

Risk Factors of Delayed HIV Diagnosis in Taiwanese Men Who Have Sex with Men

Yi-Chun Lo¹, Pei-Ying Wu², Wen-Chun Liu², Shan-Chwen Chang^{2,3}

1. Seventh Branch, Centers for Disease Control, Taiwan.

2. Center for AIDS Prevention and Control, National Taiwan University Hospital

3. Department of Internal Medicine, National Taiwan University Hospital

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Abstract

Early diagnosis of human immunodeficiency virus (HIV) infection has great clinical and public health impact. Early HIV diagnosis and timely administration of antiretroviral therapy can result in not only the reduction of morbidities and mortalities in HIV-infected patients, but also decrease of patients' viral load and risk of HIV transmission in public health aspects. However, a large proportion of HIV-infected patients still receive their first HIV diagnosis at advanced stage. In Taiwan, there has been an increase in the annual number of new HIV cases among men who have sex with men (MSM). In this study, structured interviews were conducted on 164 newly diagnosed HIV-infected MSM who received medical care at the National Taiwan University Hospital, to collect data on socio-demographic factors, clinical status, relationships with family and partners, self awareness of risk, and utilization of screening services before HIV diagnosis. Risk factors of late HIV diagnosis ($CD4 < 200/\mu L$) were analyzed. The study showed that 46% of newly diagnosed HIV-infected patients had late HIV

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Correspondence: Shan-Chwen Chang, MD, Ph.D.; Address: 7, Chung-Shan South Road, Taipei City, Taiwan, R.O.C.

E-mail: changsc@ntu.edu.tw

diagnosis. In multivariate analysis, three factors were significantly associated with late HIV diagnosis: age more than 24 years [Odds ratio (OR)=3.26; 95% confidence interval (CI): 1.08-9.83], diagnosis because of symptoms (rather than diagnosis through screening) [OR 5.70; 95% CI 2.53-12.8], last unprotected sex more than 6 months before HIV diagnosis [OR 6.19; 95% CI 2.70-14.2]. Late HIV diagnosis is prevalent among HIV-infected MSM in Taiwan. Health policy should focus on enhancing self-awareness of risk and utilization of screening services among MSM to facilitate early HIV diagnosis in this risk population.

Keyword: HIV infection, men who have sex with men, late diagnosis, HIV screening

Introduction

Early diagnosis of human immunodeficiency virus (HIV) infection has great clinical and public health impact. Early HIV diagnosis and timely administration of antiretroviral therapy can result in not only the reduction of morbidities and mortalities in HIV-infected patients, but also decrease of patients' viral loads and risk of HIV transmission. Moreover, health education and counseling accompanied with early HIV diagnosis may induce HIV-infected patients to practice safe sex or join harm reduction program, which may translate into a lower chance of HIV transmission [1-2].

However, there are still a large proportion of HIV-infected patients who received their first HIV diagnosis at advanced stage. Many studies in Western countries have concluded that late HIV diagnosis is highly prevalent; even in developed countries such as the United States, the United Kingdom, Italy and Canada, among HIV-infected patients, 24-45% were not aware of their HIV status until they were at the stage of AIDS [3-5]. Furthermore, the proportion of patients

with late HIV diagnosis among all HIV-infected patients remained stable in the past decade [5]. A report from the National Taiwan University Hospital showed that among their HIV-infected patients seen between 1994 and 2003, up to 68.2% had an initial CD4 lymphocyte count lower than 200/ μ L, with the median as low as 71/ μ L [6]. It indicated that late HIV diagnosis is still a common problem in Taiwan. In general, the reasons for late HIV diagnosis include delayed health seeking behaviors of HIV-infected individuals and poor recognition of HIV related clinical manifestations by healthcare providers. At-risk population of HIV infection may lack the awareness of their HIV risk. They may worry about discrimination, violation of privacy, deprivation of employment, and difficult medical access because of economic or work-related factors. In addition, mistrust of the medical professional, concerns of medical expenses and adverse drug effects may also be possible factors of late HIV diagnosis. We need to understand factors associated with late HIV diagnosis in Taiwan in order to develop solutions to target this problem.

The number of HIV-infected patients in Taiwan increased dramatically in 2003~2005; the majority were injection drug users (IDU). After the implementation of harm reduction programs, including methadone replacement therapy, needle exchange program and strengthening health education, the Taiwan Centers for Disease Control successfully controlled the HIV epidemic among IDU in 2006 and 2007. Analysis from the cases reported in 2006 and 2007 showed reduction of HIV case numbers in IDUs, heterosexuals and mother-to-child transmission, but continued surge of new HIV cases only among men who have sex with men (MSM, including male homosexuals and bisexuals), with a 20% increase from 2005 to 2006 and a 13% increase from 2006 to 2007. Among the 728 reported HIV cases between January and May in 2008, MSM

comprised of 46.4%, and have become the most important mode of HIV transmission. Meanwhile, MSM are acquiring HIV infection at a younger age.

In the “2008-2009 Goals and Focuses of Communicable Diseases Policy” released by the Department of Health, “reduction of HIV infection among MSM” was the first point in the chapter entitled “HIV prevention and control”. If early HIV diagnoses can be achieved, leading to decreasing risk behaviors in HIV-infected patients, it will be beneficial to HIV prevention and control among MSM. This study aimed to examine the risk factors of early and late HIV diagnosis among MSM in Taiwan, which may serve as a reference to policymakers in order to facilitate early HIV diagnosis.

Materials and Methods

Study population and setting

HIV-infected patients who received out-patient or in-patient care at the National Taiwan University Hospital were enrolled to this study if they were newly diagnosed with HIV infection within 3 months before the first visit to this hospital and had homosexual or bisexual practice as the mode of transmission. Case enrollment was started in August 2006. The study period was between August 2006 and July 2008.

Study methods and variables

The study was conducted using structured interview. Objectives of the interview were explained to all study participants by the researcher at the first encounter. After informed consent was obtained, a private interview was performed to collect detailed personal information. The study variables included social and demographic factors (sex, age, mode of transmission, education, employment, income, family, whether sexual orientation is known by any family

member or not) and clinical status (utilization of HIV screening services, initial CD4 lymphocyte count, presence of syphilis or hepatitis viral coinfection, history of sexually transmitted diseases [STD] and history of illicit drug use). The private interview was accompanied by counseling and health education to increase the patient's understanding of the disease, improve safe sex practice, and increase medical compliance.

Definitions

HIV infection is defined as detection of HIV-1 antibodies and confirmed by the western blot or polymerase chain reaction. Study participants were classified by initial CD4 lymphocyte count into early-diagnosis (ED) group ($CD4 \geq 200/\mu L$) and late-diagnosis (LD) group ($CD4 < 200/Ml$) for comparison and analysis. Unprotected sex was defined as any sexual intercourse without complete and correct use of condoms.

Statistical analysis

Statistical analysis was performed using SPSS version 15.0 (SPSS, Chicago, IL, USA). We conducted bivariate analysis using Wilcoxon rank sum test for non-categorical variables and χ^2 analysis or Fisher's exact test for categorical variables. All comparisons were two-tailed and p -value < 0.05 was considered significant. Multivariate analysis was performed using forward-conditional binary logistic regression.

Results

During the two-year study period from September 2006 to July 2008, we enrolled 164 HIV-infected MSM, including 20 (12%) bisexuals. There were 89 (54%) in the ED group and 75 (46%) in the LD group. After interviewing the first twelve participants and discussion with experts, information on family, sexual

partners and illicit drug use were added. The use of these additional questions began with subject 13. Data collection of the additional questions was performed to the first twelve participants retrospectively; several of these were lost to follow up or declined to answer. Therefore, the number of participants with additional data available was not equal to the total number of study participants.

Comparisons of socio-demographic variables between ED group and LD group were summarized in Table 1. Among all study participants, 31 (19%) were aged less than 18 years. There were no statistically significant differences between the two groups in age distribution, risk factors of HIV infection (homosexual or bisexual), education, employment and average monthly income. The majority in each group were aged between 20 and 40 years, city residents, with college degrees or above, and with average monthly income of more than 30,000 NT dollars. Compared with LD group, patients in ED group were younger (33 vs. 29 years old, $p = 0.02$). The LD group was older, had more bisexuals, and had more rural residents ($p = 0.08, 0.07, 0.07$ respectively); but none of these differences were statistically significant.

Table 1. Comparisons of socio-demographic variables among HIV-infected MSM between ED group and LD group

Variables	LD group (N=75)	ED group (N=89)	<i>p</i> -value
Age (years), median (range)	33 (19-57)	29 (18-48)	0.02
15-19	1 (1%)	4 (4%)	0.08
20-29	27 (36%)	45 (51%)	
30-39	35 (47%)	32 (36%)	
40-49	9 (12%)	8 (9%)	
50-59	3 (4%)	0 (0%)	
Risk factors of HIV infection			0.07
Homosexual	62 (83%)	82 (92%)	
Bisexual	13 (17%)	7 (8%)	
Residence			0.07
City	66 (88%)	80 (90%)	
Rural area	9 (12%)	9 (10%)	
Education			0.71
College and above	50 (67%)	74 (83%)	
Senior high school or equivalent	20 (27%)	13 (15%)	
Junior high school and below	5 (7%)	2 (2%)	
Employment			0.52
Yes	62 (83%)	70 (79%)	
No	13 (17%)	19 (21%)	
Average monthly income (NT dollars)			0.13
<15,000	13 (17%)	15 (17%)	
15,000~30,000	8 (11%)	20 (22%)	
>30,000	54 (72%)	54 (61%)	

Abbreviations: MSM, men who have sex with men; LD, late diagnosis; ED, early diagnosis; NT, New Taiwan.

Comparisons of clinical variables between ED group and LD group were summarized in Table 2. Patients in ED group had a significant higher likelihood to be diagnosed by screening than those in LD group (72% vs. 25%, $p < 0.0001$). Both groups had a similar seroprevalence of syphilis (positive rapid plasma reagin [RPR] or the venereal disease research laboratory [VDRL] tests), hepatitis B virus (HBV) and hepatitis C virus; and, the percentages of patients with history of STD

were not significantly different between the two groups. Both groups had seroprevalence of syphilis of more than 40% and HBV carriage rate of 15~20%. More than 40% of the patients in both groups had history of STD, predominantly genital warts, syphilis and gonorrhea. Of the 155 participants asked about history of illicit drug use, 76 (49%) answered "yes". In univariate analysis, patients in ED group were statistically significantly more likely to have a history of illicit drug use compared to those in LD group (57% vs. 38%, $p = 0.018$). The most common illicit drugs used were 4-methylenedioxymethamphetamine (MDMA), ketamine and marijuana; none used heroin.

Table 2. Comparisons of clinical variables among HIV-infected MSM between ED group and LD group

Variables	LD group (N=75)	ED group (N=89)	<i>p</i> value
Mode of HIV diagnosis			<0.0001
Screening diagnosis	19 (25%)	64 (72%)	
Symptomatic diagnosis by physicians	56 (75%)	25 (28%)	
Serologic test for syphilis (RPR or VDRL)			0.94
Reactive	19 (25%)	23 (26%)	
Non-reactive	56 (75%)	66 (74%)	
Hepatitis viral infection			
HBV carrier	15 (20%)	14 (16%)	0.48
HCV seropositive	2 (3%)	2 (2%)	0.87
History of STD			
Yes	31 (41%)	36 (40%)	0.91
No	44 (59%)	53 (60%)	
Type of STD			
Ano-genital warts	12 (16%)	13 (15%)	
Syphilis	9 (12%)	16 (18%)	
Gonorrhea	4 (5%)	3 (3%)	
Non-gonococcal urethritis	7 (9%)	6 (7%)	
Ano-genital herpes	2 (3%)	0 (0%)	
Others (genital ulcer, chancroid)	1 (1%)	1 (1%)	
History of illicit drug use	(N=66)	(N=89)	0.02
MDMA	22 (33%)	47 (52%)	
Ketamine	10 (15%)	31 (35%)	
Marijuana	7 (11%)	24 (27%)	
Cocaine	0 (0%)	1 (1%)	
Amphetamine	2 (3%)	0 (0%)	
Heroin	0 (0%)	0 (0%)	

Abbreviations: MSM, men who have sex with men; LD, late diagnosis; ED, early diagnosis; RPR, rapid plasma regain; VDRL, venereal disease research laboratory; HBV, hepatitis B virus; HCV, hepatitis C virus; STD, sexually transmitted diseases; MDMA, 4-methylenedioxymethamphetamine.

Table 3 summarized comparisons of variables about relationship with family and partners between ED group and LD group. Patients in ED group had a

significantly higher likelihood than those in LD group to have both parents alive and unseparated, a regular sexual partner at HIV diagnosis, a younger age of sexual debut and unprotected sex in the past 6 months ($p = 0.001$, <0.001 , 0.02 , <0.001 respectively). There was no significant difference between two groups in terms of living with family or not, sexual orientation known by any family member or not, and cumulative number of sexual partners since sexual debut.

Table 3. Comparisons of variables about family relationship and partners among HIV-infected MSM between ED group and LD group

Variables	LD group (N=75)	ED group (N=89)	<i>p</i> value
Living with parent(s)	(N=66)	(N=88)	0.23
Yes	38 (58%)	42 (48%)	
No	28 (42%)	46 (52%)	
Parents	(N=64)	(N=88)	0.001
Both alive and unseparated	37 (58%)	71 (81%)	
Separated or had one parent deceased	21 (33%)	17 (19%)	
Both deceased	6 (9%)	0 (0%)	
Sexual orientation known by any family member	(N=64)	(N=88)	0.23
Yes	30 (47%)	50 (57%)	
No	34 (53%)	38 (43%)	
Having a regular sexual partner at HIV diagnosis	(N=75)	(N=89)	<0.001
Yes	16 (21%)	46 (52%)	
No	59 (79%)	43 (48%)	
Age of sexual debut, years, median (range)	(N=64)	(N=88)	0.02
≤15	21(14-30)	19 (13-32)	0.047
16-20	3 (55%)	8 (9%)	
21-25	28 (43%)	54 (61%)	
26-30	22 (34%)	19 (22%)	
>30	11 (17%)	6 (7%)	
>30	0 (0%)	1 (1%)	
Cumulative number of sex partners since sexual debut	(N=64)	(N=89)	0.74
≤10	23 (36%)	28 (31%)	
11-50	27 (42%)	37 (42%)	
>50	14 (22%)	24 (27%)	
Timing of last unprotected sex practice before HIV diagnosis	(N=65)	(N=89)	<0.001
<1 month	11 (17%)	33 (37%)	
1~6 month	11 (17%)	38 (43%)	
>6 month	43 (66%)	18 (20%)	

Abbreviations: MSM, men who have sex with men; LD, late diagnosis; ED, early diagnosis.

Regarding self-awareness of HIV risk and utilization of screening services, comparisons between the two groups were shown in Table 4. Patients in ED group had a significantly higher percentage than those in LD group in recognizing their high risk of HIV acquisition (78% vs. 48%, $p < 0.001$). As for the utilization of screening services, patients in ED group had a higher likelihood to have considered HIV screening (69% vs. 49%, $p = 0.013$), to have been tested for HIV (73% vs. 52%, $p = 0.006$) and to have regular HIV screening (37% vs. 21%, $p = 0.03$).

Table 4. Comparisons of self awareness of HIV risk and utilization of screening services among HIV-infected MSM between ED group and LD group

Variables	LD group (N=75)	ED group (N=89)	<i>p</i> value
Self-awareness of high HIV risk			<0.001
Yes	36 (48%)	69 (78%)	
No	39 (52%)	20 (22%)	
Considered HIV screening			0.013
Yes	37 (49%)	61 (69%)	
No	38 (51%)	28 (31%)	
Tested for HIV before			0.006
Yes	39 (52%)	65 (73%)	
No	36 (48%)	24 (27%)	
Regular HIV screening			0.03
Yes	16 (21%)	33 (37%)	
No	59 (79%)	56 (63%)	

Abbreviations: MSM, men who have sex with men; LD, late diagnosis; ED, early diagnosis.

Multivariate analysis was performed to examine the relationships between early HIV diagnosis and study variables. The results were summarized in Table 5. In multivariate analysis, three factors were significantly associated with late HIV diagnosis: age more than 24 [Odds ratio, (OR) 3.26; 95% confidence interval (CI) 1.08-9.83], symptomatic diagnosis (rather than diagnosis by screening) [OR 5.70;

95% CI 2.53-12.8], last unprotected sex more than 6 months before HIV diagnosis [OR 6.19; 95% CI 2.70-14.2].

Table 5. Risk factors of late HIV diagnosis among HIV-infected MSM in multivariate analysis

Risk factors of late HIV diagnosis	Odds ratio	95% CI	<i>p</i> value
Age \geq 25 (vs. age 13-24)	3.26	1.08-9.83	0.036
Symptomatic diagnosis (vs. screening diagnosis)	5.70	2.53-12.8	<0.001
Last unprotected sex more than 6 months before HIV diagnosis (vs. within 6 months before HIV diagnosis)	6.19	2.70-14.2	<0.001

Abbreviations: MSM, men who have sex with men; CI, confidence interval;

Discussion

This study was conducted on 164 newly diagnosed HIV-infected MSM in Taiwan to collect data on socio-demographic factors, clinical status, relationships with family and partners, self awareness of risk, and utilization of screening services before HIV diagnosis. HIV diagnoses in our study participants were made between May 2006 and July 2008. Analysis from Taiwan CDC's report shows that there were 1349 newly reported HIV-infected MSM (including homosexuals and bisexuals) nationwide between May 2006 and July 2008. Therefore, the number of our study participants comprised of 12.2% of the total number of reported HIV-infected MSM during the same period.

The study showed that 46% of newly diagnosed HIV-infected patients had late HIV diagnosis, which is higher than reported in other countries (24-45%). While most foreign studies used national or regional health statistics for analysis, the higher prevalence of late HIV diagnosis is most possibly because the setting of this study was a medical center which often had patients with advanced HIV diseases from the emergency room or referred from other hospitals. Furthermore, our study focused on MSM, while most foreign studies enrolled patients with

other modes of HIV transmission. However, most foreign studies demonstrated that MSM were at a lower risk of late HIV diagnosis than heterosexuals, probably because of their increased knowledge of HIV infection and self awareness of risk [7-10]. In the Chinese societies, prevalence of late HIV diagnosis was only reported in Hong Kong. Compared with the overall HIV-infected population in Hong Kong, MSM had a lower prevalence of late diagnosis (MSM: 34.5%; overall: 58.2%) [11]; hence the higher prevalence of late HIV diagnosis among MSM in Taiwan might not be explained by ethnic or cultural factors. Unlike other countries, Taiwan provides free antiretroviral therapy (ART) which has dramatically improved the survival of HIV-infected patients [12, 13]. Further investigation is needed to evaluate whether free ART leads to decreased alertness of HIV infection and subsequent late HIV testing or late medical presentation among MSM.

In multivariate analysis, risk factors of late HIV diagnosis were age more than 24 years, symptomatic diagnosis (rather than diagnosis by screening), last unprotected sex more than 6 months before HIV diagnosis.

In accordance with US CDC, our study defined young MSM as those aged between 13 and 24 years [14, 15]. Young MSM is at a high risk of HIV infection, but many foreign studies have concluded that older age is a risk factor of late HIV diagnosis [7-10, 16-18]. A study showed that diagnosis of HIV infection among patients aged more than 60 years were often not considered by physicians until they were at advanced stage [19]. It remains unexplained why MSM between the age of 25 and 60 also had an increased risk of late HIV diagnosis, which warrants further studies.

Our study also confirmed that HIV screening plays an important role in early HIV diagnosis, because symptomatic diagnosis by physicians is highly likely to

indicate late HIV diagnosis. In spite of the authorities' constant campaign for regular HIV screening among high risk population, 36% of HIV-infected MSM in this study did not recognized themselves to be at high risk, and 40% never even considered HIV screening. Only 30% undertook regular HIV screening. Last unprotected sex more than 6 months before HIV diagnosis may lead MSM to have a false sense of security because of the lack of recent unprotected sex; these people overlooked the long latency of HIV infection, resulting in late diagnosis. Critical issues include how to improve MSM's self awareness of risk; how to enhance MSM's utilization of screening services, such as increasing screening sites, providing screening services at night and on holidays; how to strengthen pre-test and post-test counseling and safe sex promotion, with emphasis on individualizing risk reduction strategies to avoid increase of unsafe behaviors after a negative test result. We suggest that, after successful control of HIV epidemic in IDU, more efforts are needed to address these issues among MSM in Taiwan.

Our study has several limitations. First, the study site was a single hospital; caution should be taken when our results are generalized to patients in other medical institutions. However, the number of participants in our study comprised of 12.2% of the total number of reported HIV-infected MSM during the same period; hence we believe our results are representative. The second limitation is that late HIV diagnosis was defined by CD4 lymphocyte count in this study, which may have caused misclassification of an acutely HIV-infected patient whose initial CD4 lymphocyte count was $<200/\mu\text{L}$ into the LD group. However, this is rare and none of our study participants in the LD group had negative or indeterminate western blot results. In addition, all of the previous studies, except those which were performed in resource-limited countries, also used $\text{CD4}<200/\mu\text{L}$

as criteria of late HIV diagnosis [20]; therefore, our study chose the same definition to be comparable with other studies. Finally, in addition to patients' self awareness and behaviors, key factors leading to late HIV diagnosis may include whether their presenting symptoms were indicative of HIV infection, and whether physicians were alert enough to inquire the patients about HIV-related risk factors. Further studies are needed to examine the importance of these factors.

Conclusion

In this study conducted among newly diagnosed HIV patients in both outpatient and inpatient departments at the National Taiwan University Hospital, we found that late HIV diagnosis was prevalent among HIV-infected MSM in Taiwan. Risk factors of late HIV diagnosis were age more than 24 years, symptomatic diagnosis, and last unprotected sex more than 6 months before HIV diagnosis. Health policy should focus on enhancing the self awareness of risk and utilization of screening services among MSM to facilitate early HIV diagnosis in this risk population.

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