Clinical Research

Predictors of syphilis infection among HIV pre-exposure prophylaxis users

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ABSTRACT

BACKGROUND Pre-exposure prophylaxis (PrEP) has revolutionized HIV prevention worldwide. However, research has shown a contradictory trend in which PrEP helps reduce HIV incidence, but increases sexually transmitted infections (STIs), especially in high-risk groups like men who have sex with men and female sex workers. This study aimed to examine the association between sex, age, occupational status, hepatitis B virus (HBV) infection, and hepatitis C virus (HCV) infection with syphilis infection among PrEP users.

METHODS The cross-sectional survey was conducted over 1 year, with 864 participants in Thu Duc City Hospital, Vietnam. The chi-square test was utilized for descriptive analysis. Binary logistic regression models estimated the association between sex, age, occupational status, HBV infection, and HCV infection with syphilis infection. Odds ratio (OR) and 95% confidence intervals (CIs) were calculated.

RESULTS Of 864 participants, 147 (18.2%) men and 68 (23.7%) employed individuals were tested positive for syphilis. The findings indicated that men (OR = 13.805; 95% CI = 1.886–101.024), employed individuals (OR = 1.838; 95% CI = 1.191–2.834), and HBV infection (OR = 2.076; 95% CI = 1.108–3.891) were significantly associated with an increased risk of syphilis infection.

CONCLUSIONS Men, employed individuals, and individuals infected with HBV face a higher risk of syphilis infection among PrEP users.

KEYWORDS hepatitis B, hepatitis C, pre-exposure prophylaxis, sexually transmitted infections, syphilis

HIV prevention remains a major public health challenge. Pre-exposure prophylaxis (PrEP) has effectively reduced HIV transmission in high-risk populations and is increasingly prescribed. An HIV preventive package encompasses sexually transmitted infection (STI) screening, risk-reduction counseling, and condom promotion.[1] Since 2017, oral PrEP services have been available in Vietnam and are now provided in 29 of 63 provinces with 32,000 individuals enrolled in 2021.[2] In Vietnam, PrEP is a key prevention strategy for an at-risk population of HIV, especially men who have sex with men (MSM), transgender people, injecting drug users (IDUs), female sex workers, and heterosexual individuals with high-risk partners of HIV.[2]

Globally, STI rates are rising, with notable surges in syphilis, gonorrhea, and chlamydia among MSM with multiple sexual partners, particularly in high-income countries. Moreover, an increase in combined bacterial STIs has been reported alongside with the initiation of

PrEP usage. Despite these findings, data from low- and middle-income countries remain limited.[3] Individuals with high-risk perceptions might engage in biomedical prevention methods, such as PrEP, to lower their perceived risk for HIV acquisition. However, they may also engage in riskier behavior, including reducing condom use, gaining new sexual partners quickly, engaging in sexual activity more often, changing to higher-risk sexual roles (for example, from oral to anal sex) or sexual positions (such as changing to being the receptive partner in anal sex), or exhibiting a combination of this behavior.[4] Research has shown that syphilis is an independent risk factor for future HIV acquisition.[5]

The highest increase in syphilis infection occurred among individuals aged 20–29 between 1999 and 2012,[6] with those aged 25–34 were considered at higher risk.[7] Garfinkel and Blumstein[8] highlighted that men diagnosed and treated for STIs are more likely to be screened for syphilis than women. Previous studies showed that men are 5 times higher to contract with syphilis than women.[7,9] Syphilis can cause serious problems and raise the risk of HIV acquisition and transmission.[10] Severe side effects linked to untreated syphilis may contribute to HIV infection acquisition and spread.

Syphilis infection is increasing in Vietnam, as one report showed a very high prevalence (17.6%) in transgender women.[11] Previous studies have explored syphilis prevalence and related factors among key populations such as MSM, IDUs, sex workers, transgender people, and pregnant women. The increase in PrEP utilization and the advent of a new era of HIV treatment, characterized by reduced fear of HIV acquisition, has coincided with a significant surge in STI rates. A study from Thailand[12] found a high incidence of STIs, including syphilis, among PrEP users in Southeast Asia. Ong et al[13] reported that PrEP does not prevent STIs, as users were more likely to engage in condomless sex, as well as reduce condom use during their sexual practices.[14,15] However, there are few reports on the factors associated with syphilis infection among PrEP users in Vietnam. Understanding these factors is crucial for developing targeted interventions and optimizing PrEP programs in the country. Therefore, this study aimed to examine the influence of sex, age, occupational status, hepatitis B virus (HBV) infection, and hepatitis C virus (HCV) infection on syphilis infection among PrEP users. Thus, a question was provided in this study as follows: what factors (gender or occupation) influence syphilis infection in HIV PrEP users?

METHODS

Sample size and sampling

Data collection was approved by Thu Duc City Hospital, Ho Chi Minh City, and conducted from December 1, 2022, to December 31, 2023. Participants were recruited through convenience sampling methods from individuals using PrEP services at the hospital. All PrEP users who visited the hospital during the study period were invited to participate until the required sample size was reached. Participants underwent medical examinations, including blood tests for STIs, HBV, and HCV. Data from patient records, including sex, age, and occupational status, were used for testing and potential diagnosis of syphilis, HBV, and HCV. Demographic information was also collected via structured questionnaires, and informed consent was obtained from all participants.

The sample size for this cross-sectional study was calculated using the formula for a single proportion with $Z = 1.96$ (95% confidence level), $p = 0.5$ (50%), and margin of error (e) = 0.05 (5%).[16] To account for possible non-response rates, the initial sample size of 770 was increased by 25%, resulting in 963 respondents. The final sample size includes 864 valid participants.

Measurements

Screening for hepatitis B surface antigen (HBsAg), HCV antibodies, HIV antigens, and antibodies was conducted using serological methods. The enzyme-linked immunosorbent assay technique was applied on the ETI-MAX system (DiaSorin, USA), while electrochemiluminescence was performed on the Cobas E601 system (Roche, Japan). All sera were tested with *Treponema pallidum* hemagglutination assay (TPHA; Sanofi Diagnostics Pasteur, France) for syphilis. A positive TPHA result was considered a lifelong indicator of current or previous syphilis infection. All tests were performed at the Laboratory of Thu Duc City Hospital, Ho Chi Minh City, Vietnam.

Ethical considerations

The study results were approved and inspected by The Thu Duc Hospital under Decision No. 2407/QĐ-BV, dated November 5, 2024.

Data analysis

The primary outcome was an aggregate variable of exposure to any STI. This variable was derived from the following serological testing results: positive marker for HBsAg, positive anti-HCV, or syphilis exposure.

Statistical analysis was conducted using SPSS software version 25.0 (IBM Corp., USA). Descriptive statistics were used to analyze sociodemographic data. Chi-square tests were conducted to examine the association between syphilis infection outcomes and other variables. Multivariate analysis was conducted using binary logistic regression to determine the relationship between age, sex, occupational status, HBV infection, and HCV infection with syphilis infection. Variables with $p<0.05$ were considered statistically significant. Odds ratio (OR) and 95% confidence intervals (CIs) were calculated.

RESULTS

Participant characteristics

This study included 864 participants for syphilis testing, resulting in 148 (17.1%) respondents being positive. Among them, 147 (18.2%) were men, and 68 (23.7%) were employed (Table 1).

Factors influencing syphilis among participants are shown in Table 1. The chi-square analysis identified a significant association between syphilis and HBV, HCV, sex, age, and occupation. This study found that sex was a significant factor, with men being 13.805 times more likely to be diagnosed with syphilis (OR = 13.805, 95% CI = 1.886–101.024). Employed individuals had higher odds of infection than unemployed participants (OR = 1.838, 95% CI = 1.191–2.834). HBV infection was associated with an increased risk of syphilis (OR = 2.076, 95% CI = 1.108–3.891), while HCV infection was not. Moreover, age was also not significantly associated with syphilis infection.

DISCUSSION

Our findings confirm that sex was significantly associated with syphilis infection, which aligns with previous studies.[17] This study also found higher syphilis infection in men than women,[9] as proven

Table 1. Predictors of syphilis

Characteristics	Syphilis (N = 864)		OR (95% CI)	*p*
	Negative, n (%) (N = 716)	Positive, n (%) (N = 148)		
Sex				**0.010**
Men	660 (92.2)	147 (99.3)	13.805 (1.886–101.024)	
Women	56 (7.8)	1 (0.7)	1.00	
Age (years)				
15–24	261 (36.5)	46 (31.1)		
25–34	277 (38.7)	60 (40.5)	1.281 (0.836–1.963)	0.255
35–44	120 (16.8)	28 (19.0)	1.295 (0.766–2.188)	0.335
45–54	46 (6.4)	10 (6.8)	1.249 (0.580–2.689)	0.570
55–64	9 (1.3)	4 (2.7)	2.364 (0.688–8.118)	0.172
>65	3 (0.4)	0 (0)	0 (0)	0.999
Occupational status				
Employed (full)	219 (30.6)	68 (45.9)	1.838 (1.191–2.834)	**0.006**
Freelancer	125 (17.5)	22 (14.9)	1.019 (0.578–1.797)	0.947
Students	133 (18.6)	17 (11.5)	0.725 (0.395–1.330)	0.299
Unemployed	239 (33.4)	41 (27.7)		
HBV				**0.023**
Negative	679 (94.8)	133 (89.9)	1.00	
Positive	37 (5.2)	15 (10.1)	2.076 (1.108–3.891)	
HCV				0.644
Negative	713 (99.6)	147 (99.3)	1.00	
Positive	3 (0.4)	1 (0.7)	1.707 (0.176–16.537)	

CI=confidence interval; HBV=hepatitis B virus; HCV=hepatitis C virus; OR=odds ratio

by the finding of studies in Vietnam with higher syphilis infection rates in men.[18,19] The higher rates in men are likely due to high engagement in risky sexual behaviors, whereas women are more likely to contract syphilis through sexual partners. Moreover, no significant association was found between age and syphilis infection, which contradicts other studies that identified age groups of 20–29[6] or 25–34[7] to be associated with syphilis.

This study suggested that HBV infection is associated with an increased risk of syphilis, while HCV infection is not. These findings align with the study of Xiao et al,[20] which found a positive association between syphilis and HBV but no relationship with HCV. Possible explanations include syphilis directly facilitating the acquisition of HBV due to its ulcerative infection and the lower prevalence of HCV infection in our study.

The implications of these findings are substantial for syphilis prevention and HIV management. Clinicians who are aware of this link may be inclined to recommend additional HIV testing for patients with syphilis who have been misdiagnosed and educate them on the heightened risk of contracting the virus. Our finding of higher syphilis rates in men, specifically in the context of PrEP use, highlights the need for targeted interventions in this group. These findings extend beyond previous studies by examining these relationships specifically within the PrEP user population, providing valuable information for healthcare providers managing PrEP programs in Vietnam and similar settings. Strategies to enhance HIV and STI testing in high-risk populations are crucial for early diagnosis of asymptomatic syphilis and prevent secondary transmissions.

This study has some limitations. Convenience sampling may have precipitated selection bias, compromising the representativeness of the sample and constraining the generalizability of the results. Furthermore, this study did not fully adjust various confounding variables that may have influenced the result and the possibility of bias. Future research should collect more comprehensive data on potential confounders and consider longitudinal designs to better elucidate the temporal relationships between PrEP use, syphilis infection, and associated factors. Future studies should also examine the influence of marital status, adherence, drug use, education, and risk-taking behaviors (tobacco use, alcohol use, and drug use), HIV-related knowledge, and condom use status on syphilis infection.

In conclusion, the high prevalence of syphilis and co-infections with HBV or/and HCV presents significant challenges to the treatment, including time, finances, and outcomes. The finding suggested that sex was significantly associated with syphilis infection, with men being at higher risk than women. This highlights the crucial role of HIV/STI prevention programs in public health. Clinicians treating HIV patients should develop syphilis prevention strategies focused on high-risk groups like men and MSM. The results also support healthcare practitioners in accurately diagnosing and treating patients to mitigate disease transmission. The study suggests the need to enhance community awareness through education and social media about HIV, STIs, and PrEP in promoting proactive measures. School-based education programs need to focus on comprehensive sexual health education, including HIV/STI prevention and risk reduction strategies. Community-based programs promoting sexual health and well-being, including counseling and support services for individuals living with HIV/STIs.

Conflict of Interest

The authors affirm no conflict of interest in this study.

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REFERENCES

1. Scott HM, Klausner JD. Sexually transmitted infections and pre-exposure prophylaxis: challenges and opportunities among men who have sex with men in the US. AIDS Res Ther. 2016;13(5).
2. Doan AH, Vu CM, Nguyen TT, Green KE, Phan HT, Janamnuaysook R, et al. Caring for the whole person: transgender-competent HIV pre-exposure prophylaxis as part of integrated primary healthcare services in Vietnam. J Int AIDS Soc. 2022;25 Suppl 5(Suppl 5):e25996.
3. Stewart J, Baeten JM. HIV pre-exposure prophylaxis and sexually transmitted infections: intersection and opportunity. Nat Rev Urol. 2022;19(1):7–15.
4. Kumar S, Haderxhanaj LT, Spicknall IH. Reviewing PrEP's effect on STI incidence among men who have sex with men-balancing increased STI screening and potential behavioral sexual risk compensation. AIDS Behav. 2021;25(6):1810–8.
5. Hoenigl M, Green N, Mehta SR, Little SJ. Risk factors for acute and early HIV infection among men who have sex with men (MSM) in San Diego, 2008 to 2014: a cohort study. Medicine (Baltimore). 2015;94(30):e1242.

6. Gao J, Xu J, Sheng Y, Zhang X, Zhang C, Li Y, et al. Increasing trend of syphilis and infection resistance: a retrospective study. Int J Infect Dis. 2013;17(11):e971–6.
7. Gomes NC, Meier DA, Pieri FM, Alves E, Albanese SP, Lentine EC, et al. Prevalence and factors associated with syphilis in a reference center. Rev Soc Bras Med Tropl. 2017;50(1):27–34.
8. Garfinkel M, Blumstein H. Gender differences in testing for syphilis in emergency department patients diagnosed with sexually transmitted diseases. J Emerg Med. 1999;17(6):937–40.
9. European Centre for Disease Prevention and Control (ECDC). Sexually transmitted infections in Europe 2013 [Internet]. Stockholm: European Centre for Disease Prevention and Control (ECDC); 2015 [cited 2025 Jan 25]. Available from: https://www.ecdc.europa.eu/en/publications-data/sexually-transmitted-infections-europe-2013.
10. Wu MY, Gong HZ, Hu KR, Zheng HY, Wan X, Li J. Effect of syphilis infection on HIV acquisition: a systematic review and meta-analysis. Sex Transm Infect. 2021;97(7):525–33.
11. Colby D, Nguyen NA, Le B, Toan T, Thien DD, Huyen HT, et al. HIV and syphilis prevalence among transgender women in Ho Chi Minh City, Vietnam. AIDS Behav. 2016;20(Suppl 3):379–85.
12. Phanuphak N, Sungsing T, Jantarapakde J, Pengnonyang S, Trachunthong D, Mingkwanrungruang P, et al. Princess PrEP program: the first key population-led model to deliver pre-exposure prophylaxis to key populations by key populations in Thailand. Sex Health. 2018;15(6):542–55.
13. Ong JJ, Baggaley RC, Wi TE, Tucker JD, Fu H, Smith MK, et al. Global epidemiologic characteristics of sexually transmitted infections among individuals using preexposure prophylaxis for the prevention of HIV infection: a systematic review and meta-analysis. JAMA Netw Open. 2019;2(12):e1917134.
14. Calabrese SK, Underhill K, Mayer KH. HIV preexposure prophylaxis and condomless sex: disentangling personal values from public health priorities. Am J Public Health. 2017;107(10):1572–6.
15. Gamarel KE, Golub SA. Intimacy motivations and pre-exposure prophylaxis (PrEP) adoption intentions among HIV-negative men who have sex with men (MSM) in romantic relationships. Ann Behav Med. 2015;49(2):177–86.
16. Lwanga SK, Lemeshow S. Sample size determination in health studies: a practical manual. Geneva: World Health Organization; 1991.
17. Ribeiro A, Trevizol A, Oluwoye O, McPherson S, McDonell MG, Briese V, et al. HIV and syphilis infections and associated factors among patients in treatment at a Specialist Alcohol, Tobacco, and Drugs Center in São Paulo's "Cracolândia". Trends Psychiatry Psychother. 2020;42(1):1–6.
18. Cẩm Vân T, Thị Ái Liên H, Thị Minh Phương P. [Clinical characteristics of patient with syphilis and related factors at National Hospital of Dermatology and Venereology]. Viet Med J. 2021;503(1):114–7. Vietnamese.
19. Vinh NM, Vi LT. [Clinical characteristics, serological response and management result in syphilis patient at Ho Chi Minh City Hospital of Dermato-Venereology (02/2020-10/2020)]. TẠP CHÍ Y DƯỢC LÂM SÀNG 108. 2023;18(6):91–8. Vietnamese.
20. Xiao Y, Li SL, Lin HL, Lin ZF, Zhu XZ, Fan JY, et al. Factors associated with syphilis infection: a comprehensive analysis based on a case-control study. Epidemiol Infect. 2016;144(6):1165–74.