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Prevalence of HIV infection among tuberculosis patients in Bali, Indonesia

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ABSTRACT

Background: During 1998-2007, TB and HIV cases in Bali had shown a significant increase respectively. In general, both of these diseases are chronic diseases that need long term treatment, and together they could worsen the patients' condition. To prevent the double burden of those patients, we need to know HIV infection prevalence among TB cases in Bali.

Method: One thousands of TB cases diagnosed at TB health services unit (UPK) at primary health centers (*puskesmas*) and public hospitals in Bali, in September-November 2008, were given information and their blood samples were taken for HIV tests. Samples were chosen proportionally according to the number of TB cases registered in each UPK. Five milliliters of blood sample were taken from each eligible patient by laboratory staff or nurse at the UPK for HIV tests which were conducted at Bali Health Laboratory. HIV test used in this study were the two types of rapid test in accordance with WHO standard.

Discussion: Thirty-nine out of 1,000 blood samples were found HIV positive. The highest HIV prevalence among TB cases was in the Buleleng District (11.5%) and followed by Denpasar City (5.1%). This prevalence showed a different figure from the HIV/AIDS cases in VCT clinics registered at Bali Provincial Health Agency, where the highest prevalence found in Denpasar, followed by Buleleng and Badung. If we compare, the difference in figure between Badung and Buleleng, might be due to the difference in routes of HIV transmission. In Buleleng, most of the cases (90%) were sexually transmitted, while in Badung 48% transmission were through injecting drug users. The IDUs seek health services at private health centers and rarely utilize public/government services such as *puskesmas* and hospitals.

Conclusion: The HIV prevalence among TB patients in Bali was 3.9%. The characteristics of the patients showed that they are mostly male, aged between 31-40 years old, have junior high school-university education, divorce or single in marital status, work in private sector, and newly infected extra pulmonary TB/AFB(-) patients. HIV positive cases were not found in all districts, mostly found in Buleleng (11.5%) followed by Denpasar (5.1%), Tabanan (1.8%), Karangasem (1.7%) and Jembrana (1.4%). The proportion of the case detection was high in hospitals, but the spread of the cases at *puskesmas* was high as well.

Keyword: TB, HIV, Puskesmas, Bali

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INTRODUCTION

Indonesia is ranked third in number of tuberculosis (TB) cases in the world. Every year, there were 256 new TB cases found per 100.000 world population.[1]

Tuberculosis is one of opportunistic infections frequently found among HIV positive patients and conversely HIV/AIDS is one of the main risk factors for TB transmission. The significant increase in the number of TB and HIV/AIDS cases that occurred concurrently in some developing countries will lead to serious health problems.

In Bali Province, a double TB-HIV epidemic has also shown similar pattern to what has happened in other developing countries. Data from Bali Provincial Health Agency showed that HIV/AIDS continues to increase, at the same time as the increase in TB cases (Figure-1).

Geographically, HIV positive cases spread in all districts. The highest cases were found in 3 districts i.e. City of Denpasar, followed by District of Badung and Buleleng. Similarly, TB cases were distributed mostly in Denpasar, which is accounted for almost a third of the total number of cases, and then followed by Buleleng.

Factors contributing to the success of TB case detections in Bali were the availability of more structured TB case finding programs through health services unit of TB, supported by teams of

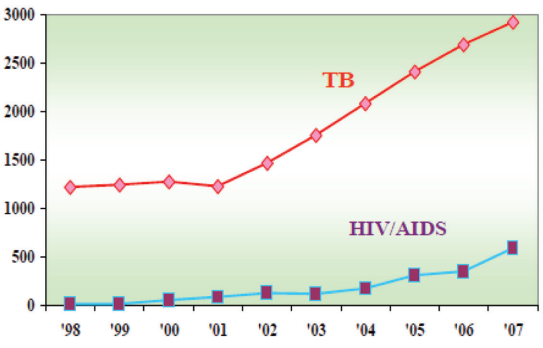

Figure 1 TB and HIV/AIDS cases in Bali, 1998-2007*

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TB, as well as DOTS facilities that are spread at primary health centers and district hospitals.

RESEARCH QUESTIONS

Tuberculosis has been known as a threatening disease in the community but has not lead to stigmatization such as happened to HIV/AIDS patients. Therefore, TB patients are voluntary coming to health services. Whereas, due to stigmatization and discrimination, HIV/AIDS patients are seldom and do not even want to seek services. Based on this notion, the research question is 'what is the prevalence of HIV infection among TB patients in Bali?

AIMS

The aims of this research are to measure the prevalence and distribution of HIV infection among TB patients in Bali.

METHODS

The research was conducted in all active health service units in the Province of Bali. The health service units are consisted of 103 primary health centers (*puskesmas*) and 17 district hospitals.

Sample size was calculated using *Epi Info Statcalc* (version 3.3.2) by considering proportion of adult TB patients who got HIV infection in Indonesia, number of adult TB patients in Bali in 2005, estimation of HIV prevalence among TB patients (0.2-1.0%), confidence level of 95%, and considering refusal and errors during examination, thus the sample size was rounded to 1,000 cases.

Research subjects were all TB out-patients found in each health service unit between July and December 2008, aged from 15 years old or more, and provided approval to participate in the study. Exclusion criteria were unable to provide consent, too sick to be given counseling or unable to understand study procedure.

Adult TB patients who were diagnosed during the study period were given information and inform consent. Blood samples were then taken from the subjects who were willing to participate. This procedure was unlinked anonymous. The blood samples were then sent to hospitals for centrifugation and stored in refrigerator. Blood serums from the hospitals and or *puskesmas* were delivered to BLK for HIV tests. This research employed test and algorithm that are regularly applied to HIV surveys in accordance with WHO standard, using two rapid tests i.e. SD-Bioline and Determine.

Table 1 Characteristics of the Sample

No	Characteristic	Percentage
1	Age (years old)	
	< 25	13.7 %
	25 – 34	27.1 %
	35 – 44	19.7 %
	45 – 54	16.5 %
	55 – 64	13.2 %
	> 64	9.7 %
2.	Sex	
	Male	58 %
	Female	42 %
3.	Education	
	Without education	13.8 %
	Primary School	33.0 %
	Junior High School	15.9 %
	Senior High School	31.2 %
	Universities	6,1 %
4.	Occupation	
	No Occupation	17.9 %
	Student	3.2 %
	Entrepreneur	21.0 %
	Civil servant/ Private employee	22.1 %
	Police officer/ soldier	1.0 %
	Farmer	19.7 %
	Housewife	15.0 %
5.	Marital status	
	Married	79.3 %
	Single	18.9 %
	Divorced	1.8 %

All patients were required to provide their approval before being involved in this study. Consent was asked to a surrogate if a patient aged between 15 and 18 years old. Subject's decision to participate in this study did not influence the standard of treatment given to them. Subjects who intend to know about their blood test results were suggested to consult with nearest VCT clinics.

Ethical clearance for the study protocol was submitted to the IRB at Kerti Praja Foundation, Denpasar.

RESULTS

A thousand blood samples were taken from TB patients in Bali, most of them (77.1%) were

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attained at primary health centers. The HIV test results showed that 3.9% of the TB patients had co-infection with HIV. Table-1 and Table-2 indicate the sample characteristics and TB patient's characteristics.

Mean of the sample age is 41.2 (15-92) years old, with the highest proportions are at age group of 25-34 years old (27.1%) and 35-44 years old (19.7%), whereas the lowest proportion is at the age group of 64 or more (9.7%). Participants were more male (58%) than female (42%). Based on educational status, almost a third of TB cases graduated from primary school (33.0%) and senior high school (31.2%). Less than one tenth of the samples completed university level (6.1%).

Three types of occupation that dominated the samples were civil servant/private employees (22.1%), entrepreneur (21.0) and farmer (19.7%). In addition, the proportion of housewives participated in this study was quite high (15.0%) that exceeded the proportion of police officer/soldier and students. Most (79.3%) of the samples were married and only 18.9% have not married or divorced (1.8%).

HIV infections were not found among TB patients in 4 districts, i.e. Badung, Gianyar, Bangli and Klungkung. The highest prevalence of HIV positive was found among TB patients in Buleleng (11.5%), followed by Denpasar (5.1%), Tabanan (1.8%), Karangasem (1.7%) and Jembrana (1.4%)

In relation to TB treatment history, almost all (92.9%) patients participated in this study, classified as new cases and only 7.1% of the cases were chronic cases or relapse.

Type of tuberculosis, based on bacteriology tests and organ affected, showed that more than a half (57.2%) of the cases were pulmonary TB with positive AFB smear tests, followed by a third (33.7%) of the cases that have negative AFB smear tests but the pulmonary Rontgen showed TB signs. Proportion of extra pulmonary tuberculosis was below one tenth (9.4%). Most (60.4%) of the cases showed symptoms 1-6 months before TB diagnosis. Proportion of patients who had symptoms appeared before 1 month was 32.0%, followed by more than 6 months (7.6%).

Table 2 **Characteristics of TB Cases**

No	TB Cases Characteristics	Percentage
1	Category of patient	
	New	92.9 %
	Chronic/ relapse	7.1 %
2	Type of Tuberculosis	
	Pulmonary TB, AFB smear +	57.2 %
	Pulmonary TB, AFB smear +, Rontgen +	33.7 %
	Extra-pulmonary TB	9.4 %
3	Duration of symptoms	
	< 1 month	32.0 %
	1-6 months	60.4 %
	> 6 months	7.6 %

DISCUSSION

Thirty-nine TB patients (3.9% of 1,000 samples)) were infected by HIV. The prevalence of HIV positive among TB patients showed a far higher figure than that estimated by WHO of 0.8%.[2] This figure is also twice as much as the results found in Yogyakarta in 2006 (1.9%).[3] Based on AIDS cases that have been reported in Indonesia up to June 2009, the prevalence of AIDS in Bali has been higher (38.9% per 100,000), ranked at second place, while Yogyakarta ranked at 12nd (7.5 per 100,000 inhabitants).[4]

HIV prevalence among TB patients by age group indicates a similar pattern to the HIV prevalence that has been reported by VCT clinic in Bali,[5] where the highest proportion occurred in the age group of 20-40 years old. While, a study of HIV prevalence in Yogyakarta showed the highest proportion was found in age group of 15-44 years old, ranged approximately between 2.7-2.8%.[3]

The proportion of HIV positive among males twice higher than females (5.1% and 2.2%, p=0.016). This difference is similar to results found in Yogyakarta; however, the difference in HIV prevalence in Yogyakarta was not significant.[3] Differences in HIV prevalence among TB patients according to sex group illustrated an appropriate figure compare to proportion of HIV positive cases reported in Bali until December 2008, with the percentage of 71.9% compare to 28.1% among males and females respectively.[5]

Prevalence of HIV infection among TB patients was dominated by educational status of junior high school or higher, the highest proportion was in the group of junior high school (6.3%), followed by senior high school (5.2%) and university (4.9%). This differs from findings in Yogyakarta which found HIV prevalence occurred mostly among university group, although the figures showed the same results as those in Bali (4.8%).[3]

None of the samples categorized as student, police officer or soldier were infected by HIV. Prevalence of HIV positive among TB patients showed that the highest proportions were found among the group of entrepreneur (6.7%), farmer (4.1%) and civil servant (3.2%). This study even

found housewives were infected by HIV (2.7%). This means that HIV heterosexual transmission occurred among housewives, although in general, housewives have no risk to HIV transmission. The result of this zero-surveillance shows a difference from the result found in Yogyakarta. The HIV positive prevalence in Yogyakarta indicated the highest proportion was among student group. This might be due to difference in sample size, where in Yogyakarta there were 117 students involved,[3] whereas in Bali, only 32 students participated in the study.

According to marital status, the highest proportion of HIV positive was found among TB patients who were divorced, where the proportion was 4 folds higher than those who were married and not married (p=0.017). If the categories of marital status classified as married and not married, the comparison of HIV prevalence is 5.3% vs 3.5%, CI 0.762%-2.972%, similar to the results found in Yogyakarta in which the prevalence of HIV positive was higher among unmarried samples than those who were married (2.6% vs 1.6%; CI 0.24%-1.51%).[3]

Chronic TB patients are those who have undergone anti tuberculosis drugs, but have not been cured. Proportion of HIV positive among chronic TB patients were 2 folds higher than those with new TB infection (5.6% vs. 3.7%, CI 0.55-4.09). This is different from the results found in Yogyakarta that the prevalence among those two groups showed same results (1.9% vs. 1.9%).[3] Theoretically, TB patients who got HIV infection frequently develop chronic diseases due to heavier immune system disorders, especially decrease in CD4 level, thus the healing process is interrupted. In addition, HIV infection also often causes the diseases to be relapsed after completion of TB treatment.[6]

In relation to the type of TB, the highest proportion of HIV positive patients was found among extra pulmonary TB patients (8.5%). This is twice higher than that occurred among pulmonary TB patients, both those who were diagnosed with AFB positive smear (3.2%) as well as those with positive Rontgen examination (3.9%), although the difference is not statistically significant (p=0.046). If the types of TB are classified into two groups i.e. positive AFB smear and negative AFB smear with extra pulmonary TB, the results become 3.2% vs 4.9%, CI 0.84-2.88. This numbers provide a similar figure to the results found in Yogyakarta (1.7% vs 2.4%, CI 0.54-1.39).[3] This result is appropriate with the epidemiological data in other regions, in which TB patients with HIV co-infection tend to show unspecific symptoms; hence it is difficult to be diagnosed.[6]

Although prevalence of HIV positive was higher among chronic TB patients, there were 5.3% HIV positive cases found among TB patients with duration of symptoms less than one month. Duration of symptom is period from the first appearance of TB symptoms until the day when patients visit health services unit. Whereas, proportion of HIV positive among those who have duration 1-6 months and more than 6 months was a half of the cases, i.e. 3.3% and 2.6% respectively. This situation is similar to epidemiological data in other places, in which HIV infection tends to make TB clinical symptoms appear faster than usual.[6]

Most of the HIV positive cases among TB patients were found in district hospitals (7.9%), while in *puskesmas*, the proportion was only one third of that found in the hospitals (2.7%). The prevalence in these two health service units shows a significant difference (RP 2.89; CI 1.57-5.32). This finding indicates a similar figure to study results in Yogyakarta, where 4.7% vs 0.8% HIV positive cases for hospitals and *puskesmas* respectively.[3] The high prevalence in hospitals might be because samples that came to hospitals are generally in bad condition, so that they seek help or treatment to hospitals. This also illustrates that *puskesmas* has a potency to detect HIV positive cases and or HIV infection has come to the middle to low socio economic communities. Specifically, in Buleleng and Denpasar, there were some *puskemas* that have proportion of HIV positive among TB patients the same as the proportion in hospitals. In average, the proportion of HIV positive cases found in Buleleng and Denpasar are 7.8% (5.0%-33.0%) and 3.7% (4.5%-12.5%) respectively. The proportion in hospitals at the same place are 33.3% and 6.8% (7.1%-22.9%), respectively. Additionally, in Buleleng, HIV positive cases were found in 5 of13 *puskesmas,* while in Denpasar, cases were found in 5 of 10 *puskesmas*. All other HIV positive cases among TB patients in Jembrana, Tabanan and Karangasem were found in *puskesmas*.

HIV positive cases were not found among TB patients in Badung. This was unpredictable, because the prevalence of HIV positive cases in this district is nearly the same as that in Buleleng. The data analysis shows that sample characteristics in three districts (Denpasar, Buleleng, and Badung), as well as distribution and number of samples per health service unit in Badung were proportional. Comparison with cumulative data of HIV/AIDS in Bali Provincial Health Agency and collaborative data of TB-HIV in 4 hospitals in Bali indicate that mode of transmission or the difference in epidemiological pattern might be the causes of the difference in prevalence of HIV positive cases among TB patients in Buleleng and

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Badung. In Buleleng, more than 90% of HIV transmission occurred through heterosexual activities, while in Badung, the heterosexual transmission is only 41.4% and nearly a half (48.5%) of them were injecting drug users. In addition, there are some supporting data that can answer why there were no HIV positive cases among TB patients in Badung including: 1) the demographic characteristics of the samples in 3 districts, showed no significant differences in terms of age and sex, while there was significant difference in terms of occupation and marital status. However, those characteristics are not factors that cause the zero HIV prevalence; 2) in Badung, there are 4 areas of *puskesmas* that have high risk for HIV transmission including *Puskesmas of* Kuta I, North Kuta, South Kuta and Mengwi I. The proprotion of TB patients recruited as the sample from those area were also quite large (13.2%-22.2%) compare to the proportion of samples in other areas of *puskesmas* in Badung, hence the samples were geographically representative; 3) The results of supervision conducted during the research in Badung, supported by results of discussion with TB program officers during initial meeting of zero-surveillance result dissemination, indicated that there were no indication of intention to choose particular TB patients for the purpose of finding HIV positive patients. In addition, patients' refusal to participate in this study in Badung was relatively low (two cases); 4) Comparison with the cumulative data of HIV/AIDS reported in Buleleng in 1987-2008, indicates a difference in mode of HIV transmission from those happened in Badung and Denpasar. In Buleleng, 90% of HIV/AIDS cases were transmitted by heterosexual infection, whereas in Badung, 50% HIV/AIDS cases were found among injecting drug users.[5]

Injecting drug users tend to be exclusive and isolated groups, thus the rate of transmission is higher in this group through needle exchanges and their treatment seeking behavior patterns shows that IDUs tend to not to come to *puskesmas*. In addition, considering that transmission risk through sexual is lower than transmission through needles, the higher prevalence of HIV positive in Buleleng than Badung might indicate the possibility that HIV epidemic in Buleleng is older than that in Badung and Denpasar. Therefore, transmission in general population in Buleleng has been wider, thus easier to find cases in *puskesmas*; 5) Collaborative data of TB-HIV in 4 hospitals in Bali from January–July 2008 showed that proportion of HIV positive cases among TB patients who got VCT in Buleleng was also far higher than that in Denpasar and Badung.[7]

CONCLUSION

1. Prevalence of HIV infection among TB patients in Bali Province is 3.9%
2. Characteristics of HIV infection among TB patients showed that the co-infections were dominant among male group, aged 31-40 years old, educational status groups of junior high school to university, divorced/single in marital status, occupation groups of entrepreneur and private/civil servant.
3. Newly diagnosed TB patients had higher proportion of HIV infection than chronic TB patients. Also, extra-pulmonary TB patients had higher proportion of HIV infection than patients with pulmonary TB with both positive and negative AFB smear.
4. HIV infections among TB patients were found in 5 out of 9 districts in Bali, with the proportion in order: Buleleng (11.5%), Denpasar (5.1%), Tabanan (1.8%), Karangasem (1.7), Jembrana (1.4%).
5. Proportion of HIV positive was higher in district hospitals than that found in *puskesmas*. However, the spread of HIV positive cases in *puskesmas* in some areas was also quite high.

RECOMMENDATIONS

1. TB surveillance in *puskesmas* needs to be continued as a surveillance system in Bali to support monitoring of HIV cases transmission in general population. This can be achieved by integrating risk factors (behavior) into the surveillance system and simplifying the implementation.
2. Developing integration between surveillance system and VCT system available in *puskesmas*. The idea is blood samples should be taken from all TB patients by anonymous unlinked procedure, to attain the magnitude of HIV problems. Moreover, TB patients who have positive risk factors should be directly offered to undergo VCT.

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