

Original Article



Epidemiological and Clinical Characteristics of Women Living with HIV in Korea

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ABSTRACT

Background: While Korea maintains a low prevalence of human immunodeficiency virus (HIV), the number of newly diagnosed cases has been steadily rising, reaching approximately 1,000 annually in recent years. The 2022 annual report from the Korea Disease Control and Prevention Agency revealed that women living with HIV (WLWH) constitute 6.4% of the total confirmed people living with the HIV population, totaling 1,219 individuals. Despite this, only a few studies have focused on WLWH in Korea. This study aims to analyze the epidemiological and clinical characteristics of WLWH in Korea.

Materials and Methods: We retrospectively collected data by reviewing the medical records of all WLWH who visited 10 urban referral hospitals across Korea between January 2005 and May 2023.

Results: A total of 443 WLWH were enrolled in this study. The predominant risk exposure was heterosexual contact, with 235 (53%) participants either married or cohabiting with a male partner at their initial clinic visit. Among the participants, 334 (77.7%) were Korean, 27 (6.1%) were Southeast Asian, and 19 (4.3%) were African. Antiretroviral therapy was initiated by 404 WLWH (91.2%). We observed 118 pregnancies in WLWH following their HIV diagnosis, resulting in 78 live births (66.1%), 18 induced abortions (15.2%), 10 pre-viable fetal losses (8.5%), and four stillbirths

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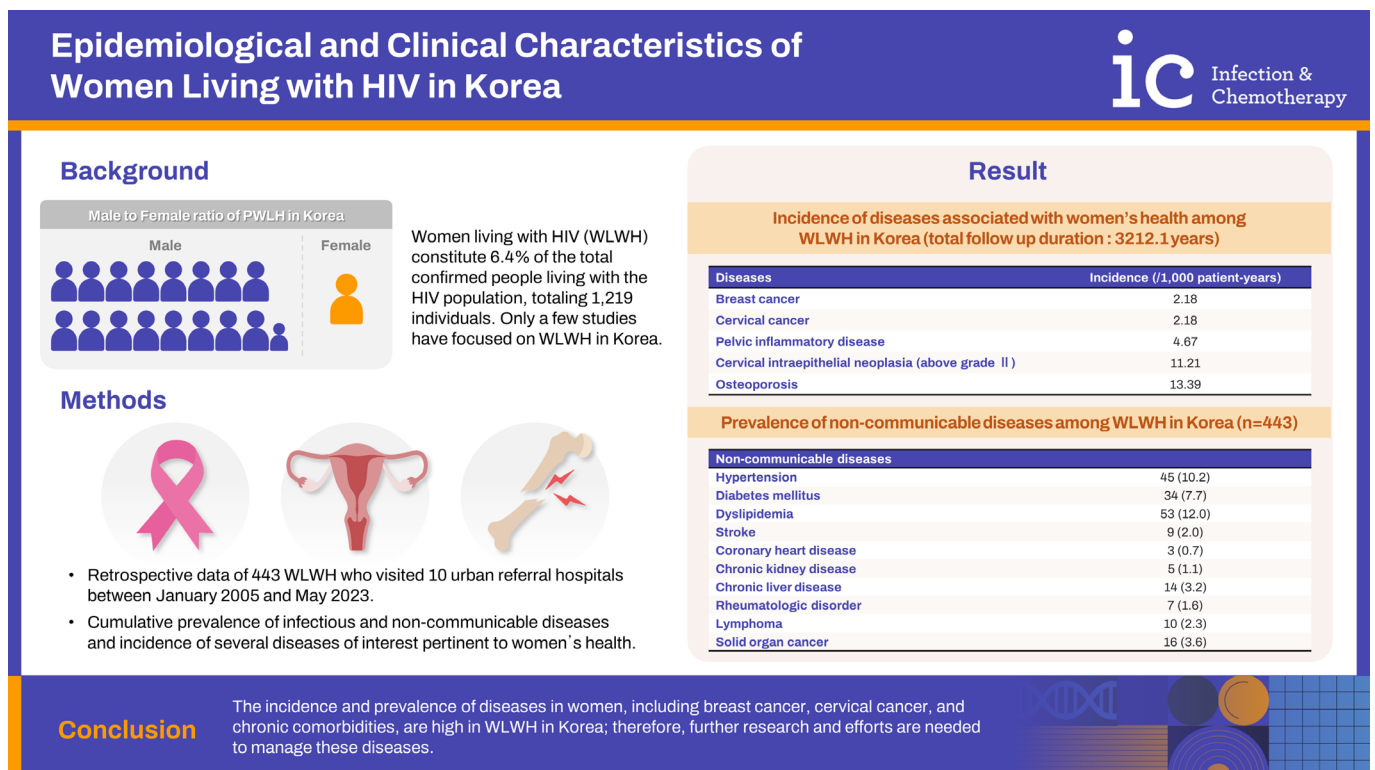
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(3.4%). Over a cumulative follow-up duration of 3,202.1 years, the incidence rates of breast and cervical cancers were both 2.18 per 1,000 person-years. Additionally, the incidence rates of pelvic inflammatory disease, cervical intraepithelial neoplasm (above grade II), and osteoporosis were 4.67, 11.21, and 13.39 per 1,000 patient-years, respectively.

Conclusion: This is the first multicenter study to investigate the clinical and epidemiological characteristics of WLWH in Korea. The incidence and prevalence of diseases in women, including breast cancer, cervical cancer, and chronic comorbidities, are high in WLWH in Korea; therefore, further research and efforts are needed to manage these diseases.

Keywords: Women living with HIV; Breast cancer; Cervical cancer; Pregnancy

GRAPHICAL ABSTRACT



INTRODUCTION

Globally, 53% of people living with human immunodeficiency virus (HIV) (PLWH) are women and girls [1]. In 2020, 4,200 women aged 15-24 years acquired HIV every week in sub-Saharan Africa. However, research focusing on women living with HIV (WLWH) remains limited. A systematic review conducted in 2016 revealed that women comprised only a median of 19.2% of participants in antiretroviral studies, 38.1% in HIV vaccine studies, and 11.1% in HIV cure studies [2]. Consequently, WLWH continues to be underrepresented in HIV clinical studies.

As of December 2023, Korea has recorded a cumulative total of 19,001 HIV-diagnosed individuals [3]. Among them, 1,219 (6.4%) are women. In 2022, 1,066 individuals were newly diagnosed with HIV in Korea, with 82 (7.7%) being women (35 Koreans and 47 foreigners). The total number of Koreans living with HIV in Korea in 2022 was 15,880, including 998 women.

While several reports have documented the clinical and epidemiological characteristics of PLWH in Korea [4-6], these studies have predominantly enrolled male PLWH due to the male-dominant epidemic of HIV infection in

Korea. Consequently, research focusing on the clinical and epidemiological characteristics of WLWH in Korea is still lacking.

A study investigating pregnancy rates and outcomes among WLWH in Korea revealed a lower pregnancy rate compared to the general population [7]. Conducted retrospectively between 2005 and 2017, this study enrolled 95 WLWH. The pregnancy rate within the study population was reported as 3.57 per 100 patient-years, with successful prevention of mother-to-child transmission of HIV through effective preventive measures.

Additionally, another study explored the epidemiology of human papillomavirus (HPV) infection among WLWH in Korea [8]. This study analyzed HPV DNA genotype and cervical cytology data from 60 WLWH and 1,938 HIV-negative women. Results indicated a higher prevalence of high-risk HPV infection and abnormal cervical cancer among WLWH compared to HIV-negative women. Given the necessity for tailored care for WLWH in the region, data specifically focusing on this demographic is essential.

Therefore, this current study aimed to describe the epidemiological and clinical characteristics of WLWH in Korea.

MATERIALS AND METHODS

1. Study population

We retrospectively enrolled all WLWH who visited 10 referral hospitals across Korea between January 2005 and May 2023. The participating hospitals were Severance Hospital, National Medical Center, Ajou University Hospital, Inha University Hospital, Wonju Severance Christian Hospital, Gachon University Gil Medical Center, Seoul Medical Center, National Health Insurance Service Ilsan Hospital, Soonchunhyang University Seoul Hospital, and Inje University Ilsan Paik Hospital. Transgender women were excluded from this study. Medical records of 443 WLWH were reviewed for this retrospective study.

2. Ethics statement

This study was approved by the Institutional Review Board of Severance Hospital (4-2023-0690), which waived the requirement for informed consent due to its retrospective design.

3. Study design, data collection, and definitions

This study utilized a retrospective cohort design. Data collected included age, HIV risk exposure, marital status, ethnicity, CD4+ T cell count, HIV viral load at the time of HIV diagnosis, and antiretroviral treatment regimens. We analyzed the cumulative prevalence of infectious and non-communicable diseases and examined the incidence of several diseases of interest pertinent to women's health, such as breast cancer, cervical intraepithelial neoplasia (above grade II), cervical cancer, pelvic inflammatory disease, and osteoporosis. Additionally, we compared the clinical characteristics of Korean and foreign WLWH.

Infectious diseases included acquired immune deficiency syndrome (AIDS) defining illness, other opportunistic infections such as herpes zoster, as well as sexually transmitted infections. AIDS-related diseases encompassed AIDS-defining illnesses according to the 1993 Centers for Disease Control and Prevention AIDS case definition, along with other relevant opportunistic diseases diagnosed by attending infectious disease doctors at each hospital [9]. Prolonged herpes simplex virus infection refers to chronic ulcer lasting longer than 1 month, or to cases of bronchitis, pneumonitis, or esophagitis. The non-communicable diseases evaluated included hypertension, diabetes mellitus, dyslipidemia, chronic kidney disease, chronic liver disease, rheumatological disease, cerebrovascular disease, cardiovascular disease, and solid organ cancer. Hypertension was defined as a diastolic blood pressure ≥ 90 mmHg and/or systolic blood pressure ≥ 140 mmHg [10], while diabetes was defined as a fasting blood glucose level ≥ 126 mg/dL [11]. Dyslipidemia was defined using any one of the following criteria: total cholesterol ≥ 240 mg/dL, triglyceride ≥ 200 mg/dL, high-density lipoprotein cholesterol < 40 mg/dL, and low-density lipoprotein cholesterol ≥ 160 mg/dL according to National Cholesterol Education Programme ATP-III guidelines [12]. Chronic kidney disease was defined as decreased kidney function demonstrated by glomerular filtration rate (GFR) of < 60 mL/min per 1.73 m² for at least 3 months or an estimated GFR < 60 mL/minute by chronic kidney disease epidemiology collaboration equation [13]. Chronic liver disease encompassed chronic hepatitis B and C, alcoholic liver disease, non-alcoholic fatty liver disease, and liver cirrhosis, according to the American Association for the Study of Liver Diseases guidelines [14]. Rheumatologic diseases included rheumatoid arthritis, psoriasis, psoriatic arthritis, ankylosing spondylitis, inflammatory bowel disease-associated spondyloarthritis, reactive

arthritis, systemic lupus erythematosus, Sjögren's syndrome, dermatomyositis, polymyositis, systemic sclerosis, vasculitis, gout, calcium pyrophosphate crystal deposition disease, and fibromyalgia diagnosed by rheumatology specialist using diagnostic criteria of the American College of Rheumatology [15]. Cerebrovascular disease comprised cerebral infarction and cerebral hemorrhage, whereas cardiovascular disease included stable angina, unstable angina, coronary artery disease, acute myocardial infarction, and peripheral artery obstructive disease. Osteoporosis, for participants >50 years of age, was defined as a bone mineral density of 2.5 T-scores below the average values for young participants [16]. Pelvic inflammatory disease was diagnosed by a gynecologist according to a previously published diagnostic criteria [17]. Solid cancers, including breast cancer and cervical cancer, were diagnosed based on relevant clinical, radiological, and pathological findings, among other criteria. Data on pregnancy outcomes were collected, with the number of weeks of pregnancy determined by examinations conducted at the Department of Obstetrics and Gynecology of each hospital. Follow-up duration was calculated from the first date of visit to the last visit.

4. Statistical analysis

The incidence rate per 1,000 patient-years was calculated by dividing the number of new cases within a specified period by the follow-up time. Continuous variables were presented as medians and interquartile ranges. Categorical variables were presented as frequencies and percentages. Continuous and categorical variables were analyzed using independent samples *t*-tests and Chi-square tests, respectively. All *P*-values were two-tailed, with a significance level set at <0.05. Statistical analyses were conducted using SPSS for Windows (version 26, SPSS Inc, Chicago, IL, USA).

RESULTS

A total of 443 WLWH were enrolled in the study, with a mean age of 39.3 years. The majority of participants who knew their route of infection reported acquiring HIV through heterosexual contact (Table 1). Upon initial visit, the survey on marital status revealed that 53.0% of the individuals were either married or cohabitating. Among the enrolled participants, 77.7% were Koreans, with foreigners originating from Southeast Asia, Africa, China, and Central Asia. The mean CD4+ T cell count at initial visit was 240

Table 1. Demographic, epidemiological, and clinical characteristics of women living with HIV in Korea (n=443)

Characteristics	Values
Age at first visit, years	39.3±13.3 (0-75)
HIV risk exposure	
Heterosexual contact	240 (54.2)
Unknown	200 (45.1)
Others	3 (0.0)
Marital status at first visit	
Single	95 (21.4)
Married/living together	235 (53.0)
Divorced/widowed	39 (8.8)
Unknown	74 (16.7)
Ethnicity	
Korean	344 (77.7)
Caucasian	11 (2.5)
Chinese	14 (3.2)
Southeast Asian	27 (6.1)
Central Asian	14 (3.2)
African	19 (4.3)
Other	5 (1.1)
Unknown	9 (2.0)
CD4+ T cell count at first visit, n=395, cells/mm ³	240 (89-453)
HIV viral load at first visit, n=348, copies/mL	
<50	9 (2.6)
50-1,000	38 (10.9)
1,000-100,000	189 (54.3)
100,000-1,000,000	100 (28.7)
>1,000,000	12 (3.4)
Antiretroviral therapy during follow up	
Yes	404 (91.1)
No	23 (5.2)
Unknown	16 (3.6)

Data are presented as mean±standard deviation (interquartile range) or number of participants (%).

HIV, human immunodeficiency virus.

Table 2. Incidence of diseases associated with women's health among women living with HIV in Korea

Disease	Incidence (cases per 1,000 patient-years)
Breast cancer	2.18
Cervical cancer	2.18
Pelvic inflammatory disease	4.67
Cervical intraepithelial neoplasia (above grade II)	11.21
Osteoporosis	13.39

HIV, human immunodeficiency virus.

cells/mm³, and the HIV viral load predominantly ranged from 1,000 to 100,000 copies/mL. Antiretroviral therapy was initiated by 91.2% of participants after HIV diagnosis.

The incidence rates of diseases of interest associated with women's health were analyzed (Table 2). Over a total follow-up period of 3,212 person-years, the incidence rates were as follows: breast cancer and cervical cancer both occurred at a rate of 2.18 cases per 1,000 person-years.

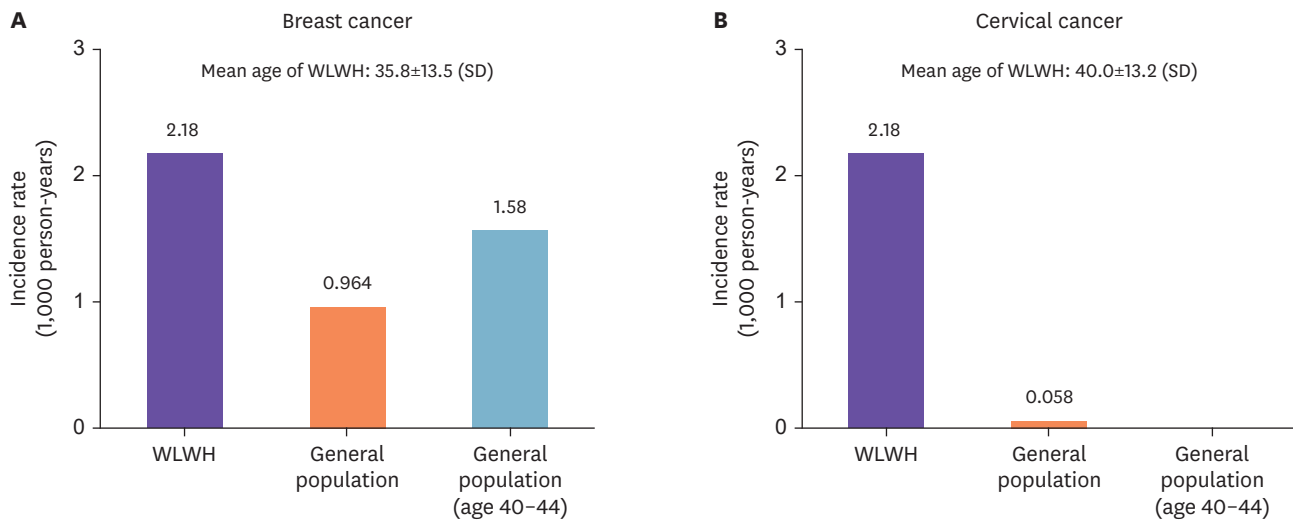


Figure 1. Comparison of the incidence of breast cancer and cervical cancer between WLWH and the general population in Korea. (A) The mean age of WLWH diagnosed with breast cancer was 35.8 ± 13.54 years (SD). Compared with the general population and individuals aged 40–44 years in the general population in 2020, the incidence rate of breast cancer in WLWH was higher than that in both groups. (B) The mean age of WLWH diagnosed with cervical cancer was 40.0 ± 13.2 years (SD). Compared with the general population, the incidence rate of cervical cancer was much higher among WLWH than in the general population in 2020. WLWH, women living with HIV; SD, standard deviation.

The incidence of pelvic inflammatory disease was 4.67 cases per 1,000 person-years, and that of grade 2 or higher cervical intraepithelial neoplasia was 11.2 cases per 1,000 person-years. Osteoporosis occurred at a rate of 13.39 cases per 1,000 person-years.

We compared the incidence rates of breast and cervical cancers among WLWH in this study with the crude incidence reported in the National Cancer Registry for 2020 in the general population (Fig. 1) [18]. The comparison revealed higher incidence rates of both cancers in WLWH. The average age at diagnosis of breast cancer in WLWH was 35.8 years, and even when compared with the incidence rates in the general population aged 40–44 years, the rates of breast and cervical cancers were higher in WLWH.

Among AIDS-related diseases, the prevalence rates of *Pneumocystis jirovecii* pneumonia, tuberculosis, invasive candidiasis, and cytomegalovirus (CMV) disease were 11.5%, 8.4%, 7.1%, and 7.1%, respectively (Table 3). Regarding non-communicable diseases, the prevalence rates of chronic conditions such as hypertension, diabetes mellitus, and dyslipidemia were 10.2%, 7.7%, and 12.0%, respectively. During the study period, 118 pregnancies were recorded, with stillbirths occurring after 20 weeks recorded in 3.4%, pre-viable fetal losses before 20 weeks recorded in 8.5%, and induced abortions recorded in 15.2%. Additionally, 29 participants (5%) died during the

study period, with 15 deaths attributed to AIDS-related diseases and 14 deaths to non-AIDS-related diseases.

The characteristics of Korean and foreign women infected with HIV were compared (Table 4). The mean age was 40.6 years for Koreans and 34.6 years for foreign WLWH. The prevalence of osteoporosis, hypertension, and dyslipidemia was significantly higher in Koreans compared to foreigners. However, for CMV disease, foreign WLWH exhibited a higher incidence than that in Koreans.

DISCUSSIONS

This study represents the first multicenter investigation into the clinical and epidemiological characteristics of WLWH in Korea. It sheds light on various aspects such as marital status, ethnicity, pregnancy outcome, prevalence of AIDS-related and non-AIDS-related diseases, and incidences of diseases relevant to women's health. By enrolling 443 WLWH who visited 10 hospitals since 2005, this study captured data from approximately 36% of the 1,219 WLWH diagnosed as of December 2023 in Korea [3]. While there is a limitation in not accounting for WLWH who did not visit hospitals, the data can still be considered representative of WLWH characteristics in Korea.

Among those whose risk of exposure was identified, the majority acquired HIV through heterosexual contact.

Table 3. Prevalence of infectious and non-communicable diseases and pregnancy outcomes among women living with HIV in Korea (n=443)

Characteristics	n (%)
Infectious diseases	
Invasive candidiasis	32 (7.1)
Cytomegalovirus disease	32 (7.1)
Tuberculosis	37 (8.4)
Pulmonary	23 (5.2)
Extrapulmonary	14 (3.2)
Non-tuberculosis mycobacterium	18 (4.1)
Pulmonary	5 (1.1)
Extrapulmonary	13 (2.9)
Herpes simplex virus infection (Prolonged)	6 (1.4)
<i>Pneumocystis jiroveci</i> pneumonia	51 (11.5)
Syphilis	28 (6.3)
Primary	2 (0.5)
Secondary	12 (2.7)
Latent	14 (3.2)
Herpes zoster	20 (4.5)
Progressive multifocal leukoencephalopathy	11 (2.5)
Non-communicable diseases	
Hypertension	45 (10.2)
Diabetes mellitus	34 (7.7)
Dyslipidemia	53 (12.0)
Stroke	9 (2.0)
Coronary heart disease	3 (0.7)
Chronic kidney disease	5 (1.1)
Chronic liver disease	14 (3.2)
Rheumatologic disorder	7 (1.6)
Lymphoma	10 (2.3)
Solid organ cancer	16 (3.6)
Pregnancy outcomes	
Pregnancy cases after being diagnosed with HIV	118
Pregnancy outcomes	
Live birth	78 (66.1)
Stillbirth	4 (3.4)
Pre-viable fetal loss	10 (8.5)
Induced abortion	18 (15.2)
Unknown	8 (6.8)

HIV, human immunodeficiency virus.

Furthermore, on their first visit, 53% of participants were married or cohabiting, whereas 8.8% were divorced or widowed. However, the influence of marital status on HIV infection could not be evaluated. A study conducted in a hyperendemic area such as South Africa showed that those who are married and living with their spouses have a reduced risk of HIV infection compared to those with other marital statuses [19]. In Korea, where HIV infection carries a significant stigma [20], a diagnosis of HIV could potentially effect marital status. Female sex workers are at a high risk of contracting HIV in many regions, such as sub-Saharan Africa [21]. However, no reports currently address their role in HIV transmission in Korea. Additionally, this study did not collect data on female sex workers.

In this study, the incidence of cervical and breast cancer among WLWH in Korea was found to be numerically higher than the reported incidence in the general population. Cervical cancer, being an AIDS-defining disease associated with HPV infection, is well-known to have a significantly higher incidence rate among WLWH compared to the general population [8]. However, the incidence of breast cancer in this population has not been consistently reported to be higher than that in the general population. For instance, a study from the United States reported a slightly lower breast cancer incidence among WLWH compared to the general population [22]. Similarly, another study from Tanzania indicated a significant decrease in breast cancer incidence during the AIDS epidemic [23]. In another study analyzing the Korean National Health Insurance Service database, breast cancer incidence among Korean WLWH was not higher than that in the general population [24]. Given the substantial improvement in survival rates among PLWH since the introduction of ART in recent decades [25], the disease burden of AIDS-unrelated cancers, such as breast cancer, might increase. However, since our study was not specifically designed to compare the incidence rate of

Table 4. Comparisons of characteristics and prevalence of clinical outcomes between Korean and foreigner WLWH in Korea

Characteristics	Korean (n=344)	Foreigners (n=99)	P-value
Age, year (mean±SD)	40.63±13.94	34.60±9.60	<0.001
CD4 T cell count at first visit, cells/mm ³ , mean (IQR)	322 (107-469)	260 (42-429)	0.618
Osteoporosis	41 (11.9)	2 (2.0)	0.003
Fetal loss	9 (11.0)	5 (13.9)	0.758
Induced abortion	15 (12.5)	3 (8.3)	0.265
Cytomegalovirus disease	18 (4.1)	14 (14.1)	0.003
Hypertension	43 (12.5)	2 (2.0)	0.002
Diabetes mellitus	31 (9.0)	3 (3.0)	0.054
Dyslipidemia	50 (14.5)	3 (3.0)	0.002

Data are presented as the number of participants (%) unless otherwise indicated. WLWH, women living with HIV; SD, standard deviation; IQR, interquartile range.

WLWH with that in the general population, including both Korean and foreign WLWH, we were unable to investigate whether the incidence of breast cancer was significantly higher than that in the general population. Therefore, additional research on breast cancer among WLWH in Korea is warranted.

Despite the younger average age of Korean WLWH compared to foreign WLWH, the prevalence of chronic non-communicable diseases such as osteoporosis, hypertension, diabetes mellitus, and dyslipidemia was higher among Korean WLWH. However, CMV disease was more prevalent among foreign WLWH. This finding suggests that foreign WLWH were more likely to be diagnosed late with AIDS. Additionally, chronic non-communicable diseases might be underdiagnosed and not properly managed among foreign WLWH. It is also possible that Korean WLWH might seek hospital care more actively than foreign WLWH. More efforts are needed for early diagnosis of HIV infection, early initiation of antiretroviral therapy, and proper management of chronic non-communicable diseases among foreign WLWH.

Given that the mean age of the participants was lower than that of foreigners, the prevalence of chronic age-related comorbidities might be lower. However, even after considering the age difference between the two groups, the prevalence of chronic age-related comorbidities was observed to be higher in infected Korean WLWH. This suggests the necessity for appropriate management policies not only for diseases affecting women but also for chronic age-related diseases in WLWH.

During the study period between January 2005 and May 2023, 118 pregnancies were recorded among 443 WLWH, with induced abortions occurring in 15.2% of cases. This study did not collect data on mother-to-child transmission of HIV. A previous study investigated the pregnancy outcomes in HIV-infected Korean women between 2005 and 2017 [7]. In the study, there were 21 pregnancies among 95 HIV infected Korean women of child-bearing age. Among these 21 pregnancies, five ended in induced abortion, and 16 resulted in childbirth, including two preterm deliveries at 24 and 35 weeks of gestation, respectively. There were no HIV-infected infants in the study. These studies indicate a low pregnancy rate and a high rate of induced abortion among WLWH in Korea.

This study had several limitations. First, it exclusively enrolled patients who visited 10 referral hospitals,

potentially overlooking the characteristics of WLWH who did not seek care at these facilities. Second, due to its retrospective design, only data available in medical records could be collected, potentially leading to incomplete information where relevant details were not recorded. Third, while the incidence rate of diseases affecting women was calculated, this study lacked a control group without HIV infection, preventing comparisons with the general population. The incidence rates of breast and cervical cancers in the general population, as shown in **Figure 1**, were based on crude incidence rates from national cancer incidence statistics. Finally, long-term surviving Korean PLWH have high unmet needs for mental health care and quality of life [26]; however, this study did not investigate these issues. Further research addressing the mental health and quality of life of WLWH in Korea is necessary.

Despite these limitations, this is the first multicenter study to investigate the clinical and epidemiological characteristics of WLWH in Korea. The findings highlight the high incidence and prevalence of diseases among women, including breast cancer, cervical cancer, and chronic comorbidities, among WLWH in Korea. The findings underscore the need for further research and efforts to manage these diseases.

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Conflict of Interest

JYC is editorial board of Infect Chemother; however, he did not involve in the peer reviewer selection, evaluation, and decision process of this article. Otherwise, no potential conflicts of interest relevant to this article was reported.

Author Contributions

Conceptualization: SMA, JYC. Data curation: SMA, YSL, MH, JAL, JES, YJB, JHH, JYA, DHO, SJJ, JHB, NSK, HKCh, YSP, BSC, YKK, JSY, YHC, JYC. Formal analysis: SMA, YSL, JAL, JES, YJB, JHH, JHK, JYA, DHO, SJJ, JHB, NSK, YSP, BSC, JSY, YHC, JYC. Investigation: SMA, YSL, MH, JAL, JES, YJB, JHH, JHB, BSC, YKK, YHC, JYC. Methodology: SMA, YSL, JAL, YJB, JHH, JHK, JYA, DHO, SJJ, NSK, HKC, YSP, BSC, YKK, JSY, YHC, JYC. Project administration: SMA, JYC. Resources: SMA, JYC. Software: SMA, JYC. Supervision: JYC. Validation: SMA, YSL, MH, JAL, JHH, JHK, SJJ, YSP, JSY, JYC. Visualization: SMA, JYC. Writing - original draft: SMA, JYC. Writing - review & editing: SMA, YSL, MH, JAL, JES, YJB, JHH, JYA, DHO, SJJ, JHB, NSK, HKC, YSP, BSC, YKK, JSY, YHC, JYC.

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