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Prevalence of Opportunistic Infections and Associated Factors in HIV-Infected Men Who Have Sex With Men on Antiretroviral Therapy in Bach Mai Hospital, Hanoi, Vietnam: A Case-Control Study

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Abstract

Objective: To investigate the distribution of opportunistic infections (OIs) and factors associated with acquiring OIs in human immunodeficiency virus (HIV)-infected men who have sex with men (MSM) in comparison to those of heterosexual patients.

Method: A cross-sectional study was conducted on 82 HIV-infected MSM and 120 HIV-infected heterosexual men in Bach Mai Hospital, Hanoi, Vietnam. Demographical characteristics and clinical data were collected and analyzed using appropriate statistics (Mann–Whitney, Chi-square, Fisher's exact test, and logistic regression).

Results: The prevalence of OIs among MSM and heterosexual patients were 63.4% and 81.7%, respectively. The most frequent OI in the MSM group was human papilloma virus (HPV) (11%), followed by hepatitis B virus (8.5%), mycobacterium tuberculosis (7.3%), and Talaromycosis (2.4%).

Conclusions: Multivariate logistic regression analysis showed that buying sex (odds ratio (OR) = 4, 95% confidence interval (CI): 1.13–14.25) and injecting drugs (OR = 13.05, 95% CI: 2.39–71.21) were associated with increased odds of having OIs in heterosexual patients while increasing age (OR = 1.1, 95% CI: 1.01–1.24) was correlated to increased odd of acquiring OIs in the MSM group. HIV-infected MSM accumulates OIs with increasing age, while heterosexual individuals increase opportunistic infections by buying sex or injecting drugs.

Keywords

HIV infection, MSM, Vietnam, opportunistic infection

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Human immunodeficiency virus (HIV) prevalence and incidence have been reported to be relatively high in men who have sex with men (MSM) (Beyrer et al., 2012; Solomon et al., 2015; UNAIDS, 2018). The estimated prevalence of newly HIV-infected MSM is 18% in the Middle East and North Africa, 50% in North, South, and Central America, 30% in Asia and the Pacific, 40% in Latin America, 22% in the Caribbean, and 17% in Western and Central Africa (Beyrer et al., 2012; UNAIDS, 2018). Enormous efforts have been made to increase the use of antiretroviral treatment, to introduce pre-exposure prophylaxis (PrEP), and to enforce and preserve human rights of the MSM population. Gay men and other MSM still accounted for 17% of all new HIV infections in 2018 globally (UNAIDS, 2018).

Opportunistic infections (OIs) occur as the result of immune-suppression and are believed to be responsible for the development of HIV-associated morbidities and mortalities (Mitiku et al., 2015). The most frequent OIs in HIV-infected patients in Vietnam are oral candidiasis,

tuberculosis, wasting syndrome, lower respiratory tract infection, cryptococcosis, and penicilliosis (Louie et al., 2004). The OIs are classified according to severity as WHO clinical stage I to IV (WHO, 2007). The more severe infections are thought to be associated with poor disease prognosis, and the degree of severity is dependent on pathogen exposure conditions, virulence of the pathogens, and the status of the immune system (Chaisson & Moore, 1997).

Antiretroviral therapy (ART) has been reported to restore the immune system and suppress viral replication as well as decreases the incidence of OIs and is thought to have the most profound effect on reducing OI-related mortality in HIV-infected patients (Autran et al., 1997; Hogg et al., 1999; Korencak et al., 2019). For those patients that still become carriers of OIs, treatment failure is considered one of the most common causes. These patients have decreased CD4 T cell counts and increased HIV viral loads as the result of failure of the immune system to protect against pathogens (Benson et al., 2004). There are patients who become infected with OIs despite high levels of CD4 T cell counts and viral suppression (Benson et al., 2004), showing that the risks of acquiring OIs are not only due to low CD4 T cell counts and high HIV viral load.

It has been unclear whether the amounts of OIs in MSM differ from those of HIV-infected heterosexual men. The distribution of OIs among heterosexual men has been studied extensively but that of OIs among HIV-infected MSM in Vietnam has not been known. Louie et al. (2004) have reported the most frequent opportunistic infections among HIV-infected adults including heterosexual men were oral candidiasis, tuberculosis, wasting syndrome, lower respiratory tract infection, cryptococcosis, and penicilliosis. Guancuagco et al. (2017) also confirmed the similar distribution of OIs among HIV-infected heterosexual patients and emphasized the regional differences between various countries including Japan, Philippines, and Vietnam. Other studies focusing on the single aspect of OIs also have been reported in HIV-infected heterosexual patients in Vietnam including fungal infection, Cryptococcus neoformans, and other biomarkers such as plasma lipopolysaccharide (LPS), sCD14, and antiflagellin IgG for studying the pattern of microbial translocation (Abdurahman et al., 2014; Ashton et al., 2019; Limper et al., 2017).

The factors associated with acquiring OIs have not been studied extensively. The risks associated with sexually transmitted infections (STIs), which prevalence has always been reported to be higher in MSM than in heterosexual men (Everett, 2013) have also been investigated in various studies. Factors associated with increased prevalence of STIs among HIV-infected MSM include unprotected sex, having diverse sex partners, increased consumption of drugs and alcohol, selling and buying commercial sex, and structural factors such as social stigma and discrimination, limited access to healthcare, and lower social status regarding education, housing, and employment (Bautista et al., 2004; Koblin et al., 2006). Risk of anal chlamydia was increased with unprotected anal intercourse, while increased risk of having herpes simplex virus 2 (HSV-2) was linked to multiple sexual partners and the risk of anal gonorrhea increased with unprotected sex (Castillo et al., 2015).

There have been limited studies focusing on the distribution of OIs among in HIV-infected MSM in comparison to that of heterosexual men in Vietnam. This study is an attempt to investigate the difference in the distribution of OIs among HIV-infected MSM in comparison to HIV-infected heterosexuals in Bach Mai Hospital, Hanoi, Vietnam. The results have long-term implications for designing the most suitable prevention program in order to reduce OIs and improve general health of HIV-infected vulnerable MSM in Vietnam.

Methods

Study Design and Setting

The study was designed as a cross-sectional study including all HIV-infected MSM patients enrolled and treated at the outpatient's clinic at Centre of Infectious Disease, Bach Mai Hospital, Hanoi, Vietnam from January to June 2019. All MSM patients and 120 randomly chosen heterosexual patients ($n = 82$ and $n = 120$, respectively) were included in the study. The majority of MSM ($n = 76$, 92.7%) and heterosexual ($n = 185$, 91.6%) patients are treated with first-line antiretroviral therapy with the

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most frequent regimen tenofovir disoproxil fumarate (TDF) + lamivudine (3TC) + efavirenz (EFV). Only one MSM and two heterosexual patients are currently treated with abacavir (ABC) + lamivudine (3TC) + efavirenz (EFV), one heterosexual patient is treated with zidovudine (AZT) + lamivudine (3TC) + nevirapine (NVP), and six patients are currently using second-line ART zidovudine (AZT) + lamivudine (3TC) + lopinavir/ritonavir (LPV/r) and tenofovir disoproxil fumarate (TDF) + lamivudine (3TC) + lopinavir/ritonavir (LPV/r).

Ethical permission to conduct the study has been obtained by the Institutional Review Board of Dinh Tien Hoang Institute of Medicine, Hanoi, Vietnam, registration number IRB-007. All participants were asked for written consent after having had the study explained, read, and understood the minimal risks involved in the study, and informed about the confidentiality of the data. Each patient was assigned with an ID number and the personal information was confidentially kept by the project principal investigator until data were entered into the study databases.

Sample and Data Collection

There were total sample population of HIV-infected MSM ($n = 80$) registered at outpatient's clinic of Centre of Infectious Disease, Bach Mai Hospital. Since the numbers of heterosexual patients were higher than MSM, a ratio of 1 MSM per 1.5 heterosexual individuals was chosen for the study. Interviewers were present at outpatient's clinic every day in order to conduct face-to-face interviews with all selected patients and fill in the questionnaire papers. Since there was two newly diagnosed HIV-positive MSM, a total of 82 patients included in MSM group. Regarding the data collection of heterosexual men, if any heterosexual patients refused to participate in the study, researchers went back to the list of patients and randomly chose the substitution in order to obtain the planned number of 120 heterosexual men.

The demographic and clinical data were collected from medical records that had been filed properly by medical staff at each visit of patients. The clinical data included: CD4 T cell count, HIV viral load, duration of ART, serum level of liver enzymes alanine transaminase (ALT) and aspartate transaminase (AST), creatinine, hemoglobin, HIV/OI co-infection, clinical stage, opportunistic infections (OIs), and sexually transmitted infection (STI). The clinical stage was determined according to the WHO clinical staging system for HIV/AIDS (WHO, 2005). The opportunistic infections (OIs) and sexually transmitted infections (STIs) were also accessed based on the WHO guideline (WHO, 2005).

Demographic information, socioeconomic status, and behavior data were collected by a questionnaire "Biobehaviour survey guidelines for populations at risk for HIV" designed by WHO (Global HIV Strategic Information Working Group, 2017). The use and validity of the questionnaire have been well reported in Vietnam and other countries (Hakim et al., 2018; Volkmann et al., 2018). The demographic data collected included: age, body mass index (BMI), birthplace, living place, employment status, education, income, having partner, alcohol consumption, and use of injectable drugs. Other characteristics regarding sexual activity were also collected including age at sexual debut, last sexual activity, buying sex, using condom, and using lubricant.

Data Analysis

The data were managed by Epidata 3.1 (Epidata, "The Epidata Association" Odense, Denmark", https://www.epidata.dk/index.htm) and analyzed by Stata 12.0.20 (Stata Corp LLC, Texas, USA) for descriptive statistics, statistical inference, and logistic regression. The descriptive statistics were used to summarize the variables, whereas the statistical inferences (Man–Whitney, Chi-square, and Fisher's exact tests) were used to compare different variables between MSM and heterosexual groups. Potential associated factors that were found to be significant in univariate analysis, or with a p value $<.15$, were entered in a forward stepwise selection multivariate logistic regression model to identify independent factors associated with increased odds of acquiring OIs or STI. All reported probability (p) values are two-sided; p values of $<.05$ considered to be statistically significant.

Results

General Demographical Characteristics of HIV-Infected MSM and Heterosexual Participants

Table 1 presents the general characteristics of the studied HIV-infected MSM and heterosexual men. Generally, MSM were younger than heterosexual men (median: 28, interquartile range (IQR): 24–32 and 38, IQR: 35–42, $p < .01$) and mostly lived in urban areas ($n = 58$, 70% vs. $n = 43$, 35.8%, $p < .01$). MSM had higher mean incomes than the heterosexual group (353USD, IQR: 172-645 vs. 231USD, IQR: 172-322.5, $p < .01$). Heterosexual individuals consumed more alcohol and there was a higher percentage of injecting drug abuse than in the MSM group ($n = 73$, 60.8% vs. $n = 20$, 24.4%, $p < .01$) and ($n = 56$, 46.7% vs. $n = 2$, 2.4%, $p < .01$), respectively.

The MSM group had lower levels of sexual activity in the last 6 months compared to the heterosexual men ($n = 38$, 46.3% vs. $n = 95$, 79.2%, $p < .01$). The majority of the heterosexual group used condom frequently ($n = 66$,

Table 1. The Demographic Characteristic of HIV-Infected MSM and Heterosexual Participants Treated at Bach Mai Hospital, Hanoi, Vietnam.

Characteristics		Total (n = 202)	MSM (n = 82)	Heterosexual (n = 120)	p value
Age (median, IQR)		35 (28–40)	28 (24–32)	38 (35–42)	<.01[a]
BMI (median, IQR)		20.9 (19.3–22.7)	21.3 (19.4–22.9)	20.6 (19–22.7)	.52[a]
Birthplace (n,%)	Urban	67 (33.2)	34 (42.5)	33 (27.5)	.04[b]
	Rural	135 (66.8)	48 (58.5)	87 (72.5)	
Living place (n,%)	Urban	101 (50)	58 (70.7)	43 (35.8)	<.01[b]
	Rural	101 (50)	24 (29.3)	77 (64.2)	
Employment status (n,%)	Unemployed	6 (3)	0 (0)	6 (5)	<.01[c]
	Student	9 (4.5)	8 (9.8)	1 (0.8)	
	Farmer	10 (5.0)	1 (1.2)	9 (7.5)	
	Retired/disability pension	1 (0.5)	1 (1.2)	0 (0)	
	Government employee	8 (4.0)	3 (3.7)	5 (4.2)	
	Freelance	102 (50.5)	33 (40.2)	69 (57.5)	
	Private company employee	66 (32.7)	36 (43.9)	30 (25.0)	
Education (n,%)	Elementary school	10 (5.2)	1(1.2)	9 (8.2)	<.01[b]
	Secondary school	28 (15.2)	7 (8.6)	21 (20.4)	
	High school	59 (31.9)	14 (17.1)	45 (43.7)	
	University/college or higher	95 (48.7)	60 (68.2)	35 (32.7)	
Total income per month (USD)		332 (172–322.5)	353 (172–645)	231 (172–322.5)	<.01[a]
Having partner (n,%)	Yes	84 (41.6)	56 (68.3)	28 (23.3)	<.01[b]
	No	118 (58.4)	26 (31.7)	89 (74.2)	
Alcohol consumption (n,%)	Yes	93 (46.0)	20 (24.4)	73 (60.8)	<.01[b]
	No	109 (54.0)	62 (75.6)	47 (39.2)	
Injecting drug (n,%)	Yes	58 (28.7)	2 (2.4)	56 (46.7)	<.01[b]
	No	135 (66.8)	80 (97.6)	55 (45.8)	

Table 2. The Behavioral Characteristic of HIV-Infected MSM and Heterosexual Participants Treated at Bach Mai Hospital, Hanoi, Vietnam.

Characteristics		Total (n = 202)	MSM (n = 82)	Heterosexual (n = 120)	p value
Age at sex debut (median, IQR)		20 (19–22)	20 (18–23)	20 (19–22)	.29[a]
Last sexual activity (n,%)	0–6 month	133 (65.8)	38 (46.3)	95 (79.2)	**<.01**[c]
	6–12 month	27 (13.4)	18 (22.0)	9 (7.5)	
	>12 month	41 (20.3)	26 (31.7)	15 (12.5)	
	Refuse to answer	1 (0.5)	0 (0)	1 (0.8)	
Buying sex (n,%)	Yes	71 (35.1)	13 (15.9)	58 (48.3)	**<.01**[b]
	No	131 (64.9)	69 (84.1)	62 (51.7)	
Using condom (n,%)	Yes	96 (47.5)	30 (36.6)	66 (69)	**<.01**[c]
	No	106 (52.5)	8 (21.2)	29 (30.5)	
Using lubricant (n,%)	Yes	68 (33.7)	58 (70.7)	10 (8.3)	**<.01**[c]
	No	15 (7.4)	5 (6.1)	10 (8.3)	
	Refuse to answer	119 (58.9)	19 (23.2)	100 (83.3)	

[a]Mann–Whitney test.
[b]Chi-square test.
[c]Fisher's exact test.
IQR = interquartile range; MSM = men who have sex with men.
Bold value: p is considered to be significant difference $p < 0.05$.

Table 3. Clinical Characteristics of HIV-Infected MSM and Heterosexual Participants Treated at Bach Mai Hospital, Hanoi, Vietnam.

Clinical characteristics	Total			MSM			Heterosexual			*p* value (Mann–Whitney)
	Median	IQR		Median	IQR		Median	IQR		
CD4 T cell count (cesIls/µl)	474	293	613	498	341	646	425	260.5	602.5	**.03**
HIV viral load (copies/ml)	ND			ND			ND			NA
Duration of ART (months)	44	26	64	29.5	14	44	58	35	83.5	<**.01**
SGPT/ALT (IU/L)	39	27	62	36.5	26	52	41.5	28	64	.09
SGOT/AST (IU/L)	31.5	24	41	28	23	35	35	26	52	<**.01**
Creatinin (umol/l)	81.5	75	90	81	74	87	82	75	91	.19
Hemoglobin (g/l)	156	148	163	157	149	163	154	147	161.5	.16

ART = antiretroviral therapy; HIV = human immunodeficiency virus; IQR: interquartile range; MSM = men who have sex with men; NA = not available; ND = not defined; ALT = alanine transaminase; AST = aspartate transaminase.

69%); whereas only 36.6% ($n = 38$) of MSM frequently used condom ($p < .01$). Around 70.7% ($n = 58$) in MSM group used lubricant compared to only 10% ($n = 5$) of the heterosexual men ($p < .01$). Regarding buying sex, 48.3% ($n = 58$) of the heterosexual men reported to use commercial sex as compared to 15.9% ($n = 13$) of the MSM group ($p < .01$) (Table 2).

Clinical Characteristics of HIV-Infected MSM and Heterosexual Patients

All of the patients were on ART and the viral load was suppressed to under detectable levels. Both groups had high levels of CD4 T cell counts. Among other clinical markers, only AST was significantly different between the two groups (28 IU/L, IQR: 23–35 in MSM vs. 35 IU/L, IQR: 26–52 in heterosexual men, $p < .01$) (Table 3).

Distribution of STIs and OIs Among HIV-Infected MSM and Heterosexual Participants

There was a high prevalence of OIs in both groups ($n = 52$, 63.4% in MSM vs. $n = 98$, 81.7% in heterosexual men, $p < .01$) and most patients were in clinical stage I. The most frequent OIs in the MSM group were HPV infection ($n = 9$, 11%), followed by hepatitis B virus (HBV) infection ($n = 7$, 8.5%), mycobacterium tuberculosis ($n = 6$, 7.3%), and Talaromycosis infection ($n = 2$, 2.4%). Instead, the most frequent OIs in the heterosexual group were mycobacterium tuberculosis ($n = 31$, 25.8%), followed by Varicella-Zoster virus infection ($n = 18$, 15%), Talaromycosis, and Thrush and dermatitis (each contributed to 12.5% of the total infection, $n = 15$). While the MSM individuals were significantly more often infected with HPV (11% vs. 3%, $p = .04$), the heterosexual group individuals were more likely to be infected with Mycobacterium tuberculosis, Talaromycosis, and Toxoplasma gondii Encephalitis (7.3% vs. 25.8%, $p < .01$; 2,4% vs. 12.5%, $p = .01$ and 1.2% vs. 10%, $p = .01$, respectively).

There was no significant difference in percentage of STIs between the groups (MSM: $n = 44$, 53.7%, heterosexual: $n = 59$, 49.2%). The frequency of syphilis was significantly higher in the MSM than in the heterosexual group ($n = 26$, 31.7% vs. $n = 3$, 3.0%, $p < .01$). HCV infections were more frequent in heterosexual men ($n = 66$, 55%) than in the MSM group ($n = 4$, 4.9%) ($p < .01$) (Table 4).

Factors Associated With Sexually Transmitted Infections

Age, using lubricants, levels of liver enzyme ALT, AST, and injecting drug were all found to be independently associated with increased odds of acquiring STIs when subjected to univariate logistic regression analysis for the pool data of MSM and heterosexual groups: age (odds ratio (OR) = 1.05, 95% confidence interval (CI): 1.01–1.09); levels of liver enzyme ALT (OR = 1.01, 95% CI: 1.00–1.02) and AST (OR = 1.02, 95% CI: 1.00–1.03); and injecting drug (OR = 3.08, 95% CI: 1.61–5.88). Using lubricant was protective, reducing the odds of having STIs to 0.26 (95% CI: 0.07–0.9) (Table 5). When analyzed by multivariate logistic regression, none of the factors showed significant association with presence of STI (Table 6). Thus, analyzing each group separately, such associations have not been observed (data not reported).

Factors Associated With Opportunistic Infections

In the univariate logistic regression model for the pool data of MSM and heterosexual groups, independent variables that showed significant association with OI acquisition included age (OR = 1.10, 95% CI: 1.05–1.15), having a partner (OR = 2.53, 95% CI: 1.28–5.00), buying sex (OR = 3.37, 95% CI: 1.53–7.41), longer ART duration (OR = 1.01, 95% CI: 1.00–1.02), and injecting

Table 4. Frequency of Opportunistic Infection Among HIV-Infected MSM and Heterosexual Participants Treated at Bach Mai Hospital, Hanoi, Vietnam.

		Total (n = 202)		MSM (n = 82)		Heterosexual (n = 120)		
Characteristics		*N*	%	*N*	%	*N*	%	*p* value
WHO HIV clinical stage	I	201	99.5	81	98.8	120	100.0	.41[a]
	IV	1	0.5	1	1.2	0	0.0	
HIV/OIs coinfection	Yes	150	74.3	52	63.4	98	81.7	<**.01**[b]
	No	52	25.7	30	36.6	22	18.3	
Frequency of OIs	Bacterial enteric	1	0.5	0	0.0	1	0.8	1.00[a]
	Bacterial respiratory	1	0.5	0	0.0	1	0.8	1.00[a]
	Cryptococcosis	1	0.5	0	0.0	1	0.8	1.00[a]
	Cytomegalovirus	2	1.0	1	1.2	1	0.8	1.00[a]
	Herpes simplex virus	2	1.0	2	2.4	0	0.0	1.00[a]
	Human papillomavirus	13	6.4	9	11.0	4	3.3	**.04**[a]
	Mycobacterium tuberculosis	37	18.3	6	7.3	31	25.8	<**.01**[a]
	Pneumocystis Pneumonia	5	2.5	1	1.2	4	3.3	.65[a]
	Talaromycosis (Penicilliosis)	17	8.4	2	2.4	15	12.5	**.01**[a]
	Toxoplasma gondii Encephalitis	13	6.4	1	1.2	12	10.0	**.02**[a]
	Varicella-Zoster virus	23	11.4	5	6.1	18	15.0	.07[a]
	Thrush and dermatitis	20	9.9	5	6.1	15	12.5	.16[a]
	HBV	25	12.4	7	8.5	18	15.0	.17[b]
	HCV	70	34.7	4	4.9	66	55.0	<**.01**[a]
STIs	Yes	70	34.7	44	53.7	59	49.2	.53[b]
	No	192	95.0	38	46.3	61	50.8	
Frequency of STIs	Syphilis	29	14.4	26	31.7	3	2.5	<**.01**[a]
	Gonorrhea	6	3.0	4	4.9	2	1.7	.22[a]
	Chlamydia	4	2.0	4	4.9	0	0.0	**.03**[a]

[a]Fisher's exact test.
[b]Chi-square test.
HBV = hepatitis B virus; HCV = hepatitis C virus; HIV = human immunodeficiency virus; MSM = men who have sex with men; OI = opportunistic infections; STI = sexually transmitted infections.

Table 5. Factors Associated With STI Acquisition in HIV-Infected MSM and Heterosexual Men Analyzed by Univariable Logistic Regression Model.

Variables	OR	*p* value	95% CI	
Age	1.05	.01	1.01	1.09
Using lubricant	0.26	.03	0.07	0.90
Liver enzyme ALT	1.01	.03	1.00	1.02
Liver enzyme AST	1.02	<.01	1.00	1.03
Injecting drug	3.08	<.01	1.61	5.88

Table 6. Factors Associated With STI Acquisition in HIV-Infected MSM and Heterosexual Men Analyzed by Multivariable Logistic Regression Model.

Variables	OR	*p* value	95% CI	
Age	1.00	.06	0.91	1.10
Using lubricant	0.71	.11	0.47	1.07
Liver enzyme ALT	1.01	.45	0.99	1.03
Liver enzyme AST	0.98	.45	0.94	1.03
Injecting drug	2.40	.39	0.33	17.30

ALT = alanine transaminase; AST = aspartate transaminase.

drug (OR = 15.44 times, 95% CI: 3.61–66.11). Using lubricant was protective, reducing the odds to 0.49 (95% CI: 0.25–0.93) (Table 7). Using multivariate logistic regression analysis, only age (OR = 1.09, 95% CI: 1.02–1.17), buying sex (OR = 2.7, 95% CI: 1.1–6.6), and injecting drug (OR = 15.1, 95% CI: 3.2–70.0) were significantly associated with OI acquisition (Table 8). Buying sex and injecting drug increased the odds of having OIs to 4.0 times (95% CI: 1.13–14.25) and 13.05 times (95% CI: 2.39–71.21), respectively, in heterosexual patients, while age was the only factor found to be associated with increased odds of acquiring OI in the MSM group (OR = 1.1, 95% CI: 1.01–1.24) (Table 9).

Table 7. Factors Associated With OI Acquisition in HIV-Infected MSM and HIV-Infected Heterosexual Men Analyzed by Univariable Logistic Regression Analysis.

Variables	OR	*p* value	95% CI	
Age	1.10	**<.01**	1.05	1.15
Having partner	2.53	**<.01**	1.28	5.00
Buying sex	3.37	**<.01**	1.53	7.41
Using lubricant	0.49	**.03**	0.25	0.93
Duration of ART	1.01	**.03**	1.00	1.02
Injecting drug	15.44	**<.01**	3.61	66.11

Table 8. Factors Associated With OI Acquisition in HIV-Infected MSM and HIV-Infected Heterosexual Men Analyzed by Multivariable Logistic Regression Analysis.

Variables	OR	*p* value	95% CI	
Age	1.09	**.01**	1.02	1.17
Having partner	0.80	.61	0.34	1.87
Buying sex	2.76	**.03**	1.08	7.06
Using lubricant	2.58	.08	0.88	7.55
Duration of ART	0.99	.51	0.98	1.01
Injecting drug	13.84	**<.01**	2.90	66.10

Table 9. Factors Associated With OI Acquisition in HIV-Infected MSM and HIV-Infected Heterosexual Men Analyzed Separately Each Group by Multivariable Logistic Regression Analysis.

Variables (heterosexual patients)	OR	*p* value	95% CI	
Age	1.13	.07	0.99	1.28
Having partner	1.28	.74	0.30	5.52
Buying sex	4.0	**.03**	1.13	14.25
Using lubricant	1.44	.72	0.20	10.39
Duration of ART	0.99	.30	0.96	1.01
Injecting drug	13.05	**<.01**	2.39	71.21
Variables (MSM)	**OR**	***p* value**	**95% CI**	
Age	1.11	**.03**	1.01	1.24
Having partner	0.63	.4	0.21	1.87
Buying sex	2.04	.36	0.44	9.38
Using lubricant	8.72	.07	0.84	90.63
Duration of ART	0.99	.51	0.96	1.02

ART = antiretroviral therapy; MSM = men who have sex with men; OR = odds ratio; 95% CI = 95% confidence interval.

Discussion

The study showed that the prevalence of OIs was 63.4% and 81.7% in MSM individuals and heterosexual participants, respectively. Previous reports of OI prevalence have varied: Pang et al. (2018) reported the prevalence of OI to be 63.9% ($n = 954$), Ghate et al. (2009) in India reported 35.5% ($n = 457$), while in Brazil, 51% ($n = 79$) has been reported and 10% in southern India ($n = 558$) (Gadelha et al., 2002; Kumarasamy et al., 2005). The current findings presented relatively high levels of OIs compared to other findings except for the study conducted by Pang et al., who investigated the overall prevalence of OIs among HIV-infected patients. The higher prevalence of OI in current study might be due to the fact that Vietnam also is burdened by a high prevalence of infectious disease. While the age and the CD4 T cell counts were relatively lower in studies conducted by Pang et al. and Gadelha et al., it is understandable that the prevalence of OI was high among these populations. Patient groups with high levels of CD4 T cells counts were typically found to have a low prevalence of OIs. Thus, the relatively high proportion of OI acquisition in current study was surprising, as most of the patients showed relatively high levels of CD4 T cells and viral suppression. All of the participants were on the ART, and ART initiation has been reported to be associated with a reduced incidence of OIs (Ghate et al., 2009), suggesting the OI acquisition was determined by other factors in addition to CD4 T cell counts and HIV viral load.

The proportion of the major OIs found in the current study was quite consistent with the study conducted by Gangcuangco et al. (2017), in which the authors investigated the prevalence of major OIs among ART-naive HIV-infected patients in several countries, including Vietnam. Consistent with most of the findings regarding the OIs in HIV-infected patients, tuberculosis was identified as the most predominant OI in heterosexual participants, with a prevalence of 25.8%. The percentage was lower than that of the study conducted in Vietnam in 2017 and a study conducted in Ethiopia (Mitiku et al., 2015). This was generally higher than most of the studies in most other developed and developing countries like Ethiopia (9.7%, $n = 358$) (Mitiku et al., 2015). The prevalence of tuberculosis infection in HIV-infected MSM was rather low (7.3%), and comparable to the prevalence reported in other studies. The low prevalence of tuberculosis infection in the MSM group might be explained by the fact that MSM patients in the study were young, and therefore had received proper tuberculosis vaccination and good healthcare service, in comparison to older heterosexual counterparts. Nevertheless, this prevalence is still significantly higher than that of the general population (Lien et al., 2009), suggesting tuberculosis is still one of the major opportunistic infections in the HIV-infected population in Vietnam.

Following tuberculosis, Varicella-Zoster virus (15%) and Talaromycosis (Penicilliosis) (12.5%) were found to be second and third most common OIs in heterosexual participants, which was in accordance with most findings

in other studies (Mitiku et al., 2015). Varicella-Zoster virus and Talaromycosis (Penicilliosis) accounted for only 6.1% and 2.4% infection in MSM patients. Varicella-Zoster virus is one of nine herpes viruses known to infect humans, enters through respiratory system with the prevalence in the incidence rate of 1.02–1.8 cases per 100,000 inhabitants (Becerra et al., 2013) among general population. Gangcuangco et al. (2017) have emphasized the regional indifferences in Varicella-Zoster virus infection among HIV-infected patients and showed that patients from Bach Mai Hospital acquired lower levels of infection compared to those at Nagoya Medical Center (NMC, Nagoya, Japan), Lampang Hospital (LPH, Lampang, northern Thailand), and Philippine General Hospital (PGH, Manila, Philippines); however, the authors have not stratified the data into different subpopulations such as MSM and heterosexual patients. The proportion reported by Gangcuangco et al. (2017) in antiretroviral-naïve patients was much lower than that in the current study, suggesting increased infection during treatment or improvement of the screening method for Varicella-Zoster virus among HIV patients in Bach Mai Hospital currently.

Talaromycosis (Penicilliosis) has been considered to be infected in small rate among general population, its occurrence has increased due to infection of HIV, especially more common in Southeast Asia (Chastain et al., 2017). Gangcuangco et al. (2017) reported the prevalence of Penicilliosis among patients in Bach Mai Hospital of 16.6% ($n = 384$), which is much higher than that of the current study. Regional differences have also been addressed in the study comparing the prevalence of certain opportunistic infections among different hospitals, suggesting the difference in living areas of MSM and heterosexual participants might account for this variation.

In the MSM participants, HPV (11%) had the highest prevalence among OIs compared to only 3.3% of heterosexual patients. The incidence of HPV infection has been reported to be increased in HIV-positive MSM and the prevalence in the current study was significantly lower than as reported by the SUN study conducted in the United States, which is 31% ($n = 403$), compared to only 11% HPV positive patients reported in the present study (Patel et al., 2018). The general prevalence of HPV in heterosexual men has reported to be 1.3%–72.9% (Dunne et al., 2006) in systematic review of 40 publications focusing on the infection of HPV among men. The low prevalence might due to the less advanced techniques of screening for HPV and other characteristics of the participants, including lower sexual activity. There was no screening program for HPV for HIV-infected patients, especially MSM in Vietnam and they were diagnosed only if they experienced symptoms. Therefore, the real prevalence of HPV among HIV-infected MSM could be considerably higher, compared to what has been reported. Additionally, the HPV infection in men has not been considered to be an important public health problem, thus, a more and comprehensive study should be conducted on the prevalence of HPV among men in general and HIV-infected heterosexual and MSM in order to provide a complete picture regarding the infection of HPV.

The prevalence of STIs was similar to in both groups; however, the distribution of infection is not the same. HCV infected only 4.9% of MSM; however, it affected 55% of heterosexual men. The results of MSM were generally consistent with those that have been reported, however, that of heterosexual men were much higher. Platt et al. (2016) constructed a meta-analysis in 783 studies and showed the estimated prevalence of HCV was 2.4% (IQR 0.8–5.8) within general population samples, 4.0% (1.2–8.4) within pregnant or heterosexually samples, 6.4% (3.2–10.0) in men who have sex with men (MSM), and 82.4% (55.2–88.5) in people who inject drugs (PWID). Clipman et al. (2020) also suggested the risk of increased HCV infection associated with drug use. The current subpopulation has up to 46.7% ($n = 4{,}994$) heterosexual patients using drug, which might be associated with increased prevalence of HCV. However, the study conducted in South Africa support the opposite trend in HCV infection among HIV-infected MSM and confirmed the association between injecting drug use and increased risks of HCV. The lower percentage of MSM in Bach Mai Hospital using drug might explain the lower HCV infection. Syphilis has been regarded as one of the most frequent STIs among HIV-infected MSM, in current study, the prevalence of Syphilis was 31.7% and 2.5% in MSM and heterosexual participants. The results were consistent with that of different studies conducting on HIV-infected MSM and heterosexual patients. The reason for the difference has not been established. One of the reasons for the difference is that HIV-infected heterosexual patients have been infected for longer period of time, therefore they might have been treated; while the MSM, on the other hand, has recently been infected with HIV and thus they might have just currently been diagnosed (Ang et al., 2020; Roth et al., 2020). Ang et al. also confirmed that the annual incidence rate of syphilis was consistently higher among MSM than in heterosexual men and the incidence was on the rise especially in MSM group with the risk factors including younger age, race, and being an MSM. It is unknown why MSM suffer from higher risk of syphilis; however, giving that MSM in current study was younger than heterosexual counterparts, the prevalence could be reasonably higher (Gogela et al., 2018).

Regarding the factors associated with increased odds of having OIs, increased odd was found to be associated with buying sex and injecting drug in heterosexual men and with age in the MSM group. The associated factors

for developing OIs have been investigated in several studies, including occupational factors, younger age, advanced baseline WHO stage, ART adherence, recent hemoglobin status, and recent weight were all identified to be parameters that could correlate to factors in OIs occurrence (Bhuvana et al., 2015). The current study stated that older individuals were more prone to developed OI than younger, which is supported by the finding of Bhuvana et al. (2015), in which age was reported to reflect the cumulative exposure to, and thus increased risk to become infected with tuberculosis. Ghate et al. (2009) reported that older age was a strong risk factor for developing OIs. Nevertheless, Moges and Kassa (2014) reported that younger age, was one of the risk factors for the occurrence of OIs; Lawn et al. demonstrated that younger age was a strong determinant of OIs (Lawn et al., 2005). A study conducted in US patients by Palella et al. (1998) found no significant association between age and development of OIs. No findings with association between gender, CD4 T cell counts, WHO HIV stages, or HIV viral load were found and that has been proved to play significant roles and OI acquisition. Notably, age was only associated factor found in MSM and not in heterosexual men, suggesting accumulation of opportunistic infections in HIV-infected MSM may be more severe. There is a need to study these issues thoroughly, to fully understand the reasons for, and consequence of this associated factor, in order to develop proper intervention for this subpopulation.

In the current study, association between buying sex and injecting drug with an increased odd of having OIs in heterosexual participants was found. Unprotected sexual activity through commercial sex was thought to be associated with STIs. The proportion-using condom was relatively high in the heterosexual group and there was a low prevalence of STIs in this subpopulation, suggesting that other infections might spread by commercial sex involvement. Certain diseases including HBV, HCV, HPV, and Herpes simplex virus have been shown to be infected through unprotected sex with the infected partners (Poudel et al., 2011) . Additionally, the prevalence of certain opportunistic infection related to sexual transmission among sex workers have been shown to be significantly high (Bremer et al., 2016; Goldsamt et al., 2018), suggesting the possibility of high levels of transmission for the heterosexual patients using the service. In search for other studies investigating this association and showing only the heterosexual group with an increased odd of acquiring OIs when buying sex, the results might have had important implications for optimizing the caring programs for the two subpopulations.

Drug abuse using injections has always been regarded as an associated factor for increased odd of having OIs. One of the reasons is the sharing needles since certain infections can be transmitted through blood. This might explain why the heterosexual group in the current study suffered from a high percentage of opportunistic infections. The association was not found in MSM participants, which might be due to the lower percentage of drugs used in this group. The patients showed distinct factors associated with increased opportunistic infection, which can be explained by the fact that our populations differ in terms of social status, demography, education, and lifestyle, which makes them unique, compared to other HIV-infected populations as well as to other HIV-infected MSM populations that have been studied.

There are several limitations within this study. First of all, all MSM and heterosexual participants were chosen from patients enrolled at Bach Mai Hospital, while MSM was much younger and mostly from urban areas with higher education and incomes, the comparison might be affected by the selection bias of the sampling. Secondly, the participants enrolled in this study do not represent the entire population of HIV-infected MSM and heterosexual men. This should be taken into consideration when interpreting the findings. Also, the data were collected at only one time point, so no access of the incidence and the trend of OIs and STIs within the group of study could be done. Furthermore, the study was designed as cross-sectional study so that only associated factors could be evaluated. Finally, the analyses could be affected by the low numbers of patients and other potential profound variables.

Conclusion

The current findings demonstrate a high prevalence of OIs among HIV-infected MSM and HIV-infected heterosexual patients, with certain associated factors including age in MSM, buying sex, and injecting drugs in heterosexual participants. The difference in prevalence and associated factors among these two subpopulations suggests development and implementation of appropriate interventions for these patients, such as increased awareness of using condoms or decreased drug use and the OI and STI screening and health training programs. Regarding the MSM, age was the only variable associated with the increased odds of having OI, therefore a more comprehensive study should be conducted in order to provide complete picture regarding the factors associated with increased OI and thus designing a proper intervention program for this particular subpopulation. As several factors might be potentially associated with increased OIs among HIV-infected MSM have not been addressed in the study such as unprotected sex, having diverse sex partners, social stigma and discrimination, and limited access to healthcare, further study needs to develop a comprehensive picture in order to develop the best possible intervention.

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Authors' Contributions

L.O. and T.T.D. contributed equally to this article. All authors were involved in carrying out the research and writing of the manuscript and have approved the final version of this publication.

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