

Demographic factors associated to survival of HIV/AIDS patients in southernmost province of Thailand*

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- Introduction** : *HIV/AIDS is a serious public health problem that has globally caused severe illnesses and deaths within the past two decades. However, a little is known about the impact on demographic factors which is changed over time.*
- Objective** : *To investigate the demographic factors associated to survival of HIV/AIDS patients.*
- Setting** : *Provincial and community hospitals.*
- Research design** : *A prospective, hospital-based cohort study.*
- Patients** : *HIV/AIDS patients registered in both provincial and community hospitals between January 1992 and April 2010.*
- Methods** : *In total, 1,575 patients with HIV/AIDS infection were observed and followed-up in one regional and other six community hospitals, Yala province, Thailand. The outcome was timed from diagnosis of HIV/AIDS infection to death. Cox's proportional hazard model was used to analyze and investigate the association between demographic factors and death among HIV/AIDS patients.*

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- Results** : *The median survival time among the HIV/AIDS patients from diagnosis to death was 46.6 months (95%CI: 46.2 to 46.9 months). Statistically a significant corresponding risk of time from HIV/AIDS diagnosis to death was found among HIV/AIDS patients. Primarily, patients who were employees had double the chance to die (HR: 1.66; 95%CI: 1.05 to 2.62). In contrast, patients with complementary care were more likely to have longer life by about 53% (0.47; 0.28 to 0.76). Regarding the in-patients, they were 9 times more likely to die (8.94; 5.47 to 14.60). Patients who had heterosexual behavior also had double risk of death (1.86; 1.32 to 2.63). Finally, those who were at risk of infection by their sexual behaviors had double the chance to die (1.98; 1.12 to 3.48).*
- Conclusion** : *An association between demographic factors and survival time from HIV/AIDS diagnosis to death among patients with HIV/AIDS infection was found. the factors are namely: employment, complementary care, type of patient, sexual behavior, and risk of infection.*
- Keywords** : *Demographic factors, survival, death, HIV, AIDS.*

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- บทนำ** : โรคภูมิคุ้มกันบกพร่องเป็นปัญหาสาธารณสุข และทำให้มีอัตราการป่วยและตายในช่วง 20 ปีที่ผ่านมา และปัจจุบันปัจจัยทางประชากรมีการเปลี่ยนแปลงตลอดเวลา และยังไม่เป็นที่ทราบแน่ชัดถึงผลกระทบต่อการเสียชีวิตของผู้ป่วย
- วัตถุประสงค์** : เพื่อศึกษาความสัมพันธ์ระหว่างปัจจัยทางประชากรและการรอดชีพในผู้ป่วยติดเชื้อ HIV/AIDS
- สถานที่ทำการศึกษา** : โรงพยาบาลประจำจังหวัดและโรงพยาบาลชุมชน
- รูปแบบการวิจัย** : การศึกษาแบบไปข้างหน้า
- ผู้ป่วยที่ได้ทำการศึกษา** : ผู้ติดเชื้อ HIV/AIDS ที่ขึ้นทะเบียนรักษาพยาบาลในโรงพยาบาลประจำจังหวัดและโรงพยาบาลชุมชนในจังหวัดยะลา ระหว่าง ปี พ.ศ. 2535 ถึง 2553
- วิธีการศึกษา** : ผู้ติดเชื้อจำนวน 1,575 คน ได้รับการติดตามการรักษาพยาบาลในจังหวัดยะลา โดยมีตัวแปรตามคือระยะเวลาจากการวินิจฉัยว่าป่วยหรือติดเชื้อจนกระทั่งเสียชีวิต ทำการวิเคราะห์ด้วยสถิติ Cox's proportional hazard model
- ผลการศึกษา** : พบว่า ผู้ป่วยที่ติดเชื้อ HIV/AIDS มีระยะเวลาการรอดชีพเท่ากับ 46.6 เดือน (95%CI: 46.2 ถึง 46.9 เดือน) และมีปัจจัยทางประชากรที่มีความสัมพันธ์ต่อการเสียชีวิตในผู้ป่วยที่ติดเชื้อ HIV/AIDS ได้แก่ผู้ที่ประกอบอาชีพใช้แรงงานมีโอกาสการตายเป็น 2 เท่า (HR: 1.66; 95%CI: 1.05 ถึง 2.62) อย่างไรก็ตามผู้ป่วยที่ได้รับการรักษาพยาบาลที่อื่นร่วมด้วยจะมีการรอดชีวนานขึ้นประมาณ 53% (0.47; 0.28 ถึง 0.76) และในกรณีที่ผู้ป่วยในจะมีโอกาสการเสียชีวิตเป็น 9 เท่า (8.94; 5.47 ถึง 14.60) สำหรับผู้ป่วยที่มีพฤติกรรมการมีเพศสัมพันธ์กับเพศตรงข้ามมีโอกาสการเสียชีวิตเป็น 2 เท่า (1.86; 1.32 ถึง 2.63) และผู้ป่วยที่มีการติดเชื้อจากเพศสัมพันธ์มีโอกาสการเสียชีวิตเป็น 2 เท่า (1.98; 1.12 ถึง 3.48)

วิจารณ์และสรุป : จากการศึกษาค้นคว้าพบว่า การรอดชีพของผู้ป่วยที่ติดเชื้อ HIV/AIDS มีความสัมพันธ์กับปัจจัยทางประชากร ได้แก่ การประกอบอาชีพ การรักษาพยาบาลร่วม ประเภทของผู้ป่วย พฤติกรรมทางเพศ และปัจจัยเสี่ยงในการติดเชื้อ

คำสำคัญ : ปัจจัยทางประชากร, การรอดชีพ, การตาย, HIV, AIDS

HIV/AIDS has globally emerged as a major public health problem over two decades ago. The human immunodeficiency virus (HIV) infection was first reported in 1981.⁽¹⁾ At present, the epidemic has decreased in incidence. However, the prevalence of HIV-infected people is still high, and new infections gradually continue to increase.⁽²⁾ Especially with HIV/AIDS, there are a number of epidemic cases when the patients have exhibited symptoms of their illness well after original infection.⁽³⁾

More than 3 million people died of AIDS, two-thirds of them lived in Africa.⁽¹⁾ It is estimated that 33.4 million people are living with HIV/AIDS worldwide. Most of them reside in low and middle income countries. Approximately, 2.7 million people were newly infected in 2008. Furthermore, about 2 million people die of HIV/AIDS yearly.⁽⁴⁾ In the Southeast Asia Region, the prevalence of HIV/AIDS illness is much lower than in Africa.⁽⁵⁾ An approximately estimated 3.5 million people are living with HIV/AIDS. Of these, 200,000 people were newly infected with HIV and 230,000 died of AIDS related illness.⁽⁶⁾ In Thailand, the prevalence of HIV-infected and people living with HIV are declining, compared to a decade ago.⁽⁷⁾ Although, the prevalence of AIDS-related opportunistic infections decreases in AIDS-related mortality-HIV-infected people are living better and longer.⁽²⁾ However, the prevention and treatment of HIV/AIDS patients nowadays still remains problematic. Also, the determinant of deaths has emerged as a greater challenge and concern worldwide.⁽⁸⁾

In this paper, the rigorous statistical methods have been deployed to estimate the survival time from HIV/AIDS diagnosis to death among HIV/AIDS patients. It is well-known that AIDS is a leading cause

of death worldwide. Moreover, its impact on demographic factors has been noticed in some studies. During the past decades, the demographic factors of HIV/AIDS patients have changed over time and it must be monitored to proper target prevention and care. Consequently, the purpose of this study was to investigate the demographic factors associated to survival of HIV/AIDS patients in the southernmost province of Thailand where there is culture and traditional diversity.

Methods

Study design

The study began with patients registered with HIV/AIDS infection in 1992 and who reside in Yala, a province situated in the southernmost part of Thailand. The patients were routinely observed and followed up in a hospital-based study designed in both rural and urban areas. In addition, a hospital-based study was established in one regional and other six community hospitals. A total of 1,575 patients with HIV/AIDS infection were observed and followed up in this study. During the following-up period from diagnosis to death, 308 patients died (19.56%, 17.6 to 21.5).

Outcome variables

The primary outcome was timed from HIV/AIDS diagnosis to death during the follow-up period. Death was defined and diagnosed by physicians in the hospitals, and also confirmed by death certificate. Furthermore, the censored data were defined as incomplete observations that might not have been observed or experienced during the study period. The terms of follow up, refusal of treatment, termination of the study or migration during the study period were

classified as censored data in this study.

The outcome was routinely gathered and observed by the healthcare staff responsible for epidemiological surveillance and diseases control each hospital. They were trained to assess the outcome, demographic factors and risk factors of HIV/AIDS infection during the study period. The data were monthly recorded using a database, which was a rigorous standard database and developed by the Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health.

Instruments and data collection procedure

According to the instrument and collection procedure, the inter-rater reliability was checked among the different healthcare staff. The healthcare staff that collected the data presented different linguistic and religious groups; therefore, they were well qualified to test the variant subjects for the study so that healthcare staff were selected and well-trained to use the case report form and database. Monitoring and quality controls were established at the beginning of the study to ensure that there were reliability and validity.

Statistical methods

Initially, the baseline demographic information was presented as descriptive analysis. The primary outcome of time from HIV/AIDS diagnosis to death was estimated using the Kaplan-Meier method. The statistical significance of the difference between the survival curves was investigated using the Cox's model. This model was constructed using baseline demographic factors such as prognostic

factors for the time from HIV/AIDS diagnosis to death. The variables were constructed using crude analysis to demonstrate factors relating the death of the patients with HIV/AIDS.

A three-phase modeling strategy was used. Initially, a model was constructed for each of the demographic factors and all possible factors from previous studies were considered. The polytomous variables including marital status, occupation, complementary care and risk of infection were constructed into dummy variables prior to entering into the model. The continuous variable such as the age of the patients was categorized if it had a non-linear relationship. Second, the factors with a coefficient value for p -value that was less than or equal to 0.25 using the Wald's test in crude analysis were considered and entered into the initial model. Using a backward elimination method, the factors with p -value of Wald's test greater than 0.05 were eliminated respectively. The p -value of the partial likelihood ratio test was tested by model fitting. On the other hand, factors were not excluded from the initial model due to be confounding factors. Therefore, the final model included all possible factors. Also, the log-likelihood ratio was used to test the best fitting model, and the adjusted coefficient values were used to calculate the effect of demographic factors to the survival time of the HIV/AIDS patients. The results are presented as hazard ratios (HR) which are comparable to relative risk (RR) with 95 % confidence intervals. The interpretation is presented as no association if the HR included 1, negative association if the HR is greater than 1, and positive association if the HR is less than 1.

Power of the study

A Cox regression of the log hazard ratio on a covariate with a standard deviation of 1.50 based on a sample of 1,575 subjects achieves 100% power at a 0.05 significant level to detect a regression coefficient equal to 2.0 (HR = 8.94). The sample size was adjusted since a multiple regression of the variable of interest on the other covariates in Cox regression is expected to have a R-squared of 0.50. The sample size was adjusted for an anticipated event rate of 0.19.

Result

During the study period, the available data on all 1,575 HIV/AIDS patients in routine prospective

study was analyzed. A total of 8,649 person-months of follow up was available. One-fifths of the HIV/AIDS patients died (n = 308, 19.56%) during the follow-up period. The incidence rate was 2.90 times per 100 person-months (95%CI 2.55 to 3.28). The median survival time among the HIV/AIDS patients from diagnosis to death was 46.6 months (95%CI: 46.2 to 46.9 months). Of these, 292 (18.5%) were missing due to unknown the dates of diagnosis and death. Therefore, the survival time of 1,283 (81.5%) the HIV/AIDS patients was analyzed. The survival time was estimated by Kaplan-Meier where half of the HIV/AIDS patients experienced death. In addition, the time span from HIV/AIDS diagnosis to death is shown in Figure 1.

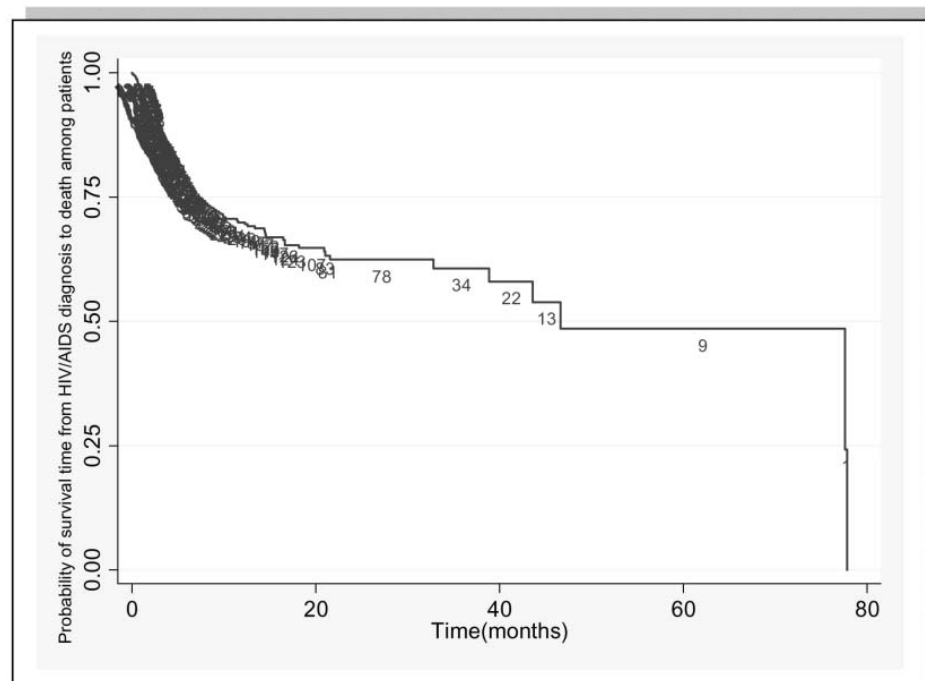


Figure 1. Kaplan-Meier's estimated survival time from diagnosis to time of death among HIV/AIDS patients.

Demographic characteristics of HIV/AIDS patients included, namely: personal factors, complementary care, sexual behavior factors and risk of transmission which is not presented in this present study. Among these patients, about two-thirds (70.86%) of them were male. A half of HIV/AIDS patients were aged 31 to 45 years old (53.24%). Their average age was 33 years old, (SD. = 10). The lowest age was 0.17 months of age and the highest age was 76 years. About one half had their marital status of separate or divorced (51.87%). Almost all HIV/AIDS patients had Thai nationality (98.92%). Half of the HIV/AIDS patients were employee (44.44%). Only one-fifth of the patients had complementary care (17.78%). Two-thirds of them were classified as in-patients (68.72%). In addition, about two-thirds of whom had risk of infection from their sexual behavior. However, only one-tenths were infected by blood donation and/or by being born to infected mothers (11.43%). Finally, of these, the proportion of living areas was quite similar in both urban and rural areas (43.43% vs. 56.57%).

To identify factors associated with the survival time of HIV/AIDS patients, all possible potential factors related to the death of HIV/AIDS patients were considered in the crude analysis. Those factors were analyzed as both categorical and continuous variables. In this study, there was only an age variable which was a continuous variable. According to the crude analysis, it showed that sex, age and marital status were not statistically significant when associated with time span from HIV/AIDS diagnosis to death which is not presented in this present study. On the contrary, a statistically significant association was found among demographic factors, i.e., HIV/AIDS patients were employee were more likely to die about 1.87 times (HR: 1.87, 95%CI: 1.19 to 2.93), compared to patients were government and company officers.

Patients who had sought complementary care were more likely to have longer life about 76 % (0.24, 0.15 to 0.39), compared to those who had not any complementary care. In addition, the HIV/AIDS patients defined as in-patients were 12 times more likely to die (11.49, 7.18 to 18.41), compared to the out-patient. Patients who had heterosexual preferences were demonstrated about 3 times more likely to die (3.02, 2.24 to 4.09). Regarding sexual behavior, patients who were heterosexual were three times as likely to die (2.77, 1.63 to 4.74), and about twice as likely if they were of invasive drug abuse (1.62, 0.89, 2.96). Finally, patients who resided in rural areas were 34% less likely to die (0.66, 0.52, 0.85), compared to those who resided in urban areas.

The final Cox's proportional hazard model demonstrated that there was statistically significant association between demographic factors and survival time from HIV/AIDS diagnosis to death as shown in Table 1. Patients who were employee were twice as likely to die (1.66, 1.05 to 2.62), compared to those who had government and company officer. On the contrary, patients who sought complementary care were more likely to survive about 53% longer (0.47, 0.28 to 0.76), compared to those who had no complementary care. However, in the case of in-patients who had been admitted to hospital, they were 9 times more likely to die (8.94, 5.47 to 14.60), compared to those who were out-patients. Furthermore, sexual behavior of the patients was a risk factor that doubled the chance of death (1.98, 1.12 to 3.48), compared to those who had been infected by blood donation and child born to infected mothers. Finally, the HIV/AIDS patients who resided in rural areas were about 16% more likely to survive (0.84, 0.64 to 1.09), compared to whom resided in urban areas.

Table 1. Adjusted hazard ratios of demographic factors associated to survival of HIV/AIDS patients in the southernmost province of Thailand.

Demographic factors	Crude HR	Adjusted HR	95%CI	p-value*
Sex				0.747
- Female	1	1		
- Male	1.06	1.07	0.78 – 1.44	
Age(years)	1.00	0.99	0.98 – 1.01	0.522
Marital status				0.323
- Single	1	1		
- Couple	1.25	1.32	0.81 – 2.16	
- Separate/divorce	0.98	1.09	0.68 – 1.73	
Race				0.108
- International	1	1		
- Thai	0.36	0.39	0.14 – 1.06	
Occupation				0.043
- Government and company officers	1	1		
- Agriculturists	1.01	1.09	0.65 – 1.84	
- Employees	1.87	1.66	1.05 – 2.62	
- Unidentified	1.25	1.40	0.83 – 2.36	
Complementary care				0.010
- No	1	1		
- Yes	0.24	0.47	0.28 – 0.76	
- Unknown	0.38	0.59	0.40 – 0.87	
Type of Patient				<0.001
- Out-patient	1	1		
- In-patient	11.49	8.94	5.47 – 14.60	
Sexual Behavior				<0.001
- Homo/bisexual	1	1		
- Heterosexual	3.02	1.86	1.32 – 2.63	
Risk of infection				0.036
- Blood donation/ child born to infected mother and others	1	1		
- Invasive drugs abuse	1.63	1.54	0.83 – 2.87	
- Sexual behavior	2.77	1.98	1.12 – 3.48	
Resident areas				0.189
- Urban area	1	1		
- Rural area	0.66	0.84	0.64 – 1.09	

Note: * p-value calculated by using partial likelihood ratio method

Discussion

The given information on demographic factors associated with survival time of HIV/AIDS patients are demonstrated in this prospective study. An adjusted analysis of Cox's proportional hazard model showed that demographic factors, for instance, employment, seeking complementary care, type of patient, sexual behaviors and risk of infection and residence area were statistically significantly when associated with survival time of HIV/AIDS patients. The statistics and the relationships shown were precise enough to detect demographic factors in the death of HIV/AIDS patients. However, the missing data were also eliminated due to the loss of the date of diagnosis and death. The missing data were, however, not large enough to affect the Cox' proportional hazard function, which was 18%. Although this present study is based on non-randomized information which might not necessarily represent the sample population the findings are consistent in areas in which the current study was conducted. Moreover, the study design may not always capture as many contextual or clinical factors to account for confounding factors, especially, CD4, T-cell and receiving an antiretroviral drug. These may increase the survival time of HIV/AIDS patients.⁽⁹⁾

The present study demonstrated that the median survival time from HIV/AIDS diagnosis to death was 46.6 months (95%CI: 46.2 to 46.9 months), compared to Silverberg's study who showed that HIV/AIDS patients had median survival time longer.⁽¹⁰⁾ In addition, the Sieleunou's study demonstrated that in worst case scenario patients who received the antiretroviral drug had longer median survival time of 58 months.⁽¹¹⁾ On the contrary, the Jougla's study

presented a shorter median survival time by about 1.4 years from AIDS diagnosis to death.⁽¹²⁾ Among the HIV-seropositive patients who had been followed up they demonstrated that there was a shorter survival time by about 10.3 months.⁽¹³⁾ Also, we found the shortest survival time of about 7 months, which was in the capital city of Thailand.⁽¹⁴⁾

Regarding the demographic factors, occupation was associated with survival time from diagnosis to death. Among the HIV/AIDS patients were employee were more likely to die (HR: 1.66, 1.05 to 2.62) compared to other categories of occupation. This related to the Coovadia's study that HIV/AIDS patients who were employee were more likely to die, and its impact was greater on people who were manual labors.⁽¹⁵⁾ In the United States, the HIV prevalence was in urban men. Especially, there was a higher level in older blacks.⁽¹⁶⁾ Bamford's study shows a higher prevalence in poor Hispanic areas.⁽¹⁷⁾

The previous studies showed that HIV/AIDS transmitted primarily among homosexual and bisexual males. Particularly, two-thirds of AIDS was transmitted by male-to-male sexual contact.^(1, 18) They had twice the risk of progressing toward AIDS than the heterosexual.⁽¹⁹⁾ However, this showed no association between sex and death. The Kitayaporn's study conducted in the capital city of Thailand showed association between sex and death among HIV/AIDS patients. The majority of them were male patients, 93%;⁽¹⁴⁾ and they had 1.4 times more likely to die.^(17, 20) On the contrary, the Vernon's study reveals that female patients with Tuberculosis were 2.47 times more likely to die.⁽²¹⁾ Also, females who received antiretroviral drug were 1.73 times more likely to die than males.⁽¹¹⁾ In addition, patients aged more than

50 year old were more likely to die by about 2.33 times.⁽²²⁾

Regarding the behavioral risk of HIV/AIDS infection, sexual behavior is a major factor among HIV/AIDS patients. In the highest proportion of sufferers HIV/AIDS was transmitted by male-to-male sexual intercourses. Previously, the virus was transmitted among the homosexual and bisexual males.⁽¹⁸⁾ It is, however, currently spread to various groups such, spouses, partners and monogamies.⁽¹⁵⁾ Also, the mode of transmission was also high in the injection drug user group.⁽¹⁶⁾

At the present, after providing a highly active antiretroviral therapy (HAART), a lower level of death among men has been shown. HAART would expect to increase life in these groups.⁽⁹⁾ Given the high levels of risk behavior among men who had sex with men through the nineteen sixties, it would expect an epidemic of substantially larger proportion than that observed in 1980 and 1990.⁽¹⁶⁾ However, the important factors among HIV/AIDS patients such as CD4 and T-cell are also associated with survival time.⁽¹⁶⁾

In the present study, HIV patients who received palliative care survived longer. Coovadia's study⁽¹⁵⁾ shows that healthcare services, insurance, taking necessary goods and health services and making them accessible amongst the general population is important. Where regions had high care costs and services were obstructed the accessibility of health care was reduced.

In conclusion, the study links five important demographic factors to death among HIV/AIDS patients. The factors are, namely: occupation, the quality of palliative care, patient type, sexual behavior of patients, and the modes of HIV transmission. A

further study is, however, needed to investigate the relationship between antiretroviral drug use and death among HIV/AIDS patients.

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