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Non-AIDS-related Comorbidities among People Living with HIV Aged 50 Years and Older: A Cross-sectional Study at Hua Hin Hospital, 2018-2019

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Abstract

With the success of combination antiretroviral therapy (cART), HIV-infected individuals are living longer and, as a consequence, are experiencing an increasing number of and more varied age-related comorbidities. Nevertheless, there are limited data regarding the profile of these chronic comorbidities among aging people living with HIV in Thailand. We therefore aimed to determine the prevalence and risk factors of non-AIDS-related comorbidities in this population. A cross-sectional study was conducted utilizing an electronic medical record database from the HIV clinic at Hua Hin Hospital. We assessed the prevalence of chronic comorbidities among HIV patients aged at least 50 years. Multivariate logistic regression analysis was performed to identify factors associated with multimorbidity. Among 307 HIV patients, nearly half (49.2%) had at least 1 comorbidity and multimorbidity was present in 22.5% of the patients. The most common comorbidities were dyslipidemia (33.9%), hypertension (21.5%) and diabetes (8.1%). Age (OR 1.11, 95% CI 1.06-1.18), duration of HIV infection (OR 1.11, 95% CI 1.04-1.19), body mass index (OR 1.10, 95% CI 1.02-1.19) and stavudine-containing regimens (OR 2.63, 95% CI 1.46-5.90) were associated with multimorbidity. The finding underscores a significant burden of non-AIDS-related comorbidities in aging HIV patients. Given the complexity of clinical care in this population, a comprehensive multidisciplinary approach is of paramount importance to optimize overall health outcomes.

Keywords: HIV, PLHIV, comorbidity, elderly, Thailand

Introduction

The availability of combination antiretroviral therapy (cART) has effectively reduced AIDS-related mortality worldwide and made HIV a manageable chronic disease. Globally, AIDS-related deaths have declined by 33% since 2010 and people living with HIV (PLHIV) who are on cART and virally suppressed are living longer and enjoying a better quality of life.[1] As a result, they have almost a normal life span similar to non-HIV infected populations, and the proportion of PLHIV aged more than 50 years has increased from 8% in 2000 to approximately 17% in 2016 with an expected notable upward trend.[2-4]

However, these aging PLHIV are facing new challenges from other comorbidities such as cardiovascular diseases (CVD), neurodegenerative diseases and malignancies. In addition to the traditionally recognized risk factors that cause these comorbidities, the accelerated aging process due to chronic immune activation and persistent systemic inflammation caused by HIV infection itself and side effects from long-term use of ART also play a role in the development of these chronic diseases.[5] These non-AIDS-related comorbidities among aging PLHIV have been reported in several studies and when compared to non-HIV-infected populations, the onset of the diseases is earlier and the disease prevalence is higher among the seropositive population.[6-9] Consequently, the HIV management strategy has shifted to optimize the long-term clinical outcome and to improve the overall quality of life of this aging population.

HIV/AIDS is one of the important public health issues in Thailand given the high burden of disease. It is estimated that the number of PLHIV is approximately 480,000 or 1.1% of the adult population, accounting for 9% of PLHIV in Asia and the Pacific region.[10] Nevertheless, Thailand is one of the developing countries that has successfully responded to the HIV epidemic through multisectoral collaboration between the government, the Thai Ministry of Public Health (MOPH), the National Health Security Office (NHSO)

and non-governmental organizations (NGOs). Intervention programs implemented by the MOPH have considerably reduced the number of new HIV infected cases over the past few decades. In 2018, the estimated number of people newly infected with HIV was 6,400, which is a 59% reduction compared to 2010.[10,11] It is estimated that AIDS-related deaths have also decreased to 18,000 per year in 2018 or a 39% decline since 2010.[11]

Previous studies conducted in Thailand reported a high prevalence of aging-related comorbidities among PLHIV.[12-15] However, these studies either had a small sample size, focused on specific diseases, or included young HIV patients. Moreover, to the best of our knowledge, there has been no published study focussing specifically on aging PLHIV populations and conducted in non-urban areas of Thailand which are known to have a different HIV distribution and population characteristics from the metropolitan area such as access to healthcare, socio-economic status and health literacy. Hua Hin Hospital is a governmental general hospital with a 340-bed capacity. It is situated in Hua Hin District, Prachuap Khiri Khan Province, western Thailand. The hospital provides a wide range of specialty healthcare services for patients, serving primarily the population of 60,000 in Hua Hin area and also receives patient referrals from the adjacent district hospitals, which have lower levels of healthcare. In 2019, the outpatient HIV clinic of Hua Hin Hospital serviced 1,376 HIV patients, while at the provincial level, it is estimated that there are approximately 4,000 PLHIV.[16]

Since there have been limited studies on the aging PLHIV population and age-related comorbidities in Thailand, and given the number of HIV patients and the proportion of aging PLHIV in Thailand are increasing each year, evidence-based data are needed to inform strategic planning, policy development, and resource allocation. The objective of this study was to assess the prevalence of non-AIDS-related comorbidities among aging PLHIV who were registered at the HIV clinic of Hua Hin Hospital and to explore the factors associated with multiple comorbidities.

Methods

Study Design and Study Population

We conducted a cross-sectional study at Hua Hin Hospital, Prachuap Khiri Khan Province, Thailand. The study population consisted of clinic records of all HIV-positive patients aged 50 years and older who attended the outpatient HIV clinic during 1 Jul 2018 to 30 Jun 2019. Patients were excluded if they were referred to other hospitals for HIV care or died before the study period began.

The data were collected from HIV clinic patient records and the electronic medical records database. The HIV patients were identified from the international classification of diseases, tenth revision (ICD-10) diagnostic code for human immunodeficiency virus (HIV) disease (B20-B24) and the HIV clinic appointment registry. The diagnosis of HIV in each patient was confirmed based on the anti-HIV test result in the record. For the non-AIDS-related comorbidities diagnoses, we used a composite definition from the medical records, laboratory results and the ICD-10 diagnostic code. Given that there might be some recording and coding errors, we also checked for the consistency between clinical diagnosis in the electronic medical records and laboratory results. There was no direct contact with the patients during the study period.

Outcome Measurement

Three categories of variables were collected: (1) the socio-demographic data of patients including gender, age, race, body mass index (BMI), type of health coverage and healthcare utilization over past 12 months, (2) the HIV-related characteristics and HIV-treatment data including ART data, CD4 count, viral load, duration of HIV infection since diagnosis, retention in care and viral suppression status, and (3) non-AIDS-related comorbidities of clinical relevance in the aging HIV-positive population. The chronic comorbidities included hypertension, diabetes mellitus, dyslipidemia, obesity, acute coronary syndrome, neurological disease (epilepsy, dementia and Parkinson disease), liver disease (chronic hepatitis B virus (HBV), hepatitis C virus (HCV) infection or cirrhosis), chronic kidney disease, bone disease (osteopenia or osteoporosis) and non-HIV-related malignancy. Apart from the diagnosis of comorbid diseases, the number of co-medications that the patients use on a daily basis was also collected. Co-medication was defined as non-antiretroviral medication prescribed during the study period. Multimorbidity was defined as having at least 2 of these non-AIDS-related chronic diseases and polypharmacy was defined as the concurrent use of 5 or more medications.[17,18]

Statistical Analysis

Exploratory data analyses were conducted to examine the distributions of the variables. Continuous variables were summarized by mean, standard deviation, median, and range according to their distributions while categorical variables were

described by frequency and percentage. Multivariate logistic regression was performed to identify factors associated with multimorbidity. To select independent variables into the model, we used the stepwise method which predicts the best model that yielded the lowest Akaike information criterion (AIC) as a penalized measure of model fit. Subsequently, the goodness of fit of the predictive model was determined by diagnostic plots.

In order to provide a valid statistical analysis in the presence of missing data, a multiple imputation (MI) method was implemented under the assumption that the unobserved values were missing at random (MAR). We used the Predictive Mean Matching approach for MI and after deriving the imputation model, we evaluated the plausibility of the imputed data by graphically comparing its distribution with the observed values.[19,20] A sensitivity analysis was conducted to examine differences between the original model with missing values and the imputed. Statistical significance was defined with an alpha level set at 0.05. All analyses were performed using the R language and environment version 3.6.3 (Foundation for Statistical Computing, Vienna, Austria).[21]

Ethical Approval

The data were collected during a 3-month period from 1 Jul to 30 Sep 2019 after ethical approval from the Institutional Review Board of the University of California, Los Angeles (reference number 19-001205) and permission to conduct the study from the ethics committee of Hua Hin Hospital.

Table 1. Socio-demographic and characteristics of PLHIV aged 50 years and older in Hua Hin hospital, Thailand, 2018-2019 (n=307)

Characteristic	n (%)
Age (years)[t]	55.0 (50.0, 83.1)
Gender	
Male	139 (45.3)
Female	168 (54.7)
Race	
Thai	300 (97.7)
Myanmar	2 (0.7)
Other	5 (1.6)
BMI (kg/m^2)*	22.3 ± 3.6
Health Insurance Schemes	
Universal Coverage	193 (62.9)
Social security	76 (24.8)
Civil Servant Medical Benefit	30 (9.8)
Others	8 (2.6)
Duration of diagnosed infection (years)*	8.3 ± 4.5
Late presentation (CD4 <350 cells/mm^3), (n=246)	
Yes	199 (80.9)
No	47 (19.1)
AIDS-defining events	
Yes	181 (59.0)
No	126 (41.0)
Last CD4 <200 cells/mm^3, (n=300)	
Yes	20 (6.7)
No	280 (93.3)
Last CD4 count (cells/mm^3)[t]	501.5 (38.0, 1514.0)
Current HIV viral load, (n=291)	
0-20 copies/ml	244 (83.9)
21-500 copies/ml	41 (14.1)
>500 copies/ml	6 (2.1)

*Note: [t] Data are shown in median with range. * Data are presented in mean with standard deviation.*

Table 2. Antiretroviral therapies and healthcare service utilization of PLHIV aged 50 years and older in Hua Hin hospital, Thailand, 2018-2019 (n=307)

Characteristic	n (%)
ART[a] duration (years)*	7.3 ± 4.3
0-1 years	19 (7.6)
1-5 years	72 (28.9)
5-10 years	80 (32.1)
10-15 years	70 (28.1)
>15 years	8 (3.2)
Number of ART regimens*	1.5 ± 0.7
Time from diagnosis to ART initiation (years)[t]	0.2 (0.0, 12.0)
ART regimen, (n=306)	
NRTI[c] + NNRTI[d]	274 (89.5)
NRTI + PI[e]	31 (10.1)
PI	1 (0.3)
Viral suppression, (n=291)	
Yes	285 (97.9)
No	6 (2.1)
Retention in care	
Yes	290 (94.5)
No	17 (5.5)
Healthcare utilization	
HIV clinic	300 (97.7)
Number of visits*	7.0 ± 2.6
Outpatient department	121 (39.4)
Number of visits*	3.7 ± 2.8
Hospitalization	21 (6.8)
Number of hospitalizations*	1.1 ± 0.3

*Note: [A] Antiretroviral therapy, [c] nucleoside reverse transcriptase inhibitor, [d] non-nucleoside reverse transcriptase inhibitor, [e] protease inhibitor. * Data are presented in mean with standard deviation. [t] Data are shown in median with range.*

Results

The records of 307 patients were included in this study, which accounts for 22.3% of all patients attending the HIV clinic at Hua Hin Hospital. The median age of the patients was 55.0 years (range 50.0–83.1 years). Almost half (45.3%) were male and 62.9% received care under the universal health coverage insurance scheme. Around one-quarter (26.4%) were diagnosed with HIV after the age of 50 years. The mean known duration of HIV infection was 8.3 ± 4.5 years, and 59% had a history of AIDS-defining events. The median CD4 count at presentation was 117 cells/mm^3 (1.0-1018.0 cells/mm^3) and 80.9% were late presenters (CD4 <350 cells/mm^3). The median CD4 cell count at the last visit was 501.5 cells/mm^3 and the median value of the change in CD4 count measured between the last CD4 count and CD4 count at presentation was 345 cells/mm^3 (-582.0-1273.0 cells/mm^3). The majority (83.9%) had HIV viral load <20 copies/ml (Table 1).

The distribution of antiretroviral therapies and healthcare utilization are shown in Table 2. The mean duration of receiving ART was 7.3 ± 4.3 years with only 3.2% of the patients receiving treatment for more than 15 years. The median time from HIV diagnosis to ART initiation was 0.2 years (range 0–12 years). The mean number of ART regimens was 1.5 ± 0.7. According to the Thailand national HIV treatment guideline 2017, the triple therapy regimen is recommended for all HIV patients with Tenofovir/Emtricitabine/ Efavirenz or Tenofovir/Lamivudine/Efavirenz as a first line regimen.[22] The majority (89.5%) of patients received regimens based on nucleoside Reverse Transcriptase Inhibitors (NRTI) plus a non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI). The most common treatment regimen was Tenofovir/Lamivudine/ Efavirenz (56.2%) and Lamivudine was prescribed to most of the patients (92.2%). Regarding the treatment target, 97.9% of the patients achieved viral suppression and 94.5% remained in HIV care. The mean (SD) number of HIV clinic visits in the past 12 months was 7.0 (2.6) and 7 patients missed their last appointment at the HIV clinic. In the previous year,

121 patients (39.4%) attended the outpatient department, and 21 patients (6.8%) were hospitalized.

Nearly half of the patients (49.2%) had a diagnosis of at least 1 comorbidity of interest and 7.8% had 3 or more comorbidities (Figure 1). Sixty-nine patients (22.5%) were multimorbid and the prevalence of multimorbidity increased with age: 14.2% (50-54 years), 30.4% (55-59 years) and 31.7% (≥60 years), respectively. The mean number of comorbidities was 0.8 and the median was 0 (range 0-5). The mean number of comorbidities increased slightly with age (Figure 2). The most common comorbidities were dyslipidemia (33.9%), hypertension (21.5%) and diabetes mellitus (8.1%) (Table 3).

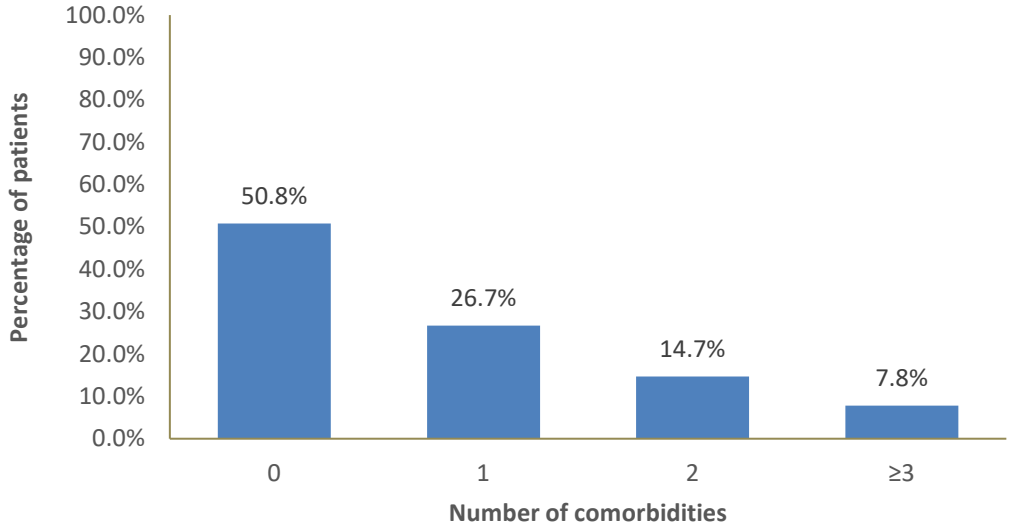

Figure 1. The percentage of patients and number of comorbidities of PLHIV aged 50 years and older in Hua Hin hospital, Thailand, 2018-2019

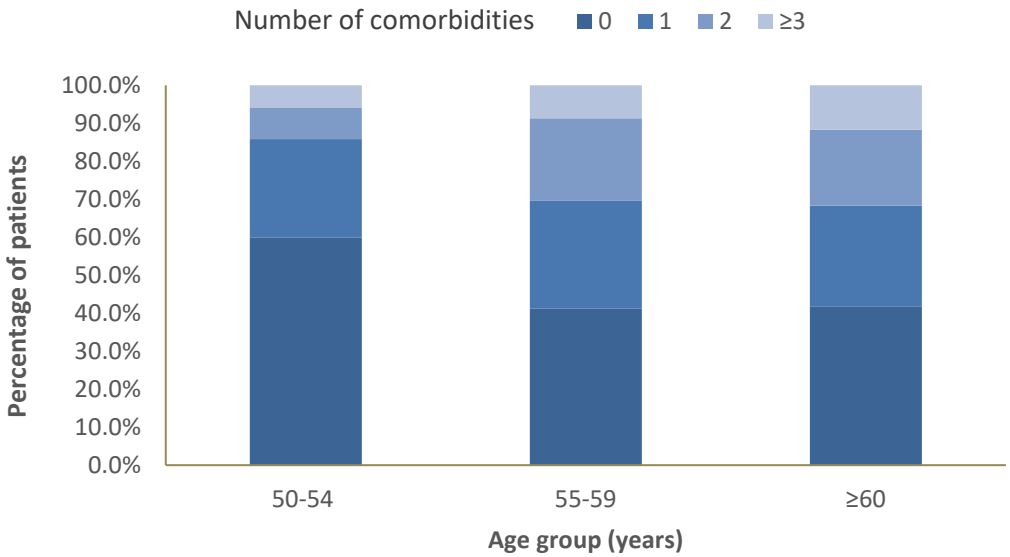

Figure 2. The distribution of the number of comorbidities of PLHIV aged 50 years and older, by age group, in Hua Hin hospital, Thailand, 2018-2019

In addition, 2.3% of the patients were obese while 12.7% were underweight (BMI <18.5 kg/m^2) and 15.3% were overweight (BMI 25.0–29.9 kg/m^2). Nearly 70% were receiving at least one non-ART medication and approximately one-third (34.5%) had polypharmacy; these patients were prescribed 5 or more drugs on a daily basis.

Results of the multivariate logistic regression analysis is presented in Table 4. According to the predetermined criteria for model selection, both initial and imputed models were found to be optimally fit for the data. Considering the imputed model, use of a stavudine-containing regimen was a strong predictor of multimorbidity (OR 2.63, 95% CI 1.46–5.90; *p*-value 0.02) while age (OR 1.11, 95% CI 1.06–1.18; *p*-value

<0.001), BMI (OR 1.1, 95% CI 1.02–1.19; *p*-value 0.009) and duration of HIV infection (OR 1.11, 95% CI 1.04–1.19; *p*-value 0.002) were weakly associated with the occurrence of multimorbidity. A sensitivity analysis was conducted since approximately 20% of the study subjects did not have an initial CD4 count or date of HIV diagnosis. The strength of association was not drastically different between the models except for the stavudine-containing regimen variable.

Table 3. Non-AIDS-related comorbidities and comedications in PLHIV aged 50 years and older in Hua Hin hospital, Thailand, 2018-2019 (n=307)

Characteristic	n (%)
Non-AIDS related comorbidities*	0.8 ± 1.0
50-54 years	0.6 ± 0.9
55-59 years	1.0 ± 1.0
≥60 years	1.1 ± 1.1
Multimorbidity	
Yes	69 (22.5)
No	238 (77.5)
Distribution of non-AIDS related comorbidities	
Dyslipidemia	104 (33.9)
Hypertension	66 (21.5)
Diabetes mellitus	25 (8.1)
Chronic hepatitis C	16 (5.2)
Chronic kidney disease	10 (3.3)
Obesity	7 (2.3)
Acute myocardial infarction	5 (1.6)
Chronic hepatitis B	5 (1.6)
Non-AIDS-defining Malignancy	3 (1.0)
Stroke	3 (1.0)
Other heart diseases	2 (0.7)
Cirrhosis	1 (0.3)
Epilepsy	1 (0.3)
Polypharmacy	
Yes	105 (34.5)
No	199 (65.5)

*Note: *Data are presented in mean with standard deviation.*

Table 4. Multivariate logistic regression regarding multimorbidity of PLHIV aged 50 years and older in Hua Hin hospital, Thailand, 2018-2019

	Initial Model			Imputed Model		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Age (years)	1.07	1.01-1.15	0.02	1.11	1.06-1.18	<0.001
BMI[c]	1.13	1.04-1.24	0.005	1.10	1.02-1.19	0.009
Duration of HIV infection (years)	1.13	1.05-1.22	0.002	1.11	1.04-1.19	0.002
Stavudine-containing regimen	2.02	0.79-4.96	0.12	2.63	1.46-5.90	0.02
P-value	<0.0001			<0.0001		
Adjusted-R^2	0.26			0.15		
AIC[d]	249.88			305.85		

Note: [c] BMI stands for body mass index; [d] AIC stands for akaike information criterion.

Discussion

This study explored the prevalence of non-AIDS-related comorbidities among aging PLHIV and factors associated with multimorbidity. Almost half of the patients had at least 1 comorbidity and approximately 20% had multimorbidity. These findings are in agreement with previous studies conducted in Asia in

which the prevalence of chronic conditions ranged from 40-60%.[15,23,24] However, some studies conducted in other regions reported a considerably higher prevalence of age-related comorbidities and multimorbidity.[25-27]

Consistent with previous studies, the most common chronic comorbidities were dyslipidemia, hypertension, and diabetes.[23,24,28] The prevalence of these diseases in our study was comparable with the results from another HIV-positive Asian regional cohort study.[29] However, when compared to other previous reports from Thailand, the results from our study are somewhat different.[12,15] A previous study conducted in 2018 showed considerably higher prevalence of chronic diseases: 69.8%, 27.3% and 23.9% of the patients had dyslipidemia, hypertension, and diabetes, respectively. This discrepancy might be explained by differences in the inclusion criteria for the study subjects as this study focused on HIV patients aged 50 years and older. The difference might also be attributable to the rate of screening uptake and coverage at the HIV clinic. According to the fifth Thai national health examination survey (NHES V) conducted in 2014, the prevalence of hypercholesterolemia, hypo-HDL-cholesterolemia and hypertriglyceridemia among Thais older than 15 years of age were 43.8%, 25.4% and 31%, respectively. And although the prevalence of hypertension and diabetes were 24.7% and 8.9% respectively, this study showed a comparable prevalence of these comorbidities to the general Thai population, which is in agreement with the findings from a study conducted in Portugal.[25,30] Nevertheless, some studies indicated that the prevalence of non-AIDS-related comorbidities were significantly higher among PLHIV.[26,31]

We found that the duration of HIV infection, age and BMI had a modest but significant positive association with multimorbidity. Similar findings were reported in other studies concerning the effect of HIV infection and aging associated with chronic metabolic conditions.[25,26] Interestingly, approximately 17% of the patients had excessive weight. However, the proportion was much lower than those reported in developing countries.[32,33] As obesity is one of the major modifiable risk factors for cardiovascular diseases, it is essential to focus on optimizing HIV patients' body weight as well. Nevertheless, we did not include ART duration in the model given that it was highly correlated with HIV infection duration. Some studies have shown an independent effect of ART duration in association with metabolic comorbidities.[27,34]

Of note, the occurrence of metabolic syndrome among PLHIV is known to be partly attributable to long-term use of certain ARTs, such as nucleoside reverse transcriptase inhibitors (NRTIs) and protease inhibitors. Similar to findings of the current study, HIV patients who received a stavudine-containing ART regimen were more likely to have multimorbidity. Other studies also showed similar associations between chronic conditions and the use of NRTIs.[35-37]

Our study is subject to some limitations. As the data were extracted from an electronic medical record database, some important variables that can potentially influence the outcome, such as mode of transmission and socioeconomic status such as education level, were not collected. We were also unable to include traditional risk factors of metabolic diseases such as smoking, alcohol consumption and physical activity into the model since these factors were not well-documented in the electronic medical record. Moreover, information on previous ART regimens and duration of cumulative exposure were not captured, so we were unable to assess the association of these variables with the comorbidities. In addition, external validity is an important concern. One should be cautious when extrapolating the results to another population since the study was conducted in a non-urban setting of Thailand where population characteristics may differ from those in metropolitan areas. Lastly, due to the cross-sectional design of the study, we cannot make any causal inferences from the findings; only associations can be made from this study.

Implication for Practice and Policy

The main objective of this study was to determine the prevalence of non-age-related diseases among PLHIV aged 50 years and over and assess the associated factors of multimorbidity. Accordingly, the practical implication derived from this research is that a specific screening protocol implementation for chronic age-related diseases is strongly recommended since early detection and treatment will be greatly beneficial for the aging HIV population. In the Thai government hospital setting, clinical care for chronic diseases is generally incorporated into HIV clinic services for practical purposes. Furthermore, a multidisciplinary approach for clinical care is also crucial since older PLHIV are also affected by other conditions such as geriatric syndromes. The issues of frailty, neurocognitive impairment, and falls should be also taken into consideration.

Secondly, in order to track the performance of an HIV clinic service, a comprehensive and timely data collection system is necessary. Consequently, the conceptual framework for service quality improvement and annual operation plan can be developed according

to the Reach, Recruit, Test, Treat, and Retain (RRTTR) approach. Moreover, data regarding traditional risk factors for metabolic diseases is particularly important in order to evaluate the effectiveness of treatment and prevention services. With this system established, the HIV clinic team will be able to address gaps and opportunities for improvement, which will inform policy decisions regarding resource allocation and hospital strategic planning.

Lastly, future research could further evaluate the impact of HIV on chronic comorbidities among aging PLHIV by comparing the disease prevalence with an HIV-negative control group. The study could be extended longitudinally to monitor treatment outcomes, incidence of multimorbidity and effectiveness of the screening and intervention program. It could also be expanded to the provincial level to address other aspects of health issues such as nutritional status, psychosocial wellbeing, or geriatric syndromes by incorporating additional assessment tools in order to provide comprehensive clinical care and improve the overall quality of life of aging PLHIV.

Suggested Citation

Duriyaprapan P. Non-AIDS-related comorbidities among people living with HIV aged 50 years and older: a cross-sectional study at Hua Hin hospital, 2018-2019. OSIR. 2020 Dec;13(4):127-36.

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