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Metabolic abnormalities among HIV-infected patients: The rational of national health security for people living with HIV

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ABSTRACT

In the era of highly active antiretroviral therapy (ART), traditional risk factors for metabolic syndrome are presented as increasing age. In low- and middle-income countries, the restricted benefit package of national health security for human immunodeficiency virus (HIV) does not facilitate the early detection of metabolic disorders. In order to assess the rational of national health security for metabolic abnormalities among people living with HIV (PLHIV), this retrospective study aims to determine the occurrence of metabolic abnormalities and its predicting factors. The study was approved by the hospital ethics committee and conducted at the internal medicine clinic, Pathum Thani Hospital, Thailand. Patients with HIV having had at least 1 year of first-line ART, and having their fasting glucose, fasting lipid profile, and blood pressure assessed before ART were recruited into the study. Those with any abnormal metabolic component prior to ART or absent history of ART were excluded. The metabolic abnormalities were defined as any of the following: elevated triglyceride, reduced high-density lipoprotein (HDL), elevated blood pressure, elevated fasting glucose, or on drug treatment for these metabolic abnormalities. The occurrence of metabolic abnormalities was found in 102 of 340 patients (30.0%). Hypertension (11.4%) was the most common abnormality. Age became the single predictor of metabolic abnormalities (odds ratio [OR] = 1.03, 95% confidence interval [CI] = 1.00–1.06). Aging patients with HIV should be the target group for monitoring

and treating metabolic abnormalities. The revision of the benefit package on metabolic abnormalities is urgently needed to promote a better quality of life.

Keywords: *HIV; HAART; metabolic syndrome; NRTIs; NNRTIs*

INTRODUCTION

Human immunodeficiency virus (HIV) attacks the body's immune system, specifically the CD4 cells. In 2017, 36.9 million people globally were living with HIV, and 59% of all people living with HIV (PLHIV) were provided with antiretroviral therapy (ART).[1] Thailand, one of the countries with the highest prevalence of HIV in Asia and the Pacific, accounts for 9% of the region's total population of PLHIV.[2] HIV incidence per 1000 population was 0.09 [0.08 – 0.10]. PLHIV were 480,000, and 75% of them are on ART.[3] The incidence rate of metabolic syndrome (MetS) in patients on ART was 1.2 per 100 person-months, and most of them had a low level of high-density lipoprotein (HDL).[4]

The development of highly active antiretroviral therapy (HAART), a treatment regimen of combined ART, improved the quality of life and increased the life expectancy of PLHIV.[5] Only 49.6% of the deaths were due to acquired immunodeficiency syndrome while the rest was due to age-related illness, especially cardiovascular disease.[6] This increases the importance of age-related illness among these patients.[6] In the era of HAART, several traditional risk factors of MetS are presented, which finally lead to MetS, cardiovascular events, and mortality.[5,7] In addition, both HIV infection and ART can cause metabolic abnormalities.[8] The previous study showed that the highest prevalence of metabolic component in patients treated with the first-line HAART group and the ART-naive group were 53.2 and 14.8%, respectively.[9] Prevalence of MetS in PLHIV, ranging from 11.2 up to 45.4%, was reported,[7] and 24.2% of patients on first-line HAART regimens were diagnosed with MetS.[9] Furthermore, MetS prevalences across subgroups were as follows; 23.7 and 26.7% in men and women, respectively, and 25.8, 17.2, and 17.9% in protease inhibitor (PI) users, nonnucleoside reverse transcriptase inhibitor (NNRTI) users, and nucleoside reverse transcriptase inhibitors (NRTI) users, respectively. However, there is no significant difference in the prevalence of MetS in high or low proportion of smokers, 8% versus 22.2%, $P = 0.193$.[10]

Dyslipidemia, insulin resistance, and diabetes mellitus (DM) have been observed among patients treated with HAART, especially PIs.[5] Furthermore, the annual cumulative incidence of events related to coronary artery disease was significantly higher in patients treated with PI than patients treated with other ART.[5] Therefore, the World Health Organization (WHO) recommended first-line ART regimens for adults consisting of two NRTIs plus one NNRTI.[11] However, it was reported that NRTI and NNRTI can increase the risk of DM.[12] Dyslipidemia has been observed in NNRTI-based therapy, although to a lesser degree when compared to PI.[13] Therefore, prevention of MetS by monitoring metabolic components appears to be an effective strategy. However, there are some limitations in this regard in low- and middle-income countries.

According to the universal health coverage in Thailand, the benefit package for patients with HIV is the free basic medical services available to all HIV patients. The basic blood chemistry testing, consisting of fasting plasma glucose (FPG) , serum total cholesteral, and serum triglyceride, have been performed in patients with HIV taking into consideration age and comorbidities as follows: age <35 years without any comorbidity: annually; age

<35 years with comorbidities: twice a year; and age >35 years: twice a year. For screening and monitoring metabolic disorders in PLHIV, blood chemistry testing is recommended within the first 3 months after starting or changing ART and every 3 months during the first year,[14,15] in contrast to the benefit pakage for HIV in Thailand. Moreover, adverse effects of ART were manifested differently in different races.[16] Therefore, strong evidence from the local database is needed to challenge the revision of the laboratory screening, especially in the aging HIV population. Is the national health security for metabolic abnormalities among the Thai PLHIV appropriate? The study hypothesis is that there is a high occurrence of metabolic abnormalities in PLHIV and that there are other predisposing factors of metabolic abnormalities apart from age. This retrospective study aims to determine the occurrence of metabolic abnormalities and predict factors responsible for metabolic abnormalities among patients with HIV.

METHODS

This retrospective study was conducted at the internal medicine clinic at the outpatient department of Pathum Thani Hospital, from September 2018 to Febuary 2019. The study was conducted in accordance with the principles for human experimentation, as defined in the Declaration of Helsinki and approved by the hospital ethics committee on 06 September 2018 (approval number: 0032.203.3/16076). The privacy of the research participants was ensured with an adequate level of confidentiality. The study conducted in the South West region of Cameroon showed that the highest prevalence of metabolic component in patients treated with the first-line HAART group and the ART-naive group were 53.2 and 14.8%, respectively.[9] In order to determine the occurrence of metabolic abnormalities in patients with HIV after first-line HAART, the incidence was estimated to be 33% with a 95% CI and the precision to be within 5% of the true value. The sample size calculation was as follows:

$$n = \frac{z^2 \times p \times (1-p)}{d^2}$$

where
n = sample size
z = 1.96 ($\alpha = 0.05$)
p = the prevalence of impaired fasting glucose
d = error allowance

Therefore, a sample size of at least 339 patients with HIV was required for this study.

Intensive training was provided for two data collectors, Pharm D students, using a set of practice medical records before the study started. The electronic predefined case record forms (eCRFs) were prepared for data collection with the electronic log book for patients' confidentiality and patient tracing. The electronic medical records were screened by a medical statistician according to inclusion and exclusion criteria before random sampling by data collectors. Patients with HIV having had at least 1 year of the first-line ART, and having FPG, fasting lipid profile, and blood pressure assessment before starting ART were recruited into the study. Those with any abnormal metabolic component prior to ART or absent history of ART were excluded. Clinical characteristics were obtained from electronic medical records and laboratory data were obtained from the electronic laboratory report using the eCRFs. The scheduled meetings were arranged to resolve data clarification and conflicts.

The outcomes of interest

The outcomes of interest were the occurrence of metabolic abnormalities after at least 1 year of the first-line HAART and its predicting factors among patients with HIV.

Definition

The metabolic abnormalities were defined as at least one metabolic component of the following: blood

pressure over 130/85 mmHg or hypertention, fasting triglyceride level over 150 mg/dL or dyslipidemia, and fasting blood sugar over 100 mg/dL or DM.[17]

Statistical analysis

Data analysis was performed by Statistical Package for the Social Sciences 15.0 (SPSS, Chicago, IL). Categorical variables were summarized as frequencies and percentages, and then analyzed using the chi square test or the Fisher's exact test. Continuous variables were summarized as mean ± standard deviation (SD) or median and interquartile range (IQR) values, and compared using *t*-test or the Mann–Whitney U-test where appropriate. Then, a*ll variables with* statistically significant relationships with metabolic abnormalities were included in the logistic regression model. The *variables with* statistical significance in this model indicated "the predictor" to the metabolic abnormalities. All tests for significance were two-sided, and $P < 0.05$ was considered to be of statistical significance.

RESULTS

A total of 340 patients were recruited into this study. The first patient was recruited on 10 September 2018 and of the last patient was recruited on 11 January 2019. After at least 1 year of first-line ART, 30% (102/340) of patients had metabolic abnormalities. The demographic characteristics of patients with and without metabolic abnormalities were shown in Table 1. In both the groups, most of the patients were male. Patients with metabolic abnormalities were significantly older than those without metabolic abnormalities (42.45 ± 10.34 years old vs. 38.76 ± 10.24 years old; P value = 0.003). Proportions of those who were married (45.1% vs. 30.5%; P = 0.010) and had an occupation (100.0% vs. 94.5%, P value = 0.016) were significantly higher in patients with metabolic abnormalities. Traditional risk factors such as smoking (9.7% vs. 17.2%; P value = 0.139) and alcohol consumption (9.7% vs. 17.3%; P value = 0.134) were slightly higher

TABLE 1. Bivariate Analysis of Demographic and Clinical Characteristics Associated with Metabolic Abnormalities after ART (n = 340).

Variables	Total (n = 340)	Metabolic abnormalities (n, %)		P
		No (n = 238)	Yes (n = 102)	
Male	200 (58.80)	144 (60.90)	55 (53.90)	0.700
Age (year[a])	39.76 ± 10.75	38.76 ± 10.24	42.45 ± 10.34	0.003*
Married	118 (34.90)	72 (30.50)	46 (45.10)	0.010*
Having an occupation	372 (96.20)	225 (94.50)	102 (100.00)	0.016*
Smoking	35 (14.90)	28 (17.20)	7 (9.70)	0.139
Alcohol	35 (15.00)	28 (17.30)	7 (9.70)	0.134
% Weight change[a,b]		+3.96 ± 10.74	+4.98 ± 10.36	0.570
Having comorbidities	59 (24.70)	39 (23.50)	20 (27.40)	0.519
Having opportunistic infection	135 (39.70)	95 (39.90)	40 (39.20)	0.904
Duration between diagnosis and initial treatment (year[a])	4.01 ± 0.84	4.05 ± 0.81	4.21 ± 0.82	0.008*
ART[c] duration (months[a])	41.14 ± 9.68	41.55 ± 9.27	43.03 ± 10.05	0.018*
Baseline CD4 (cell/mm^{3}[a])	336.56 ± 242.14	327.88 ± 255.40	342.15 (219.80)	0.429

[a]*Mean ± SD.*
[b]*Weight differences between the latest measurement and before starting ART.*
[c]*ART, antiretroviral therapy*
**statistical significance*

in those without metabolic abnormalities while weight differences between the latest measurement and before ART initiation was slightly higher in the metabolic abnormality group (4.9% ± 10.36 vs. 3.9% ± 10.74; P value = 0.570). Furthermore, these patients had significantly longer average duration between diagnosis and initial treatment (4.21 ± 0.82 years vs. 4.05 ± 0.81 years; P value = 0.008) as well as ART duration (43.03 ± 10.05 months vs. 41.55 ± 9.27 months, P value = 0.018). Baseline blood chemistries and CD4 were similar in both groups.

The distribution of metabolic abnormalities was shown in Figure 1. Of 102 patients, hypertension (39; 11.5%) was the single most common metabolic abnormality while the combination of hypertension and hypertriglyceridemia was the most common combination of metabolic abnormalities (9; 2.7%). MetS was found in one patient (0.3%).

ART in these patients was similar except the proportion of patients treated with either efavirenz or nevirapine in the regimen containing lamivudine and stavudine, which was significantly greater in the metabolic abnormality group (3; 2.98 vs. 0, P value = 0.011) (Table 2).

Logistic regression analysis showed that age was the single predictor of metabolic abnormalities in these patients (OR = 1.03, 95% CI = 1.00, 1.06, P value = 0.024).

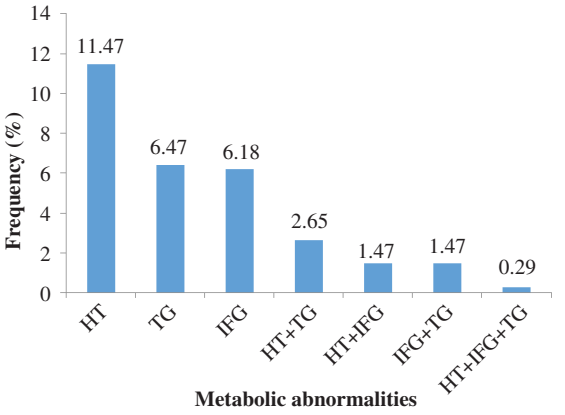

FIG 1. The distribution of metabolic abnormalities (n = 102). HT, hypertension; IFG, impaired fasting glucose; TG, hypertriglyceridemia.

DISCUSSION

This is the first finding of the occurrence of metabolic abnormalities in patients with HIV after first-line ART in Thailand. About one-third of them had metabolic abnormalities, and it was likely to be underestimated due to the restricted benefit package for PLHIV. The fact that gender was of no consequence in patients with and without metabolic abnormalities supported a previous study in Thailand.[18,19] However, in Western and African countries, females are at a higher risk of MetS, compared to males.[20,21] Living with family and having an occupation tend to increase the occurrence of metabolic abnormalities in this study. Similarly, previous studies showed that marriage is associated with weight gain in both men and women and is strong predictor for MetS.[22,23] In addition, MetS was significantly increased in the unemployed.[24] In line with a previous finding, no association was found between current smoking and alcohol consumption.[25] The inconsistent research findings were found among non-HIV patients.[26,27] Mild-to-moderate alcohol consumption of beer and wine had a positive effect on lipids and fasting insulin.[28] Moderate weight gain observed in our patients may increase the risk of MetS, as shown in a previous study.[29] Generally, PLHIV are motivated to engage in health-promoting behaviors because intensive lifestyle modification significantly improved cardiovascular risk indicators in patients with HIV and MetS.[30] Therefore, the traditional risk factors of MetS were found in small proportions and were not associated with metabolic abnormalities. Although there were significant differences in duration between HIV diagnosis and the initial treatment, and ART duration between the two groups, they were nonsignificantly different after logistic regression analysis. It was supported by a previous finding that the prevalence of

TABLE 2. ART in HIV-infected Patients with and without Metabolic Abnormalities (n = 340).

ART			Metabolic abnormalities after HAART (n, %)		P
NRTI		NNRTI	No (n = 238)	Yes (n = 102)	
TDF	FTC	EFV	111 (46.64)	39 (38.24)	0.554
		NVP	1 (0.42)	0	
	3TC	EFV	57 (23.95)	30 (29.41)	0.442
		NVP	3 (1.26)	3 (2.94)	
	AZT	EFV	4 (1.68)	1 (0.98)	0.642
	d4T	EFV	1 (0.42)	0	
	ddI	EFV	1 (0.42)	1 (0.98)	
3TC	AZT	EFV	29 (12.18)	12 (11.76)	0.762
		NVP	25 (10.50)	12 (11.76)	
	d4T	NVP	6 (2.52)	1 (0.98)	0.011*
		EFV	0	3 (2.98)	

ART, antiretroviral therapy; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; TDF, tenofovir disoproxil fumarate; FTC, emtricitabine; EFV, efavirenz; NVP, nevirapine; 3TC, lamivudine; AZT, zidovudine; d4T, stavudine; ddI, didanosine.
**statistical significanc*

MetS was not significantly different between longer and shorter durations of diagnosed HIV infection (32.0% vs. shorter: 19.1%, P = 0.251), as well as longer or shorter duration of ART (25.6% vs. 14.2%, P = 0.192).[10] CD4 cell > 350 cells/mm^3 was a risk factor for dyslipidemia as well as CVD,[31,32] and low CD4 cell counts observed in this study showed no association with metabolic abnormalities in bivariate analysis. After 12 months of ART, abnormal lipid profile[33] and insulin resistance[34] were detected, the prevalence of which could be influenced by ART.[35] NNRTI-based regimens were less likely to induce dyslipidemia.[36] In addition, TDF, 3TC, and FTC had positive effects on lipid profile.[37] However, hypertriglyceridemia was the second most metabolic abnormality found in our patients. Although ART containing didanosine and TDF were least commonly used in this study due to the risk of hyperglycemia,[38,39] hyperglycemia was found in 9.4% of the patients. In addition, increased risk of DM by NRTI and NNRTI was reported in a study of patients with HIV, mostly among black patients.[12] Therefore, HIV infection may have a major impact on metabolic abnormalities in our patients.

Age was the single predictor of metabolic abnormalities, which was supported by a previous study,[40] especially in patients treated with regimens not based on PI. In the era of HARRT, the life expectancy of PLHIV and people with age-related illness has increased.[34] With increasing age, the risk of hypertension increased,[41] which is supported by the highest rate of hypertension in this study. Furthermore, it is recommended to screen for hyperlipidemia and hyperglycemia at the inception of HIV care, after treatment initiation and modification.[15,17,42,43] However, laboratory testing provided by the benefit package for PLHIV is not sufficient for an early detection of all metabolic components. Delayed detection of metabolic abnormalities may lead to adverse cardiovascular outcomes. Our result highlighted that the national benefit package for aging patients with HIV should be revised in order to promote effective screening for metabolic abnormalities. FPG and/or HbA1c should be monitored within 1–3 months after initiation or modification of

ART, and then once or twice a year.[14,44] In patients having impaired FPG or DM, FPG should be monitored every 3 months or HbA1c should be monitored every 6 months.[14,44] Fasting lipid profile should be monitored within 3 months after initiation or modification of ART, then every 3 months in the first year, and once or twice a year thereafter.[15,45] In patients having a triglyceride level of > 200 mg/dL, fasting lipid profile should be monitored within 3 months after initiation of ART[15,45] and within 6–8 weeks after initiation or dose increases for statins, and subsequently every 6–12 months.[46] Due to the economic burden in this resourse-constrained country, patients aged ≥ 35 years should be prioritized as the finding in HIV-1-infected Thai adults showed that they are at high risk for MetS.[19] In addition, waist circumference and body mass index should be monitored at each visit. Lifestyle modification consisting of diet control, exercise, smoking cessation, and alcohol abstinence is strongly recommended.[47]

There are some limitations to this study due to incomplete entries in the electronic medical records such as marital status, waist circumference, height, and weight. The metabolic abnormalities may be underestimated because of the limitation of laboratory testing according to national health security for PLHIV. Furthermore, the result might have limited generalizabiltiy as the study was conducted only among Thai patients with HIV.

CONCLUSION

Age-related risk factors should be monitored and treated in order to prevent or slow down metabolic disorders in PLHIV. Therefore, improvement of the benefit package for aging PLHIV, especially blood tests for metabolic abnormalities, is urgently needed to promote a better quality of life and to diminish the long-term cost of health services.

CONFLICTS OF INTEREST

All authors have disclosed no conflicts of interest.

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REFERENCES

1. Global HIV & AIDS statistics -2018 fact sheet. http://www.unaids.org/en/resources/fact-sheet (accessed on: February 24, 2020).
2. Global information and education on HIV and AIDS. HIV and AIDS in Thailand. https://www.avert.org/professionals/hiv-around-world/asia-pacific/thailand (accessed on: February 24, 2020).
3. Country factsheets Thailand 2018. https://www.unaids.org/en/regionscountries/countries/thailand (accessed on: February 25, 2020).
4. Jacobson DL, Tang AM, Spiegelman D, et al. Incidence of metabolic syndrome in a cohort of HIV-infected adults and prevalence relative to the US population (National Health and Nutrition Examination Survey). J Acquir Immune Defic Syndr 2006;43(4):458–66. http://dx.doi.org/10.1097/01.qai.0000243093.34652.41
5. Kramer AS, Lazzarotto AR, Sprinz E, Manfroi WC. Metabolic abnormalities, antiretroviral therapy and cardiovascular disease in elderly patients with HIV. Arq Bras Cardiol 2009;93(5):519–26. http://dx.doi.org/10.1590/S0066-782X2009001100019
6. Gill J, May M, Lewden C, et al. Causes of death in HIV-1-infected patients treated with antiretroviral therapy, 1996–2006: Collaborative analysis of 13 HIV cohort studies. Clin Infect Dis 2010;50(10):1387–96. http://dx.doi.org/10.1086/652283
7. Paula AA, Falcao MC, Pacheco AG. Metabolic syndrome in HIV-infected individuals: Underlying mechanisms and epidemiological aspects. AIDS Res Ther 2013;10:32. http://dx.doi.org/10.1186/1742-6405-10-32
8. Grunfeld C, Kotler DP, Arnett DK, et al. Contribution of metabolic and anthropometric

abnormalities to cardiovascular disease risk factors. Circulation 2008;118:e20–8. http://dx.doi.org/10.1161/CIRCULATIONAHA.107.189623

9. Mbunkah HA, Meriki HD, Kukwah AT, et al. Prevalence of metabolic syndrome in human immunodeficiency virus–Infected patients from the South-West region of Cameroon, using the adult treatment panel III criteria. Diabetol Metab Syndr 2014;6(1):92. http://dx.doi.org/10.1186/1758-5996-6-92
10. Nguyen KA, Peer N, Mills EJ, Kengne AP. A meta-analysis of the metabolic syndrome prevalence in the global HIV-infected population. PLoS One 2016;11(3):e0150970. http://dx.doi.org/10.1371/journal.pone.0150970
11. World Health Organization. Updated recommendations on first-line and second-line antiretroviral regimens and post-exposure prophylaxis and recommendations on early infant diagnosis of HIV: Interim guidelines. Supplement to the 2016 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization, 2018. http://www.who.int/iris/handle/10665/277395 (accessed on: December 27, 2019).
12. Butt AA, McGinnis K, Rodriguez-Barradas MC, et al. HIV Infection and the risk of diabetes mellitus. AIDS 2009;23(10):1227–34. http://dx.doi.org/10.1097/QAD.0b013e32832bd7af
13. Zou W, Berglund L. HIV and highly active antiretroviral therapy: Dyslipidemia, metabolic aberrations, and cardiovascular risk. Prev Cardiol 2007;10(2):96–103. http://dx.doi.org/10.1111/j.1520-037X.2007.03071.x
14. Aberg JA, Gallant JE, Ghanem KG, et al. Primary care guidelines for the management of persons infected with HIV: 2013 update by the HIV medicine association of the Infectious Diseases Society of America. CID 2014;58:e1–34. http://dx.doi.org/10.1093/cid/cit665
15. Maggi1 P, Biagio AD, Rusconi S, et al. Cardiovascular risk and dyslipidemia among persons living with HIV: A review. BMC Infect Dis 2017;17:551. http://dx.doi.org/10.1186/s12879-017-2626-z
16. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report. Circulation 2002 Dec;106(25):3143–421. http://dx.doi.org/10.1161/circ.106.25.3143
17. Beer L, Mattson CL, Bradley H, et al. Understanding cross-sectional racial, ethnic, and gender disparities in antiretroviral use and viral suppression among HIV patients in the United States. Medicine (Baltimore) 2016;95(13):e317. http://dx.doi.org/10.1097/MD.0000000000003171
18. Teekawong C, Apidechkul T, Cassely M, Chansareewittaya K. Prevalence and factors associated with metabolic syndrome among HIV/AIDS infected patients who use ARV, Nan Province, 2015–2016. Siriraj Med J 2017;69(6):319–29.
19. Jantarapakde J, Phanuphak N, Chaturawit C, et al. Prevalence of metabolic syndrome among antiretroviral-naive and antiretroviral-experienced HIV-1 infected Thai adults. AIDS Patient Care STDs 2014;28(7):331–40. http://dx.doi.org/10.1089/apc.2013.0294
20. Alvarez C, Salazar R, Galindez J, et al. Metabolic syndrome in HIV-infected patients receiving antiretroviral therapy in Latin America. Braz J Infect Dis 2010;14(3):256–63. http://dx.doi.org/10.1016/S1413-8670(10)70053-2
21. Dohou H, Shm D, Codjo Hl, et al. Prevalence and factors associated with metabolic syndrome in people living with HIV in Parakou in 2016. SM Atheroscler J 2017;1(1):1005.
22. Wilson SE. Marriage, gender and obesity in later life. Econ Hum Biol 2012;10(4):431–53. http://dx.doi.org/10.1016/j.ehb.2012.04.012
23. Bhanushali CJ, Kumar K, Wutoh AK, et al. Association between lifestyle factors and metabolic syndrome among African Americans in the United States. J Nutr Metab 2013;2013:516475. http://dx.doi.org/10.1155/2013/516475
24. Park HS, Oh SW, Cho S-I, Choi WH, Kim YS. The metabolic syndrome and associated lifestyle factors among South Korean adults. Int J Epidemiol 2004;33(2):328–36. http://dx.doi.org/10.1093/ije/dyh032

25. Bosho DD, Dube L, Mega TA, et al. Prevalence and predictors of metabolic syndrome among people living with human immunodeficiency virus (PLHIV). Diabetol Metab syndr 2018;10:10. http://dx.doi.org/10.1186/s13098-018-0312-y
26. Oh SW, Yoon YS, Lee ES, et al. Association between cigarette smoking and metabolic syndrome. Diabetes Care 2005;28(8):2064–6. http://dx.doi.org/10.2337/diacare.28.8.2064
27. Slagter SN, van Vliet-Ostaptchouk JV, Vonk JM, et al. Combined effects of smoking and alcohol on metabolic syndrome: The LifeLines cohort study. PLoS One 2014;9(4):e96406. http://dx.doi.org/10.1371/journal.pone.0096406
28. Freiberg MS, Cabral HJ, Heeren TC, et al. Alcohol consumption and the prevalence of the metabolic syndrome in the U.S. Diabetes Care 2004;27(12):2954–9. http://dx.doi.org/10.2337/diacare.27.12.2954
29. Zabetian A, Hadaegh F, Sarbakhsh P, et al. Weight change and incident metabolic syndrome in Iranian men and women; a 3 year follow-up study. BMC Public Health 2009;9:138. http://dx.doi.org/10.1186/1471-2458-9-138
30. Fitch KV, Anderson EJ, Hubbard JL, et al. Effects of a lifestyle modification program in HIV-infected patients with the metabolic syndrome. AIDS 2006;20(14):1843–50. http://dx.doi.org/10.1097/01.aids.0000244203.95758.db
31. Lichtenstein KA, Armon C, Buchacz K, et al. Low CD4+ T cell count is a risk factor for cardiovascular disease events in the HIV outpatient study. Clin Infect Dis 2010;51(4):435–47. http://dx.doi.org/10.1086/655144
32. Santiprabhob J, Tanchaweng S, Maturapat S, et al. Metabolic disorders in HIV-infected adolescents receiving protease inhibitors. BioMed Res Int 2017;2017(12):1–14. http://dx.doi.org/10.1155/2017/7481597
33. Leitner JM, Pernerstorfer-Schoen H, Weiss A, et al. Age and sex modulate metabolic and cardiovascular risk markers of patients after 1 year of highly active antiretroviral therapy (HAART). Atherosclerosis 2006;187(1):177–85. http://dx.doi.org/10.1016/j.atherosclerosis.2005.09.001
34. Palacios R, Merchante N, Macias J, et al. Incidence of and risk factors for insulin resistance in treatment-naive HIV-infected patients 48 weeks after starting highly active antiretroviral therapy. Antivir Ther 2006;11(4):529–35.
35. Pendse R, Gupta S, Yu D, Sarkar S. HIV/AIDS in the South-East Asia region: progress and challenges. J Virus Erad 2016;2:1–6. http://dx.doi.org/10.1016/S2055-6640(20)31092-X
36. Jevtovic DJ, Dragovic G, Salemovic D, et al. The metabolic syndrome, an epidemic among HIV-infected patients on HAART. Biomed 2009;63(5):337–42. http://dx.doi.org/10.1016/j.biopha.2008.09.011
37. Crane HM, Grunfeld C, Willig JH, et al. Impact of NRTIs on lipid levels among a large HIV-infected cohort initiating antiretroviral therapy in clinical care. Aids 2011;25(2):185–95. http://dx.doi.org/10.1097/QAD.0b013e328341f925
38. Abebe M, Kinde S, Belay G, et al. Antiretroviral treatment associated hyperglycemia and dyslipidemia among HIV infected patients at Burayu Health Center, Addis Ababa, Ethiopia: A cross-sectional comparative study. BMC Res Notes 2014;7:380. http://dx.doi.org/10.1186/1756-0500-7-380
39. Garcia-Benayas T, Rendon AL, Rodriguez-Novoa S, et al. Higher risk of hyperglycemia in HIV-infected patients treated with didanosine plus tenofovir. AIDS Res Hum Retroviruses 2006;22(4):333–7. http://dx.doi.org/10.1089/aid.2006.22.333
40. Husain NE, Noor SK, Elmadhoun WM, et al. Diabetes, metabolic syndrome and dyslipidemia in people living with HIV in Africa: Re-emerging challenges not to be forgotten. HIV/AIDS (Auckl) 2017;9:193–202. http://dx.doi.org/10.2147/HIV.S137974
41. Okello S, Kanyesigye M, Muyindike WR, et al. Incidence and predictors of hypertension in adults with HIV-initiating antiretroviral therapy in south-western Uganda. J Hypertens 2015;33(10):2039–45. http://dx.doi.org/10.1097/HJH.0000000000000657
42. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2019;139:e1082–143. http://dx.doi.org/10.1161/CIR.0000000000000700

43. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents living with HIV. Department of Health and Human Services. http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf (accessed on: February 24, 2020).
44. International Association of Providers of AIDS Care, IAPAC Protocols for the Integrated Management of HIV and Noncommunicable Diseases. 2018. https://www.iapac.org/files/2018/07/IAPAC-Protocols-for-the-Integrated-Management-of-HIV-and-Noncommunicable-Diseases_3.pdf (accessed on: December 17, 2019).
45. Dube MP, Stein JH, Aberg JA, et al. Guidelines for the evaluation and management of dyslipidemia in human immunodeficiency virus (HIV)–infected adults receiving antiretroviral therapy: Recommendations of the HIV Medicine Association of the Infectious Disease Society of America and the adult AIDS Clinical Trials Group. CID 2003;37:613–27. http://dx.doi.org/10.1086/378131
46. Reiner Z, Catapano AL, De Backer G, et al. ESC/EAS guidelines for the management of dyslipidaemias: The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). Eur Heart J 2011;32(14):1769–818. http://dx.doi.org/10.1093/eurheartj/ehr158
47. Department of Disease Control, Ministry of Public Health. Thailand national guidelines on HIV/AIDS treatment and prevention. 2017. http://www.thaiaids-society.org/index.php?option=com_content&view=article&id=79&Itemid=86 (accessed on: March 14, 2020).