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Original Article

The global magnitude of metabolic syndrome among antiretroviral therapy (ART) exposed and ART-naïve adult HIV-infected patients in gedio-zone, southern Ethiopia: Comparative cross-sectional study, using the Adult Treatment Panel III criteria

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ABSTRACT

Aim: The global operation of antiretroviral therapy (ART) has averted 30 million new infections and nearly 8 million deaths; however, it has an impact on metabolic syndrome (MS) acquisition. As a result, there is growing concern about MS; but strangely the magnitude of MS in HIV-infected cohort, and its differential contribution ART status in Ethiopia has yet to be abundantly studied. Hence, the aim of this study was to estimate and evaluate the difference of the overall magnitude of MS among ART exposed and ART naïve people living with HIV (PLWH).

Materials and methods: An institution based cross-sectional study was conducted at the randomly chosen two hospitals and health centers, in Gedio zone, southern Ethiopia between December 29th, 2017 and January 22nd, 2019. Data were collected using the WHO three step tools. The collected data were fed into Epidata version.3.1 and exported to SPSS version 22 for analysis. The descriptive complex sample analysis method was employed, and the prevalence and differences between groups were computed with a 95% CI.

Result: A total of 633 (n = 422 ART and n = 211 ART naive) PLWH was involved, with the response rate of 92.1%. Of whom, 22.0% (95% CI: 19.0–25.4) of PLWH had MS. It was slightly higher in the ART-exposed (22.5%, 95% CI: 18.7–26.8) than ART naïve (20.9%, 95% CI: 15.2–27.1) group.

Conclusion: The global magnitude of MS in the ART-exposed was relatively higher than ART naïve groups. This dictates the existence of HIV associated MS that necessitates immediate prevention and management strategies.

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1. Introduction

Above three-quarters of the non-communicable diseases (NCDs) deaths, 30.7 million occurred in low and middle-income countries (LMIC) with about 48% of deaths in these countries occurring before the age of 70, in 2015 [1–3]. In the Sub-Saharan Africa (SSA) region, over the next two decades, it is expected to escalate substantially [2]. In Ethiopia, NCD is estimated to account for 30% of total deaths [3].

The HIV infection environment presents a typical illustration of the interaction between infectious diseases and NCDs [2,4–7]. The worldwide implementation of antiretroviral therapy (ART) for HIV infection has averted 30 million new infections and nearly 8 million Acquired Immune Disease Syndrome(AIDS)-related deaths [2,7], and increase in life expectancy of people living with HIV (PLWH). However, it has an impact on the aging population of PLWH living longer on that therapy (ART), to developing the metabolic syndrome (MS), which is the risk markers of None-communicable disease NCD [2,7–13]. As cumulative evidence reveals, an adult with this problem will have a twofold as likely to die from and are three times as likely to have cardiovascular diseases (CVDs) and a five-fold greater risk of developing type 2 diabetes (T2DM) [2,4,10,14,15].

Metabolic syndrome (MS) is usually diagnosed based on the

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following medical conditions: central obesity, elevated blood pressure/hypertension, elevated fasting plasma glucose/DM, dyslipidemia/elevated triglycerides (TGL_c), and low high-density lipoprotein (HDL_c) cholesterol levels [7,14,16–18]. Globally, an estimated 8–35%, in the SSA 0–50% or higher, and in Ethiopia, about 40% of adult peoples above the age of 20 years are expected to be living with the syndrome [10,19]. However, the precise global magnitude of MS in the HIV-infected population is still arguable; but the available data on it can be regarded as high, ranging from 11.2% up to 45.4% [6,7], and was also assumed to be reached up to 13% to 58% in Africa [2,16]. Surprisingly, in the sub-Saharan Africa (SSA), primary data on this situation is not yet well established [7,20].

On top of that, there was no crystal clear knowledge of whether HIV infection alone has an explicit effect to develop a higher prevalence of MS remains unclear [7,14]. Nevertheless, some researchers suggested the presence of higher magnitude of MS among PLWH (10% to over 50%) [7,14], while others argued as it has comparable rates with the in general population (11–26%) [7,8,16]. In this regards, for instance, Kiama.et al.(2018) study revealed that the magnitude was higher and was nearly 60.6%, with 8.4% increment at 48 weeks initiated on ART [10]. On the contrary, NGyuen et al. (2016) study beside stated, despite the notified elevated percentage of MS in those targeted group with or without treatment (17–47%), but it was within the acceptable ranges of reported to the general population [16]. In short, the cumulative evidence supported the presence of elevated proportion MS in the HIV infected patients, and the consequence of HIV infection by itself and antiretroviral treatments perhaps contributes to this increased MS, with the prevalence's ranges in the ART-exposed (18.4–21.6%) than the ART naïve (11.8–19.9%) [7,14,16,20,21].

In this backdrop and its higher attendant economic and health system implications of the identification and monitoring of comorbid health risks of HIV and ART [2,22], MS at present is a global public health issue [2], prominently in the SSA region and Ethiopia, the epicenter of HIV infection [2,4].

In spite of these facts, much of the reports on the magnitude of the problem in HIV-infected cohort and its differential contribution, if any, of ART status is produced from resource rich nations, while little outputs exist in SSA [7,16,23,24].

Therefore, the main intent of this comparative cross-sectional study was to estimate and evaluate the difference of the overall magnitude of MS among ART-exposed and ART naïve PLWH in a resource-restricted setting. The findings from this study are believed to have significance for public health practice and to establish baseline information for policy and program development.

2. Materials and Methods

2.1. Setting and participants

This study was conducted in Gedio zone, which is located in the Southern Nations, Nationalities, and Peoples (SNNP) region, 360 km to the south of Addis Ababa, the capital City of Ethiopia, and 86 km to the south of Hawassa, the capital city of the SNNP region. An institution-based cross-sectional study was conducted in the randomly chosen two hospitals and health centers (HC) ART clinics found in the zone, namely: Dilla University referral and teaching hospital (DURH), Yirga-Cheffe primary hospital, Wenago HC and Dilla town HC; between December 29th,2017 and January 22nd,2019. As per the national guideline for HIV prevention, Care and Treatment protocol, not all people living with HIV are eligible for ART and have got access to ART immediately. Enrolment in care provides an opportunity for early assessment of eligibility for ART and timely initiation. Many care interventions are relevant across the full continuum of care for people living with HIV before initiation and during ART [25]. Once the decision to start ART has been made, in our context, we have few options of drugs 1st line, 2nd line, and 3rd line regimens. Adult 1st line regimens comprises: 1a(30) = d4t(30)-3TC-NVP,1a(40) = d4t(40)-3TC-NVP,1b(30) = d4t(30)-3TC-EFV,1b(40) = d4t(40)-3TC-EFV, 1c = AZT-3TC-NVP,1d = AZT-3TC-EFV,1e = TDF-3TC-EFV, 1f = TDF + 3TC + NVP, 1g = ABC + 3TC + EFV, and 1h = ABC+3 TC-NVP. As well, adult 2nd line regimens include: 2a = ABC-ddI-LPV/R, 2b = ABC + ddI-NFV, 2c = TDF-ddI-LPV/R, 2e = AZT-3TC-LPV/r, 2g = TDF-3TC-LPV/r, 2h = TDF-3TC-ATV/r and 2i = ABC + 3TC + LPV. The 3rd line adult regimens are:3a = DRV/r + DTG + AZT/3 TC and 3b = DRV/r + DTG + TDF/3 TC. All of those regimens are based on the nucleoside reverse transcriptase inhibitors (NRTI), none nucleoside reverse transcriptase inhibitor(NNRTI) and a boosted Protease Inhibitor(PI) [25]. HIV positive patients less than 18 years of age, less than 95% adherence rate, pregnant women and who switched ART combination regimen for any reason were excluded from the study.

During the study period, as the Gedio zone ART case team Health management Information system (HMIS) report reveals, they're a total 3597 adult PLWH (629 ART naive (370 female, 259 male) and 2968 current on ART (1813 female, 1155 male)) were existed. Of whom, while (135ART naïve and 537 ART exposed) were enrolled in the ART clinics of health centers, 412 and 2395 corresponding groups were served under the ART clinics of the hospitals. Among those PLWH on ART (2922 in the first line regimen (1790 female, 1132 male), and 453, 168, 1991, 308 and 1 were receiving (1c = AZT-3TC-NVP), (1d = AZT-3TC-EFV), (1e = TDF-3TC-EFV), (1f = TDF + 3TC + NVP), as well as (1g = ABC + 3TC + EFV) regimens correspondingly. Similarly, 46 (23 female, 23 male) in the second line regimen and 10, 24, 6, 3, and 3 were on (2e = AZT-3TC-LPV/r), (2g = TDF-3TC-LPV/r), (2h = TDF-3TC-ATV/r), (2i = ABC + 3TC + LPV/r), and OTHER therapy, in the order presented.

The sample size estimation was made using openEpi version 3.03 software and by taking the following assumptions in to account: the two population proportion identified from the previous study done in Hawassa university specialized Hospital, Sothern Ethiopia (P1 = 15.6% for ART naïve and P2 = 18.1% for ART-exposed) [23], with 1:2 ratio of the ART naïve and ART-exposed groups, 95% confidence interval, 5% level of significance, and with the power of 80% and 90, the calculated sample size for the first group became (n1 = 3378) and (n1 = 4521), respectively. However, due to the constraints of resources, we made different assumptions for our sample size estimation (Table 1supplementary file S1 word doc.). Accordingly, using all of the above assumptions, the final sample size required for ART-naive group, with power 90% to detect an increment of 13.2% of the proportion of MS in the ART group from the baseline (i.e. 15.6%) became 208. By adding 10% non-response, overall 687 (n1 = 229 and n2 = 458) HIV positive patients were proposed for the study.

To select participants, first stratification of the health care institutions of the zone according to the health care delivery levels as hospital and primary health care unit (PHCU)/health center was made. Subsequently, a simple random sampling technique of a random table method was employed, and two hospitals (i.e. Dilla University referral hospital (DURH) and Yirga/Cheffe primary hospital (Y/CHP)), as well as two health centers (Dilla Town and Wonago Health centers) were chosen for the study. Once the chronic HIV clinics were specified, so as to choose participants from the study population, a survey supplemented with the data logs at the data clerk of the ART clinics of each health facility was arranged for a month to evaluate the daily/weekly/monthly patient flow.

Using the compiled assessment monthly result, the proportional allocation of sample size (PPS) to ART-exposed and ART naïve cases required for each health institution for the study period was determined. Accordingly, the resultant estimated average monthly ART naïve and ART-exposed patients flown of each health institutions became (14 and 132 for DURH, 7 and 43 YHP, 6 and 18 for WHC, and 3 and 12 for DHC). And, the total population computed for the study period and the population proportionally allocated sample size (PPS) estimated to the former and the later comparative group to DURH, YHP, WHC, and DHC were found to be (168 and 106 vs. 1584 and 282; 84 and 50 vs. 516 and 92; 72 and 43 vs. 216 and 38, as well as 36 and 19 vs. 144 and 25), respectively. Finally, by using a consecutive sampling technique, daily recruitment and selection of subjects, in accordance with the eligibility criteria's set to each comparisons group was carried on, until the estimated sample size to each study sites was obtained (Fig. 1).

2.2. Data collection

The data collection was accomplished using the validated WHO STEPS instrument version 3.2 [26], developed to chronic disease risk factor assessment in developing countries, with modifications to the context of the Ethiopian community. It covers three different levels or 'steps' of risk factor assessment: Step 1 (questionnaire), Step 2 (physical measurements) and Step 3 (biochemical measurements).

Step 1: was used to gather demographic and behavioral characteristics of the PLWH from a representative sample.
Step 2: was employed to build on the core data in step 1 and to determine the proportion of the study population with raised blood pressure, overweight and obesity. The body weight and height were measured by wearing light clothing using the 220 SECA Scale placed on a firm, flat surface. BMI is calculated according to the formula (BMI = Body weight (kg): Body height/(m2), which is a ratio of body weight in kilograms to the square of body height in meters. Waist and hip circumferences were measured by a constant tension tape meter with millimeter precision. Waist circumference (WC) was measured by placing a tape measure around the abdomen at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest of the hip bone, with the bare or light clothing, at the end

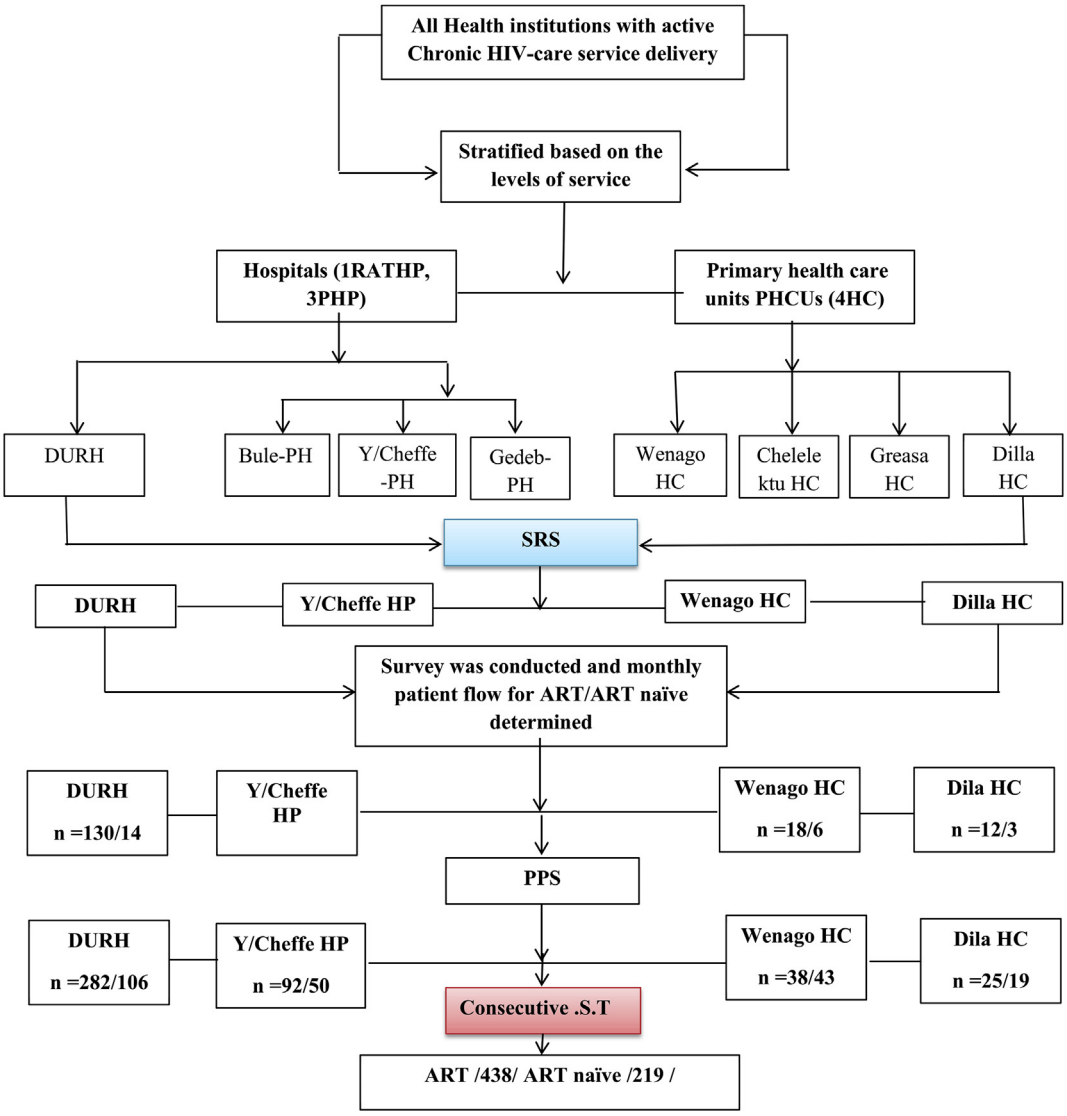

Fig. 1. Title the schematic representation of the study procedure, among PLWH, Gedio zone, South Ethiopia, 2017–2019 •

of a normal expiration. Hip circumference was measured by placing a tape measure around the hip at the maximum circumference over the buttocks or around the greater trochanter of the femoral bone. Blood pressure measurements were taken three times on the left arm of the survey participants in a sitting position, using The NUTEC BP09 Arm-type Fully Automatic Digital Blood Pressure Monitor with cuff Circumference (Approx.135 (W) 485(L) mm (medium Cuff; Fits arm Circumference 22-36Cm)). The measurements were taken after the participant had rested for 15 min, and each with 3 min of rest between the measurements. Ultimately, the mean of the three measurements was taken for analysis.

Step 3: was important to build on the core data in step 1 and step 2 and measure the proportion of the study population with diabetes, impaired fasting plasma glucose and abnormal lipid level. Laboratory tests were performed the next day or sometime after completion of STEPS 1 and 2 of the data collection process, with 8–12 h overnight fast by drawing of 3–5 mL Venus blood. The blood samples were collected into dry vacutainer tubes and centrifuged with 5000 (rpm) for 5–10 min, using a centrifuge machine in order to separate the serum from the whole blood. Subsequently, the serum stored into refrigerator at 2–8 °C or −20 °C, until analysis. The biochemical analyses were done to all serum transported from other study sites and for those samples collected at Dilla University referral and teaching hospital (DURH) clinical Diagnostic Laboratory (i.e. the centralized unit for the whole biochemistry analyses). It was made for fasting plasma glucose level and lipid profile (Total cholesterol (TC), High-density lipoprotein cholesterol (HDL-c), Low-density lipoprotein cholesterol (LDL-c) and Triglyceride cholesterol (TGL_c)) measurement, using BS-200E Clinical Chemistry Analyzer. Enzymatic colorimetric assay method was used for the measurement of TC (CHOD-PAP method) and triglyceride (GPO-PAP method), HDL-c and LDL-c measurements were done by utilizing direct homogeneous enzymatic colorimetric assay technique. Glucose level was measured by the glucose oxidase method (GOD-PAP). All the reagents, used for the glucose and lipid profile testing, were from Human Gesellschaft für Biochemica und Diagnostica mBH (Germany). Often, the quality control samples were run before running patient samples and along with patient samples in order to check the correct functioning of instruments, laboratory reagents, and technical performances. All laboratory performances were done by lab technologists by using standard operating procedures (SOPs) from sample collection to result in releasing. Finally, values of the analyzed clinical and biochemical measures got complied with the revised Adult treatment panel III standard criteria set for Europe countries.

2.3. Definition of metabolic syndrome(MS)

The presence of MS was diagnosed according to the 2005 revised National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATPIII) criteria [6]. Based on this criteria, the presence of three of the following: Waist circumference(WC) ≥ 102 cm or 40 inches (male), ≥88 cm or 35 inches (female) or BMI is > 30 kg/m2; Dyslipidemia:(Triglyceride(TGL_c) ≥ 1.7 mmol/L (150 mg/dl) Or high density lipoprotein cholesterol (HDL_c) < 40 mg/dL (male), <50 mg/dL (female)); Blood pressure (BP) systolic/diastolic(SBP/DBP) ≥ 130/85 mmHg or antihypertensive medication and Fasting plasma glucose ≥ 6.1 mmol/L (>/ = 110 mg/dl)). Or previous diagnosis of type 2 diabetes mellitus or anti-diabetic treatment.

2.4. Data processing and analysis

Every day, after completion of each step of the data, the completeness of these tools was checked by the immediate supervisor and the main author. The completed tools entered in to template formed using Epidata version3.1 software by two data clerk; eventually validation was performed using the original data as references. Subsequently, data was transformed in to Statistical Package for Social Sciences (SPSS) Version 22 for analysis. Statistical analysis was performed by the principal investigator in consultation with the primary and secondary supervisory, using appropriate methods for the complex sample design of the study. Charts were produced using Microsoft® Excel 2007. The prevalence of each component and overall metabolic syndrome were estimated and differences between groups (ART status, age, and sex groups) were calculated with a 95% CI. Sampling error, which could potentially affect the accuracy of the results of the current study, was measured by the standard error of variables. A margin of error in prevalence is represented by numeric values for the lower and upper limits of a 95% CI.

2.5. Ethical clearance

All the principles of ethics laid down in the Declaration of Helsinki (and its successive amendments) were considered. Accordingly, ethical clearance was obtained first from Addis Ababa University (AAU) College of Health Sciences school of public health Research and Ethics Committee (REC) (Ref.No.SPH257/09) then from College of health science Institutional Review Board (IRB)(-Meeting No.001/2017 and protocol No.0069/16/SPH). Furthermore, the official letter was produced and delivered by the author to the respective Southern Nations Nationalities Regional health bureaus, Gedio zone and Woreda health bureaus and all of the institutions selected to conduct the study. Data were collected unlinked anonymously, without any personal identifiers. Each individual was enrolled entirely voluntary after written consent was obtained. Any information obtained during the study was retained with the greatest confidentiality. Physical measurement was done by performing measurements at an ART clinic room that has been screened off to maintain the individual's privacy. All biochemical analysis was performed free of charge, and results were provided to the clinicians for further investigation, and possible management.

3. Result

3.1. Socio-demographic characteristics

Out of the 687 (219 ART naïve and 438 ART-exposed) proposed samples, a total of 633 adult people living with HIV (n = 422 on ART and n = 211 ART-naive) were involved, with an overall response rate of 92.1%. The mean age of the study population was 36.4 ± 8.7 years (ART naïve men, 36.4 ± 6.9 years versus women, 37.9 ± 7.8 years). This is consistent across all age groups through the highest proportion of ART-exposed women 76.1% (137) belonged to the younger age group (Age </ = 34) compared with men 74.1%) (100) (Table 2 supplementary file S2 word doc.).

As the result further reveals, out of the 302 respondents who were able to remember their stay of living with the virus since diagnosis, greater number, 278(43.9%)((123(58.3%) ART naïve and 155(36.7%) ART-exposed)) of them were below a year, with the mean reported duration of 5.31 ± 3.99 months. Besides, among those who were able to react for the time spent since ART initiation, 98 of the ART-exposed respondents were able to estimate the duration; of which 53 (8.4%) (18(7.0%) of men and 35(9.3%) of women) were exposed for less than 6 months, with reported

average exposure time of 5.69 ± 3.00 months (6.27 ± 3.09 months for men and 5.31 ± 2.90 months for women). The therapeutic schemes were based on the 1st line, 2nd line, and 3rd line regimen. All of those regimens are based on the nucleoside reverse transcriptase inhibitors (NRTI), none nucleoside reverse transcriptase inhibitor (NNRTI) and a boosted Protease Inhibitor (PI). Accordingly, overall 226 (53.5%) women and 196(46.5%) men were on both types of regimens (Table 3 supplementary file S3 word doc.).

3.2. Physical measurements

The mean and standard deviation (SD) associated with physical measurements are summarized in Table 1.

The magnitude of hypertension was found to be 56.9% (95%CI: 53.1–60.5); where 55.6% was diagnosed from elevated systolic and diastolic blood pressure (SBP ≥130 and/or DBP ≥ 85 mmHg). The ART naïve groups, had shown slightly greater proportion 57.3%(95%CI: 50.7–64.5) than ART-exposed 56.6% (95%CI: 51.7–61.4). (Fig. 2 supplementary file S1pdf. Document). The result further indicates, nearly 28%(28.9%, 95%CI: 25.3–32.7) of study population had central or abdominal obesity; higher proportion was seen among ART exposed 32.0% (95%CI: 27.7–37.0) than ART naïve 22.7% (95%CI: 17.1–28.4) groups. Of which, 21.8% of PLWH were diagnosed with elevated WC (>102 cm for men and >88 cm women), and 9.8% of them were diagnosed with elevated body mass index (BMI > 30 kg/M2), (Fig. 3 supplementary file S2 pdf. Doc.).

3.3. Biochemical measurements

In line, the study further measured the mean and standard deviation (SD) associated with the biochemical measurements and summarized in Table 2.

Thirty one point three percent (32.9%, 95%CI: 28.4–37.4 ART group compared to 28.0% ART naïve 95%CI: 21.8–34.2) of PLWH had diabetes (Fig. 4). Of whom, 26.4% (95%CI: 23.2–29.9) of participants were found to have impaired fasting plasma glucose, and the rest had history of type two DM or anti-diabetes treatment (Fig. 4 supplementary file S3 pdf. Document). Furthermore, the result indicates, generally 59.2% (95% CI: 55.5–62.7) of the study respondent were diagnosed with dyslipidemia; prominently higher magnitude, 60.4% (95% CI: 55.9–64.9) noticed in the ART exposed than ART naïve groups, which is 56.9% (95% CI: 50.2–64.0). Of which, nearly 37% (95% CI: 33.0–40.8) of them had elevated TGL_c level of ≥150 mg/dl and 34.3% (95% CI: 30.6–38.1) of them had low HDL_c level (<50 mg/dl for women and <40 mg/dl for men) (Fig. 5 supplementary file S3 pdf. Document).

3.4. The overall magnitude of the metabolic syndrome

As the study result pinpointed, the overall proportion of MS was found to be 22.0%; (22.5%, 95% CI: 18.7–26.8 in the ART-exposed and 20.9%, 95% CI: 15.2–27.1 in ART naïve group); which was found to be slightly higher in the former group than the later (Table 3) (Fig. 2). A significant differences on the prevalence estimates was observed across sexes and age groups, with a notable increase in the proportion of MS in the corresponding groups of women (23.1% 95% CI: 18.9–27.4) than men (20.2%, 95% CI: 15.6–26.1), as well as older age group than young age (Table 3) (Fig. 2).

The percentage contribution of each of the four components in the diagnosis of the overall magnitude of MS was further evaluated, and comparably higher contribution was made by dyslipidemia (20.5%) and hypertension (20.4%); followed by Diabetes mellitus (15.6%) and central obesity(12.5%). Shortly, the contribution from ART-exposed than ART naïve groups was higher to all traits of MS, except for the case of hypertension (Fig. 7 supplementary file S5 pdf. Document). In line, the result further revealed the percentage contributions made by each of the physical and the biochemical measurement to diagnose the overall magnitude of MS (Table 7 supplementary file S4 word document).

4. Discussion

Human immune deficiency virus (HIV) infection is responsible for MS and NCD risk in the general population [6,7]. Due to such reasoning, there is growing concern that MS associated with HIV and ART, place this population in a high-risk category [7]. However, the precise magnitude of MS in the HIV-infected population and its differential contribution by ART status is still arguably [2,6,7,16]. Essentially, in sub-Saharan Africa (SSA) region in general and in Ethiopia, in particular, the situation is not yet well-known [23]. Therefore, the intent of this comparative crossectional study was to estimate and compare the global magnitude of MS among ART-exposed and ART naïve people living with HIV (PLWH) in Gedio zone, southern Ethiopia. Overall, the study concluded that the global magnitude of MS among PLWH was notified as higher, with a slight difference observed in the ART-exposed than ART naïve group. As well, the contribution of dyslipidemia was found to be higher, followed by hypertension, diabetes, and central obesity that all of these traits were relatively greater in the ART-exposed than ART naïve, except for the case of hypertension.

The current study finding on the overall prevalence of MS to be higher than the study done on apparently healthy peoples in Addis Ababa, Ethiopia [27]. On top of that a lower percentage of MS was

Table 1
Mean (SD) of physical measurements, among PLWH, Gedio zone, South Ethiopia, 2017–2019.

ART status	Age groups in years	n	The mean (SD) of WC in Both Sex		The mean (SD) of BMI in Both Sex		The mean (SD) of SBP in Both Sex		The mean (SD) of DBP in Both Sex	
			Mean	SD	Mean	SD	mean	SD	mean	SD
ART naïve	</=34	78	81.5	8.0	22.39	4.92	126.7	7.9	81.9	4.9
ART-exposed		237	82.1	8.0	21.78	4.06	125.0	11.5	83.0	6.3
ART naïve	35–44	87	84.7	7.4	21.75	4.13	127.2	8.4	83.4	5.2
ART-exposed		116	85.2	7.6	22.41	4.88	128.5	11.6	83.6	6.1
ART naïve	>/=45	46	85.7	9.4	22.81	3.70	126.5	6.3	83.2	5.0
ART-exposed		69	85.4	7.5	23.16	5.38	130.9	10.5	83.9	6.3
ART naïve	All age	211	83.7	8.2	22.22	4.36	126.9	7.8	82.8	5.1
ART-exposed		422	83.5	7.7	22.18	4.54	126.9	11.5	83.3	6.3
Total		633	83.6	7.9	22.19	4.48	126.9	10.4	83.1	5.9

*WC: Waist circumference *SBP: Systolic Blood Pressure.
*BMI: Body mass index *DBP: Diastolic Blood Pressure.

Table 2
The mean and (SD) of biochemical measurements, among PLWH, Gedio zone, Southern Ethiopia, 2017–2019.

ART status	Age groups in years	n	The mean (SD) of HDL_c in Both Sex		The mean (SD) of TGL_c in Both Sex		The mean (SD) of FpGL in Both Sex		The mean (SD) of TC in Both Sex		The mean (SD) of LDL_c in Both Sex	
			Mean	SD	Mean	SD	mean	SD	mean	SD	mean	SD
ART naïve	</=34	78	53.1	23.2	133.3	29.9	96.19	26.4	168.7	40.8	138.7	32.2
ART-exposed		237	59.8	24.3	144.2	31.4	111.2	38.4	179.8	42.0	145.4	30.5
ART naïve	35–44	87	55.2	24.8	131.1	31.5	102.0	22.0	175.9	42.4	139.4	33.4
ART-exposed		116	59.9	24.2	147.2	30.8	112.8	39.0	182.7	51.4	148.6	33.3
ART naïve	>/=45	46	47.3	19.7	138.4	28.0	102.0	22.0	156.3	35.8	136.0	32.6
ART-exposed		69	54.0	20.7	149.5	37.6	116.9	42.3	185.4	44.9	147.2	34.5
ART naïve	All age	211	52.8	23.3	133.5	30.2	102.2	30.1	168.9	41.0	138.4	32.7
ART-exposed		422	58.9	23.8	145.9	32.3	112.6	39.1	181.5	45.2	146.6	31.9
Total		633	56.8	23.8	141.8	32.1	109.1	36.7	177.3	44.2	143.9	32.4

* TGL_c: Triglyceride cholesterol * HDL_c: High density lipoprotein cholesterol.
*SD: Standard deviation * LDL_c: High density lipoprotein cholesterol * FpGL: fasting plasma glucose.

Table 3
Magnitude of Metabolic syndrome (%MS), by ART status, age, and sex, among PLWH, Gedio zone, Southern Ethiopia, 2017–2019.

ART status	The magnitude of Metabolic syndrome (%MS)						Both Sex		
	Age groups in years	Sex							
		Men			Women				
		n	% MS	95% CI	n	% MS	95% CI	n	% MS	95% CI
ART naïve	</=34	35	8.6	0.0–17.1	43	14.0	4.7–25.6	78	11.5	3.8–19.2
ART exposed		100	13.0	7.0–20.0	137	14.6	8.8–20.4	237	13.9	9.7–18.6
ART naïve	35–44	47	17.0	6.4–27.7	40	30.0	15.0–45.0	87	23.0	14.8–33.3
ART-exposed		39	35.9	20.5–51.3	77	23.4	14.3–33.8	116	27.6	18.8–35.5
ART naïve	>/=45	18	33.3	11.1–55.6	28	32.1	14.3–50.0	46	32.6	19.6–47.8
ART-exposed		18	44.4	21.4–66.7	51	43.1	29.4–56.9	69	43.5	31.9–55.1
ART naïve	All age	100	17.0	9.0–25.0	111	24.3	16.2–32.4	211	20.9	15.2–27.1
ART-exposed		157	22.3	15.9–29.3	265	22.6	17.7–27.9	422	22.5	18.7–26.8
Total		257	20.2	15.6–26.1	376	23.1	18.9–27.4	633	22.0	19.0–25.4

besides identified in the present study than studies by Husain eta (2017) [2] review finding in Africa (13%–58%), Dr.J.Balachandrudu.et al. (2018) (40%) [28], Nguyen KA,(2016) (24.6–31.3%) [16], Tesfaye et al.(2014) (25%) [23] and Hirgo.et al. (2016) [20] (24.3%) [20,23]. Inconsistently lower than our report, a number of studies done among HIV- infected patients worldwide point out magnitude's ranging from 15.0 to 20.0% [16,20,23,29–31]. As well, the study report from Nigeria also shown the extremely lower magnitude of MS (12.7%) than the current study fining [32].Besides, nearly correlating with the current study result, a meta-analysis study done in the SSA by Todowede et al.(2019) [7] (21.5% 95% CI 15. 09–26.86), a crossectional study conducted in HIV-1 infected Thai adults by Jantarapakde J et al. (2014) [33] (22.2%), and Berhane T et al. (2012) cross-sectional study done in South West Ethiopia (21.1%) [34].The observed inconsistencies on the magnitude of MS could be attributed to the overlapping of range of factors such as host, HIV and/or its associated therapies, as it has been suggested by literature [7,14,16,20,21]. Apart from these, the different standard criteria employed by the studies to diagnose the overall MS, along with the diverse approaches used by the studies may be taken as a justification. This, in turn, dictates, regardless of the improvement in the quality of life conferred by immune reconstitution, the HIV infection and ART bringing the PLWH into the future risk of developing NCDs, subsequent with the acquisition of MS.

As well, in this study, we found that a slightly higher proportion of overall MS diagnosed in the ART-exposed than ART naïve counter group. Correlating with Nguyen KA,(2016) study (18.4% vs. 11.8%, p = 0.001) [16], and D.Y. Tesfaye et al.(2014) (18.1% versus 15.6%, respectively, p = 0.52) [23]; however, all are below the reported magnitude to each groups indicated by the active study result. Besides, the finding demonstrated consistency with the study reported by Jantarapakde J et al. (2014) in HIV-1 infected Thai adults (24.9% ART-exposed vs. ART naïve 15.9%) [33], and D.Y. Tesfaye et al.(2014) (25% on ART compared to 22.6% in ART-naive group; p = 0.58 by IDF) [23]. In the reverse, a study report by Ngatchou W et al. (2013) [35] done in Cameroon was notified lower rate of MS (21%) in the ART-exposed and extremely higher magnitude (47%) among the ART naïve group. The observed differences on the magnitude of MS among the two comparative groups may be attributed to the study approaches used, the standard criteria employed, the number of individuals involved, as well as the socio-economic and cultural dissimilarities associated with the host. Besides, not surprisingly, even if both the HIV-infection and ART have an independent role in the acquisition of MS complication, but the ART together with the virus might have a synergetic effect on the disease progression by aggravating the impaired metabolic processes to be underway.

Furthermore, there was also a notable increase in the prevalence of MS in the corresponding groups of women than men PLWH. Analogues with our finding, a comparative crossectional study by Hirigoet.al (2016), in the southern Ethiopia [20], a meta-study by Nguyen KA,(2016) [16], Tesfaye, et al. (2014) [23], Mbunkah, et al. (2014) [31], Jantarapakde, et al. (2014) [33], Ayodele, et al. (2012) [32], Berhane, et al. (2012) [34], and Zannou et al. (2009) [36] studies notified comparable finding. Consistency of difference of proportion across sexes, with a higher magnitude of MS seen among women than men were also reported by Abda et al. (2016) [37] study done among non HIV-infected outpatients in Jimma southwest Ethiopia. On top of that, there was also an observed

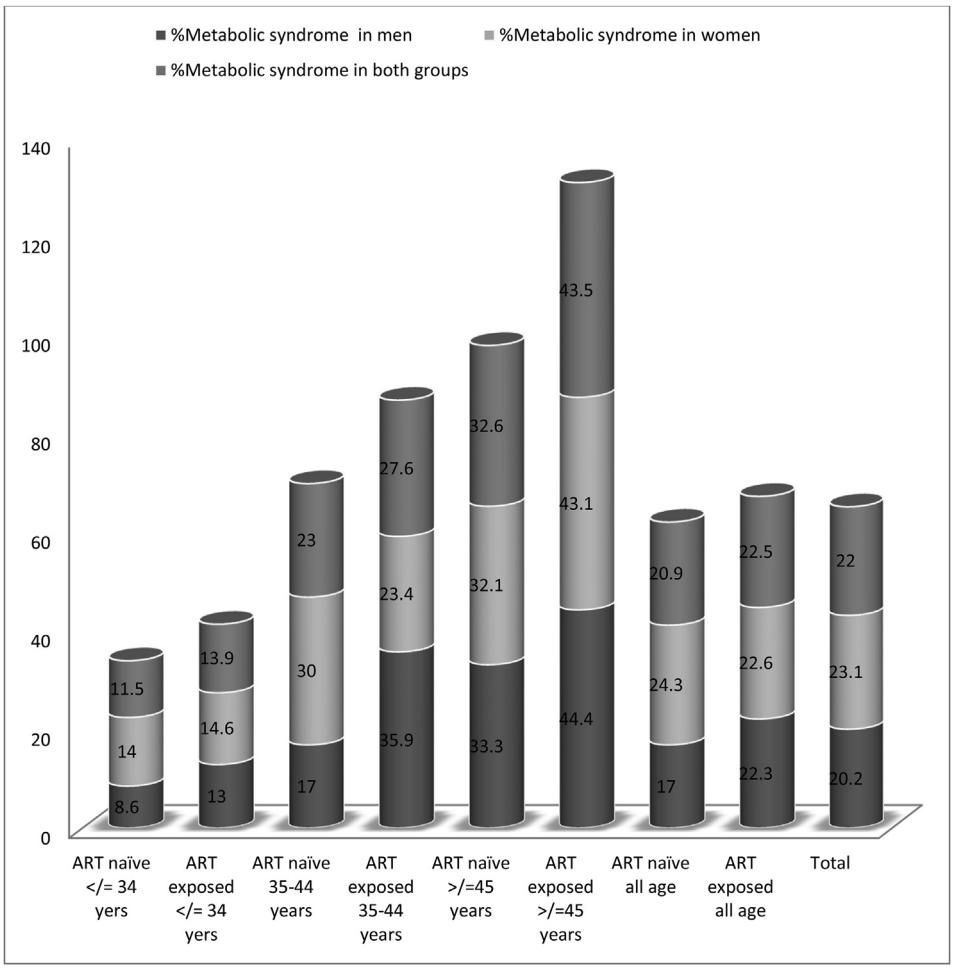

Fig. 2. Title Magnitude of Metabolic syndrome (%MS), by ART status, age and sex, among PLWH, Gedio zone, South Ethiopia, 2017–2019.

variation on the reported magnitude in between the current study report and the studies of Nguyen KA,(2016) (women 26.7%, 95%CI: 20.8–33.0 than men 23.7%, 95%CI: 19.0–28.7) [16]; Mbunkah et al. (2014) [31] (18.3% in women vs. 4.3% in men, p = 0.003), Zannou, et al. (2009) [36] (19.2% in women vs. 3.1% in men; P = 0.043), and Nguyen KA,(2016) (women 17.5%, 95%CI: 14.0–21.2 and men 14.6%, 95%CI: 11.5–18.1) [16]. The observed differences in magnitude among the two groups could be partly attributed to the biological and physiological differences inherited from being of male and female. Besides, central obesity precipitated with pregnancy and childbirth, any pregnancy induced chronic disease such as pregnancy-induced hypertension and gestational diabetes might also fever the women to have greater MS than men. In addition, as it has been suggested by Kiama.et al. study [10] done in Kenya, hormonal and environmental factors that are thought to be contributing to the occurrence of metabolic syndrome in women.

Also, the prevalence of MS in the current study reveals increased noticeably with aging, aside from it was realized higher in the older age than in the younger age. This marked disturbance in the MS with aging has also been reported by several other studies of Tesfaye et al. (2014) [23], Jantarapakde, et al. (2014) [33], by Mashinya.et al.(2015) [38], and by Dr.G.Madhavi.et al.(2018) [28]. This may be partly due to the inevitable degeneration of organ experienced by any person following with the increase in age has a consequence on the pathological organ function and that might provoke the genesis of impaired metabolic actions, and ultimately to develop MS.

Besides, the current study was also pinpointed that the contribution of dyslipidemia was found to be higher, followed by hypertension, diabetes mellitus and central obesity. The magnitude of each of the above traits was relatively greater in the ART-exposed than ART naïve, except for the case of hypertension. In spite of the variation seen on the magnitude of each traits, a cross-sectional study done in the South-West region of Cameroon using 173 treated and untreated HIV-infected out-patients by Mbunkah et al.(2014) demonstrated that dyslipidemia diagnosed from low HDL_c (43%), and hypertriglyceridemia (12.1%), followed by Hypertension (24.7%), central obesity (36.8%), and hyperglycemia (26.5%) was the most frequent traits of MS [31]. As same, Husain et al. (2017) review [2] also notified that the magnitude of each component in HIV population in Africa was estimated to range from (2.1%–26.5%) for diabetes and (20.2%–43.5%) for pre-diabetes and (13%–70%) for dyslipidemia. Another study conducted among 100 HIV patients on ART and HIV negative controls revealed that the magnitude of serum triglyceride levels are higher in HIV patients than in controls (60% vs 32), followed by hypertension (52% vs 27), fasting blood sugars (45% vs 33%), and Central obesity (33% vs 27%) in the corresponding comparative groups. However, HDL _c was reported to be low in HIV patients than controls (69%vs 32%). This may be partly associated with the development of the peripheral lipoatrophy with loss of subcutaneous fat following the use of ART is a harbinger of underlying dyslipidemia, insulin resistance, and

ultimately acquiring of diabetes. On top of that as it has been suggested by Willig AL et al. (2016) [21], [21] review report, the HIV infection as well likely induces changes in mitochondrial function, adipose tissue, and inflammatory pathways independent of ART and have increased the probable chance of occurrence of the above consequences among these subjects.

The limitations of this study mainly emerged from the observational nature and crossectional design of the study; therefore, we cannot establish a cause and effect relationship. In addition, the inherent problems raised by the institution based studies that might be failed to reflect the true prevalence estimates of the target population.

5. Conclusion

The study concluded that the global magnitude of MS among PLWH was notified as higher, with a slight difference of magnitude observed in the ART-exposed and ART naïve groups. This signifies the existence of HIV associated MS that necessitates immediate prevention and management strategies in such resource restricted area. As well, the contribution to estimate the global proportion of dyslipidemia was found to be higher, followed by hypertension, diabetes mellitus and central obesity. The magnitude of each of the above traits was relatively greater in the ART-exposed than ART naïve, except for the case of hypertension. Which implicates, in the time of entire test and treat course of action among HIV infected patient, routine follow-up of MS and its traits encompassed through the whole management system is indispensable.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

Conflicts of interest

I confirm that there is no competing of interests in this research work.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.07.051.

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