than male. Mortality in the elderly was remarkably higher than in younger, and increased continuously with age.

Keywords: Diabetes; Acquired Immunodeficiency Syndrome (HIV Disease); Chronic Kidney Disease; Cirrhosis; Critical Care; Acute Respiratory Failure; Mortality; Age

Introduction

The incidence of tuberculosis (TB) has increased around the world over the last decades. It is still a major cause of mortality worldwide. Today, TB is the leading cause of death associated with a single infectious pathogen. Previous studies have suggested that even in developed countries, its incidence in the elderly is increasing [1]. An increase in the burden of TB has not only been seen in endemic areas but also in high-income countries and intensive care unit populations. The elderly have documented very high rates of disease particularly in nursing homes [2]. Some study had

suggested that pulmonary TB in the elderly presents somewhat atypical symptoms and high mortality of the disease [3,8]. Even in developed countries where the overall incidence of TB is low, pulmonary TB remains common in the elderly [4]. Increases in the old age population due to prolonged life expectancy have increased the use of drugs that suppress immunity, decreased immunity during increased age and may further increase the incidence of pulmonary TB among the elderly in the future [5]. Many studies have been performed on the pulmonary TB in elderly [6,7]. Several factors may predispose the reactivation of pulmonary TB. These include liver

diseases, *Diabetes mellitus* (DM), chronic kidney disease (CKD), human immunodeficiency syndrome (HIV) and immunosuppressive drug intakers (IDI). Many studies found that in elderly group to be more likely to have more underlying diseases that suppress cellular immunity [9,12]. Age-related factors not only increase the risk of TB reactivation but also enhance susceptibility to TB infection, abetting outbreaks, high co-morbidity and high mortality. This study aimed to evaluate incidence and prognostic factors that might be effects of mortality in elderly smear positive pulmonary TB in Surin hospital, Thailand.

Material and Methods

Study subjects

This retrospective study was conducted at the Surin Hospital, a referral center in Thailand, where the 2016 incidence and mortality rate of TB was 62 and 3.3 per 100,000 population, respectively. The database of the data centre records was searched to identify TB patients between January 2011 and December 2017. The inclusion criteria were age >15 years, acid-fast smear positive pulmonary TB, radiographic findings suggestive of tuberculosis. The identified patients were divided into two groups. Patients: age 15 - 69 years and age higher than 69 years. The hospital's Research Ethics Committee (REC) approved the study.

Data collection

All of the medical records for the enrolled patients were reviewed. Patients who had diabetes, HIV, CKD, cirrhosis or IDIs with age more than 70 years were defined as immune-compromised host. The primary end point was short term, 40 days survival.

Statistical analysis

Inter-group difference was calculated using the Fisher's exact test for categorical variables, as appropriate. Relative risk was used. Significance testing by chi-square, Fisher's exact test and time-to-event curves were generated by the Kaplan-Meier method and compared using the log-rank test. Cox proportional hazards regression analysis and risk difference regression model was performed to identify prognostic factors for 40-day survival after admission. The potential factors included age, sex, immune-compromised status, performance of acid-fast smears of respiratory specimens and initiation of anti-TB therapy within 2 weeks of admission. Significance levels for entry into the uni-variable and multi-variable hazard ratio procedure were used. Two-sided $P < 0.05$ was considered significant.

Results

In 5844 patients of tuberculosis from 2013 to 2018 have 675 patients identified that smear positive pulmonary tuberculosis, 401 were in control group and 134 were in the elderly group, 140

patients die and 535 patients survived. In the elderly age group, female was higher than male. The elderly group had statistically significant difference higher in acute respiratory failure and chronic kidney disease, but lower in HIV disease. The baseline characteristics in elderly and control group are compared in Table 1. The incidence of smear positive pulmonary TB increasing by age groups that are presented by histogram in Figure 1. Mortality in different age groups presented in Figure 2. The mortality rate increased continuously with age, risk difference 6.5 per cent per 20 years. The elderly group are with increase in mortality rate, and relative risk 1.55 times. There had statistically significant difference between two groups in mortality by univariable Cox's regression analysis (hazards ratio = 1.56; 95% confidence interval = 1.10 - 2.20; $P = 0.012$) and by multivariable Cox's regression analysis (hazards ratio = 1.76; 95% confidence interval = 1.23-2.54; $P = 0.002$) were associated with 40 days survival after adjust sex, HIV, CKD, DM and cirrhosis. Table 2 presented hazard ratio in multivariable analysis and Figure 3. showed the survival curved after adjusted confounders. The medial survival was 17 and 35 days in elderly and control group, significant in log rank test ($P < 0.010$).

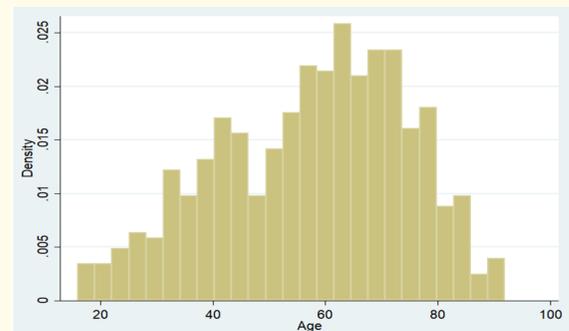


Figure 1: Histogram presented incidence of smear positive pulmonary tuberculosis in age group.

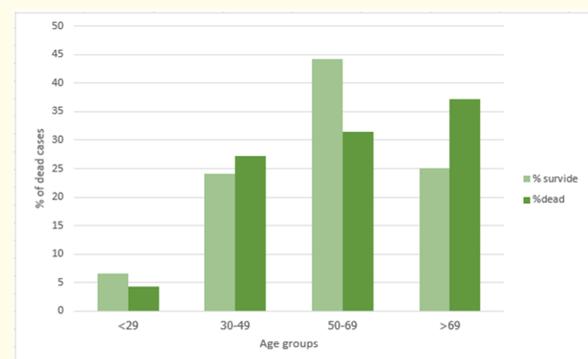


Figure 2: Mortality rate, risk difference between death and survival with age groups.

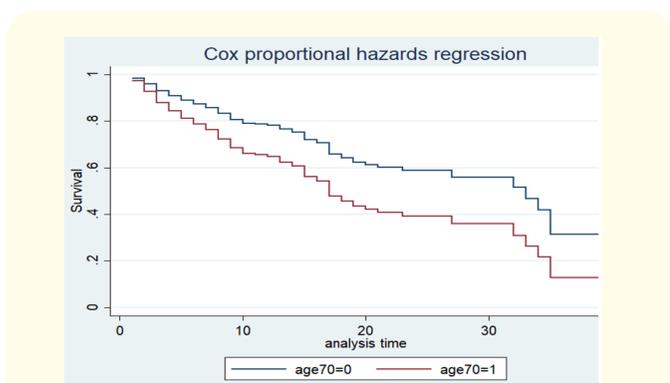


Figure 3: Multivariate Cox's Regression analysis for mortality.

	Age≤ 69		Age > 70		P-value
	(n)	%	(n)	%	
N	439		186		
SEX (M)	327	66.87	102	54.84	0.004
	50	10.22	3	1.61	<0.001
DM	58	11.86	29	11.59	0.2
CKD	29	5.93	27	14.52	0.001
Cirrhosis	15	3.07	1	0.54	0.105
ARE	112	22	57	34.34	0.002
AKI	34	6.95	17	9.14	0.332
Shock	76	15.54	34	18.28	0.415
Drug regim	474	96.93	183	98.39	0.424
dead	88	18	52	27.96	0.006

Table 1: Baseline characteristics by elderly group and control group.

M: male; HIV: human immunodeficiency virus infection

DM: diabetes mellitus; CKD: chronic kidney disease;

ARP: acute respiratory syndrome; AKI: acute kidney injury

CI: confidence interval, eGFR: estimated glomerular filtration rate

P < 0.05 for the comparison between anemic group and control group with the use of Fisher's exact test

Multivariable	Haz. Ratio	95%CI		P-value
Age > 70	1.76	1.23	2.54	0.002
Sex	1.14	0.80	1.62	0.472
CKD	1.13	0.66	1.93	0.651
	1.84	1.09	3.11	0.022
DM	0.73	0.41	1.31	0.297
Cirrhosis	2.14	0.98	4.69	0.056

Table 2: Effects of age on mortality by multivariable analysis

FIN: human immunodeficiency virus infection; DM: diabetes mellitus; CKD: chronic kidney disease; CI: confidence interval; P < 0.05 for the comparison between anemic group and control group with the use of Cox regression analysis

Discussion

Pulmonary TB is still a major cause of death worldwide. Although infection with human immunodeficiency virus is a greatest risk factor for development of this disease [13]. In this study, 65.8 per cent of pulmonary TB cases diagnosed were 60 years and older. Twenty per cent of pulmonary TB diagnosed was 65 years and older, but 60.3% of TB cases diagnosed after die were in this age group [14]. Some publications have presented mortality in elderly patients related to underlying diseases [3,9,11-12]. In this study, the elderly group had higher number of male in CKD, lower in HIV disease and no difference in DM, and cirrhosis. No cancer or immunosuppressive drug in this report, different from previous study. The control group have lower in severity of disease, in elderly group have higher in acute respiratory failure that associated to mortality in older population group. Our data confirmed the previous reports that high mortality in elderly patients. In geriatric population, many patients have underlying disease and have regular screening in chest examination and radiologic study. While in DM group had no difference in incidence or mortality. Some of patients came from home not nursing care unit with past history of long time contact from their own family. It has been suggested for screening for geriatric population, with and without symptom and classified as a separate entity. TB in the elderly may differ from TB presenting in younger population, which lead to mortality and morbidity in this age group [15,16].

When we used risk ratio, mortality in HIV patients effect as confounder. Why we have to use risk difference regression analysis in 4 difference age groups and Cox's regression analysis model with adjusted confounders.

In a retrospective data collection have some limitation in clinical data and treatment regimen to analysis. We can define as oral drugs or intravenous drugs regimen, but many detail in treatment. In this study, was evaluated in short time survival only 40 days during intra hospital, no data after long term follow up.

Age-related factors increased the risk of tuberculosis (TB) reactivation, enhanced susceptibility to TB infection, high co-morbidity and high mortality. The mortality rate increased continuously with age groups that mean age is independent factor that effect to mortality. Patients will activate TB after decreased immunity when they are older.

Conclusion

In the elderly age group, female was higher than male. Mortality in the elderly was remarkably higher than in younger, and increased continuously with age.

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