Treatment aAdherence and associated factors to antiretroviral therapy among adult people living with HIV/AIDS in Benishangul-Gumuz Regional State, Ethiopia

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ABSTRACT

Introduction. Following global efforts to increase antiretroviral therapy (ART) access and coverage, Ethiopia has made significant achievement with a 6.3% annual decline in the HIV/AIDS incidence rate between 1990 and 2016. Such success depends not only on access to ART but also on attaining optimum treatment adherence. Emerging studies in Ethiopia has shown the increasing prevalence of poor adherence and lack of the desired viral suppression, but the factors associated with non-adherence to ART are not well known, especially in the current study setup. In this study, we examined the extent and factors associated with treatment and non-adherence to ART among people living with HIV in Benishangul-Gumuz Regional State, northwest Ethiopia.

Methods. We studied 394 people living with HIV/AIDS (PLWHA) who were on comprehensive HIV care among the selected health facilities during the study period. We used binary logistic regression and subsequent multivariate logistic regression analysis to determine the factors associated with ART non-adherence, which was measured using a visual analogue scale (VAS).
Result. Overall, 39.7% of the participants were found non-adherent to ART. Strong association was found between non-adherence to ART and young age of below 25 years (AOR: 4, 95% CI: 1.21, 12.6, p = 0.02), food insecurity (AOR: 21, 95% CI: 6.1, 56.2, p <0.001), malnutrition (AOR: 0.9, 95% CI: 0.82, 0.98, p = 0.018) and opportunistic infections (AOR: 1.7, 95% CI: 1.03, 2.86, p = 0.037, p = 0.037).
Conclusion. Improving ART adherence envisages the adoption of youth-centered adherence and a development counselling approach, mitigation of recurrent opportunistic illness, and integration of nutrition and food security interventions with an HIV/AIDS program that can be implemented through a multisectoral approach to bridge the resource gap and improve the treatment outcome.

Keywords: adherence, antiretroviral therapy, food insecurity, HIV/AIDS, malnutrition, visual analogue scale

INTRODUCTION

Antiretroviral therapy (ART) has played a significant role in responding to HIV/AIDS epidemics (Granich et al., 2012; Williams, Lima & Gouws, 2011). It has increased survival and improved quality of life, and reduced the rate of disease progression and death (Oguntibeju, 2012; Dalhatu et al., 2016). Consequently, ART service expansion has received significant support at the global and national level through the commitment of the Sustainable Development Goals (SDG) (UNAIDS, 2015; The Federal Democratic Republic of Ethiopia Ministry of Health, 2015). The SDG response sets out targets for HIV treatment: 90% of people living with HIV know their HIV status, 90% of people who know their status receiving treatment and 90% of people on treatment having a suppressed viral load (UNAIDS, 2011). In line with this initiative, HIV treatment and care services have expanded dramatically (UNAIDS, 2018). In 2017, over 21.7 million people living with HIV were receiving ART globally (UNAIDS, 2018). Regardless of this increase, ensuring adherence to HIV treatment remains challenging for the HIV/AIDS response, mostly in

sub-Saharan Africa (Wang et al., 2011; Eyassu, Mothiba & Mbambo-Kekana, 2016; Fonsah et al., 2017), including Ethiopia (Alagaw et al., 2013; Peltzer & Pengpid, 2013).

Scientific literature indicate that for ART to be effective and prevent the emergence of resistant strains, a strict adherence level of ≥95% is recommended (Turner, 2002; Bangsberg, 2006). Once initiated, it must be continued daily (World Health Organization, 2010). However, irrespective of the benefits of good adherence, not all people living with HIV and AIDS (PLWHA) fully adhere to the required treatment level. Failure to attain the required adherence level results in poorer prognosis, higher morbidity, mortality and the development of resistance to ART (Iacob, Iacob & Jugulete, 2017; Nachega et al., 2011). Once resistance develops, it has dire consequences for the individual PLWHA, family, community, healthcare providers and the healthcare system. Moreover, second-line ART regimens are more expensive and have worse side effects (Karade et al., 2018; Chauhan et al., 2019).

Given the importance of adherence, a growing body of research has identified factors associated with non-adherence to ART as behaviors related to the patient itself, therapy related (medication regimens such as more than one tablet or dosing time per day and ART toxicity), poor relationships with healthcare providers and socioeconomic factors (Kim et al., 2018; Mohammed, Ahmed & Tefera, 2015; Wasti et al., 2012). Poor ART adherence was reported among underprivileged communities where socioeconomic inequalities heighten risk (Young et al., 2014) and lower quality of life is prevalent (Liping et al., 2015; Hansana et al., 2013), negatively impacting the HIV program (Wang et al., 2011b). For PLWHA, factors related to gender dimensions, education status, income, asset possession and food security have been associated with non-adherence to ART (Alagaw et al., 2013; Basti et al., 2017; Abera et al., 2015). For example, in South Africa (Eyassu, Mothiba & Mbambo-Kekana, 2016); Cameroon (Fonsah et al., 2017); and northern Tanzania (Samuel Edward et al., 2018), gender, income and level of education were reported as the determinants of ART adherence. Another study in Wolaita Sodo, Ethiopia, found lack of food was associated with poor adherence (Alagaw et al., 2013). In opposition to the culminated evidence, there are studies that have reported an absence of the impacts of socioeconomic inequalities on ART adherence in middle and low-income countries (Peltzer & Pengpid, 2013).

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Ethiopia is among sub-Saharan African countries sturdily hit by epidemics. The country has made a significant achievement in responding to the HIV/AIDS epidemic, with a 6.3% annual decline in the HIV/AIDS incidence rate between 1990 and 2016 and a total reduction of 77% (Deribew et al., 2019). Regardless of the government's commitment to end the HIV/AIDS epidemic as per the 2030 SDG initiative (that envisages a 90% suppression of viral loads to prevent treatment failure and reduce AIDS-related deaths), achieving optimum ART adherence is becoming a challenge in Ethiopia. Current evidence in the country has shown that only 32% of PLWHA on ART have suppressed viral loads (UNAIDS, 2017). Given the association between viral suppression and ART adherence, and the current indication of treatment outcomes in the country (UNAIDS, 2017), this study was aimed at investigating the extent and factors associated with non-adherence to ART among adult people living with HIV and on treatment in Benishangul-Gumuz Regional State (hereafter Benishangul-Gumuz) in northwest Ethiopia.

METHODS

Study design and population

A cross-sectional study was conducted from December 2016 to February 2017 in Benishangul-Gumuz, one of the nine regional states of the Federal Democratic Republic of Ethiopia located in the northwestern part of the country. The study was conducted among two referral hospitals and three health centers which provide comprehensive HIV care services. These health facilities were purposely targeted as they are utilized by the majority of people living with HIV. Sample size for this study was determined using the formula for the estimation of single proportion, $n = \frac{(z)^2 p(1-p}{d^2}$, where proportion (p) of HIV positive individuals with food insecurity 63% taken from the previous study in Ethiopia (Tiyou et al., 2012) margin of error (d) = 5%, and 95% confidence limit (Z = 1.96). By adding 10% to cater for non-response rate, a total of 394 respondents were enrolled into the study. Proportional to allocation method was employed to allocate the number of participants among each study sites. Based on allocated numbers, simple random sampling technique by using a sampling frame developed from the registration book of the patients was used to enrol respondents at each study sites. The study entry criteria were: ~~(a) 18 years of age or older,~~ (b) HIV positive and receiving antiretroviral therapy from the selected health facilities, and

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(c) resided in Benishangul Gumuz Regional State for at least two years, d) no psychiatric ~~cognitive~~ health problem.

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Data and measures

A structured questionnaire was used for face-to-face interviews with the target population during times participants were waiting to see ART service providers and for pharmacy refills. The study tool was checked for clarity and consistency among the selected health facilities out of the study site.

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Antiretroviral therapy adherence

Antiretroviral treatment adherence is the level to which a person is taking medicine as prescribed by a physician and as per medical recommendations in relation to timing, dosing and consistency, and correctly taking the drugs in terms of right doses and right times (Chaiyachati et al., 2014). In this study, patient self-assessments were collected using the visual analogue scale (VAS) to measure primary outcome and adherence. With the VAS approach, a series of scales with values ranging from 0 to 100% is used to assess adherence during the past 30 days (Chesney et al., 2000). The participants were asked to place an "X" inside the box above the point showing the best guess about how much of their current antiretroviral medications were taken in the past 30 days. Adherence at a VAS score of ≥ 95% over the past 30 days was defined as adherent and less than 95% as non-adherent.

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Outcome measures

To investigate the extent and factors associated with non-adherence to ART among people living with HIV and on treatment, we used socioeconomic indicators such as education, income, asset possession, employment status, dietary diversity, nutritional status and household food insecurity. Sociodemographic characteristics such as age, gender and marital status; clinical characteristics such as CD4 count, duration on ART and history of opportunistic infections were taken into consideration during the interviews and chart review for data collection. Inclusion of independent variables were based on literature reviews conducted, data availability, and theoretical relevance (Tabachnick & Fidell, 2007). We chose these independent variables because of extensive literature highlighting the relationship between these covariates and ART adherence (Fonsah et

al., 2017; Eyassu, Mothiba & Mbambo-Kekana, 2016; Alagaw et al., 2013; Peltzer & Pengpid, 2013; Bangsberg, 2006).

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Food insecurity is defined as the economic and social condition of limited or uncertain access to adequate food (US Department of Agriculture, Economic Research Service, 2019). The access component of household food insecurity was measured using the standard household food insecurity access scale (HFIAS) (Coates, Swindale & Bilinsky, 2007). This is a nine-item questionnaire assessing household food insecurity in the domains of anxiety about household food access, insufficient quality of food and insufficient food intake in the past 30 days. In this study, HFIAS was calculated by summing the score for all nine items and ranges from 0 to a maximum of 27. A higher HFIAS score indicates poor access to food and greater food insecurity.

Malnutrition is the condition that occurs when the body does not get enough nutrients (US National Library of Medicine, 2019). In this study, malnutrition refers to undernutrition. The researchers used anthropometric measurement such as weight and height to measure malnutrition. The participants' weight was measured by means of the Seka weight scale calibrated to the nearest 0.1 kg after removing heavy clothes. The participants' height was measured using the Seka measuring rod calibrated to the nearest 0.1 cm. The participants took off their shoes, stood erect and looked straight in the horizontal plane to measure their height. The body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters (kg/m^2). Participants with a BMI of less than 18.5 kg/m^2 were considered malnourished.

Household dietary diversity is the economic ability of a household to access a variety of foods during the past seven days. Household dietary diversity was measured based on the dietary measurement method (Swindale & Bilinksy, 2006; Kennedy, Ballard & Dop, 2011). Twelve questions were used to assess dietary diversity. Participants were asked to report the frequency of consumption of each of the following 12 food groups: (1) cereals; (2) roots and tubers; (3) pulses and legumes/nuts; (4) vegetables; (5) fruits; (6) meat and poultry; (7) eggs; (8) fish and seafood; (9) milk and milk products; (10) oils and fats; (11) sugar and sweets; and (12) miscellaneous. Irrespective of the frequency, participants received '1' point if they consumed at least once

during the last seven days of the foods within each subgroup, and '0' points if they never consumed the food. The household dietary diversity score (HDDS) was constructed as the sum of some food groups consumed over the past week, ranging from 0 to 12. A high value indicated a diversified diet.

Asset possession refers to a household's possession of assets elicited by asking participants a series of 13 questions about household assets and housing characteristics such as housing quality (floor, walls and roof material), source of drinking water, type of toilet facility, presence of electricity, type of cooking fuel, and ownership of modern household durable goods and livestock (e.g. bicycle, television, radio, motorcycle, telephone, refrigerator, mattress, bed and mobile phone). Following the method of Filmer and Pritchett (Filmer & Pritchett, 2001), principal components analysis was applied to define the asset wealth index among the PLWHA, and participants were sorted into three quintiles of relative asset wealth. A high value indicates more asset possession.

Data analyses

To assess factors associated with non-adherence to ART, binary adherence variables using data from VAS was created. Both descriptive and analytic statistics were used. Binary logistic regression analysis was used to find associations between the independent variables and the outcome variable. The Chi-square test of independence was used to find factors for not taking medication. All the variables showing a significant association in a binary analysis at $p < 0.05$ were extended to the multivariate linear regression model using the Wald backward method. In the final multivariate analysis, the test was two-sided and p-value <0.05 was considered statistically significant. All statistical analyses were conducted in IBM SPSS Statistics for Windows, Version 24.0.

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Ethical approval and consent to participate

Ethical clearance was obtained from the Health Studies Higher Degrees Committee of the College of Human Sciences at the University of South Africa (REC 012714-039 NHERC). Informed consent was obtained from all the individual participants included in the study.

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RESULTS

Three hundred and ninety-four study participants were recruited for this study. The response rate was 98.9%. The majority (80%) of the participants were aged between 25 and 44 years. The women participants constituted 66.4% of the total participants. Nearly 50% of the participants were married and an equal number of the participants were divorced, widowed or single. About 36.4% of them never attended school, while only 4% attended college/university. The majority of the participants (91%) lived in urban areas. Table 1 shows the characteristics of the study participants.

In terms of socioeconomic characteristics, most of the participants were poor as measured by the wealth index, a proxy measure for asset possession. About 60% of them were in the lower asset tertiles. More than a quarter of them were unemployed (31%). A large number of the participants (67.7%) lived on a ~~poor~~ mean monthly income of 1260 Ethiopian Birr (equivalent to US$45), below the World Bank poverty threshold of US$ 1.90/day (The World Bank Group, 2019). The vast majority of the study participants (76%) were food insecure and 60% had a BMI of less than 18.5 kg/m^2. The mean CD4 count was 559 (SD = 319.6) cells/mm^3, with a range of 60 to 1914. More than a quarter of them (33.6%) suffered from frequent opportunistic infection in the last three months.

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Based on a 30-day VAS at ≥95%, 39.7% of the study participants were found non-adherent to ART. Of the 296 food insecure participants, more than half (51.4%) was non-adherent; of the 235 malnourished PLWHA, 47.2% was non-adherent.

Factors associated with antiretroviral therapy adherence

As presented in Table 2, the binary logistic regression analysis and subsequent multivariate logistic regression analysis showed age, employment, food insecurity, malnutrition and opportunistic infections were strongly associated with ~~the factors in~~ non-adherence to ART.

Age groups of less than 25 years were found to be four-fold non-adherent to ART in comparison with older age groups (AOR: 4, CI: 1.2–12.6, p = 0.02). The odds of non-adherence to ART among unemployed PLWHA were almost twice higher than their peers who were employed

(AOR: 1.7, CI: 1.03–2.1, p = 0.04). Food insecurity was the other socioeconomic factor strongly found impeding ART adherence (AOR: 2.1, CI: 6.1–56, p <0.001) and malnutrition was among factors deterring PLWHA to attain the required ≥95% ART adherence level (AOR: 0.9, CI: 0.82–0.98, p = 0.018). Recurrent episodes of opportunistic infection (AOR: 1.7, CI: 1.03–2.86, p = 0.037) was a clinical factor contributing to non-adherence to ART.

Reasons for missing medication

The prevalence of non-adherence to ART in this study was 39.7% (n = 135). Among these, ~~Based on the self-reported adherence level, among those who missed taking their medication,~~ 83% missed twice a month while 4.4% missed three times or more a month. Four reasons were reported by the study participants as important reasons for missing ~~taking~~ their medications: (i) demanding work or household responsibilities (33%), (ii) ran out of medication (34%), (iii) unable to take without food (22%), and (iv) forgetfulness (11%). As seen in Table 3 which shows frequency of missing medication was found strongly associated with VAS <95%.

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DISCUSSION

In the current study, the factors associated with non-adherence and adherence to ART among PLWHA in Benishangul-Gumuz were examined. Our findings endorse higher prevalence of ART non-adherence, with only 60.3% of our study participants remaining adherent to ART, and indicates changes need to be implemented towards commitment to and realization of a 90-90-90 HIV treatment initiative. The study found age groups below 25 years were non-adherent to ART. Analogous to this finding, the results of a meta-analysis study (Ghidei et al., 2013) showed a higher risk of non-adherence among young PLWHA while older PLWHA had reduced risk of non-adherence to ART. Another study in Canada found a higher proportion of non-adherence among young PLWHA (Hadland et al., 2012). Youths are willing to engage in greater risky sexual behaviors and may also be more likely to assume the risks of poor HIV medication compliance, thus youth tailored behavioral change interventions that address the special emotional and developmental concerns of younger PLWHA could be designed.

Strong plausible evidence of the association between non-adherence to ART and food insecurity was found. Food insecure PLWHA were found twice more likely of non-adherence to ART than

their food secure counterparts. Studies in both developing and developed countries have culminated the strong association between non-adherence to ART and food insecurity effects. For example, studies in Lake Victoria,Kenya (Nagata et al., 2012) and in Atlanta, USA (Pellowski et al., 2016) showed that food insecure PLWHA miss doses of their daily medication. Similarly, studies in Congo (Musumari et al., 2014), and Jimma (southwest Ethiopia) (Tiyou et al., 2012) established a strong association between non-adherence to ART and food insecurity. Since non-adherence to ART can risk developing viral resistance (Weiser et al., 2012; Musumari et al., 2014) and food insecurity poses a significant challenge to the HIV/AIDS response (Federal Ministry of Health of Ethiopia, 2015; Pellowski et al., 2016; Kalichman et al., 2014), policymakers must take into account the issue of integrating food security with HIV treatment and prevention program.

In the current study, malnourished PLWHA were also found non-adherent to ART. Research findings in different setups have indicated the strong relationship between non-adherence to ART and malnutrition, thus the focus should be on clinical and programmatic nutrition interventions. For example, a study in northern Ethiopia (Berhe, Tegabu & Alemayehu, 2013) showed that malnutrition was significantly associated with non-adherence to ART and recommended nutritional support to such a vulnerable group. Another matched case-control study in the Central Tigray Zone, Ethiopia revealed malnutrition was among the independent factors associated with lack of adherence to ART (Weldehaweria et al., 2017). Absence of nutritional support fuels the synergistic co-existence of HIV and malnutrition that has a perverse effect on ART adherence and the wellbeing of PLWHA (Mekuria et al., 2015; Sicotte et al., 2014; Berhe, Tegabu & Alemayehu, 2013). Therefore, nutritious food support is highly regarded as a viable option to increase weight gain (Audain et al., 2015) and improve treatment outcome (Tiyou et al., 2012; Chaiyachati et al., 2014).

Our findings are similar to the study by Nachega et al., who found a strong association between non-adherence to ART and lack of employment among PLWHA living both in low-income and in high-income countries (Nachega et al., 2015). In opposition to this finding, unemployed PLWHA in Nigeria had better ART adherence than employed people and rarely missed their ART medications (Okoronkwo et al., 2013). The possible explanation for adherence among

unemployed PLWHA might be time freedom to take their medications without forgetting being a concern. Also, they are more privileged to take their medications freely without any psychological impacts that put them under stress such as the workplace environment (Okoronkwo et al., 2013). Education status, dietary diversity and asset possession were among the alterable socioeconomic factors found influencing adherence to ART, thus developing effective adherence interventions to such alterable barriers are important in achieving an optimum adherence level.

Opportunistic infections were found to affect the treatment outcome of PLWHA. According to the results of this study, those who suffered recurrent illness within the last three months were twice more likely to miss their treatment and be non-adherent to ART. This finding is consistent with the findings of other studies that reported the presence of a significant association between treatment for HIV and other infections and adherence to ART (Eyassu, Mothiba & Mbambo-Kekana, 2016). Corresponding to this finding, non-adherence to ART as a result of opportunistic infection was reported among PLWHA in Yaounde, Cameroon (Fonsah et al., 2017) and the Republic of Korea (Kim et al., 2018). The reason for non-adherence to ART among sick PLWHA include the pill burden and poor absorption (Eyassu, Mothiba & Mbambo-Kekana, 2016; Fonsah et al., 2017). It is highly recommended that strong attention and follow-up are required for ill PLWHA on medication and nutritional support to maximize the treatment outcome and improve quality of life.

The findings of this study are consistent with the evidence that urban residences, as a result of dynamic socioeconomic alteration, may lack the desired adherence level (Belayihun & Negus, 2015). Similar to this finding, a study at Gonder University in northwest Ethiopia revealed that urban residences are associated with factors of non-adherence to ART (Molla et al., 2018). To alleviate the adherence issues both in urban and rural setups, a robust and sustainable response has to be foresighted, including using community volunteers to re-engage patients in care and helping them to remain in care, and empowering PLWHA in rural areas to regularly visit their healthcare provider (Kaihin et al., 2015; Campbell et al., 2012).

The principal implication of the current study is that socioeconomic factors such as nutrition and food security play a significant role in ART adherence. However, Ethiopia's healthcare system

cannot afford such affluent program to run vertically across the health sector as a standalone. Thus, the integration of nutrition food security interventions with HIV prevention, treatment and care that can be realized through a multisector approach has to be adopted to attain viral suppression and improve adherence. Equally, innovative youth-centered adherence intervention strategies have to be developed. Strong advice on medication adherence and positive living should be promoted to minimize and prevent the frequent acquisition of opportunistic infections.

The current study has several limitations: First, even if an attempt was made to minimize social desirability bias, it might be subjected to recall and social desirability biases as ART adherence, food security and dietary diversity were assessed based on the self-reported measure. Second, the study design was cross-sectional in nature and hence cannot be used to determine causality. Malnutrition can be both a cause and effect of non-adherence to ART. Hence, future longitudinal studies are warranted to ascertain the causal directions of these variables. In spite of these limitations, the study shows that non-adherence to ART is strongly associated with socioeconomic and clinical factors, including young age, food insecurity, malnutrition and opportunistic infections.

CONCLUSIONS

The current study provides empirical findings on the factors associated with non-adherence to ART and the extent of non-adherence in Benishangul-Gumuz. High prevalence of non-adherence is strongly associated with young age, food insecurity, malnutrition and opportunistic infections; while lower odds of ART non-adherence were found among unemployed PLWHA, urban residents, lower educational level, poor asset possession and CD4 count below 350 cell/mm^3. Therefore, improving ART adherence requires the adoption of a youth-centered adherence and development counselling approach, mitigation of recurrent opportunistic illness, and integrating nutrition and food security interventions with the HIV/AIDS program that can be implemented through the multisectoral approach to bridge the resource gap and improve the treatment outcome across all setups.

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Competing interests

The authors declare no conflicts of interest.

Authors' contributions

Fikadu Tadesse designed and implemented the field research, performed the statistical analyses and drafted the manuscript. Azwihangwisi Mavhandu-Mudzusi reviewed the manuscript. Both authors contributed to the interpretation of the data and critically revising the paper, and agree to be accountable for all aspects of the work.

List of abbreviations

AIDS: acquired immuno deficiency syndrome; ART: antiretroviral treatment; BMI: body mass index; HDDS: household dietary diversity score; HFIAS: Household Food Insecurity Access Scale score; HIV: human immunodeficiency virus; PLWHA: people living with HIV and AIDS

Availability of data

The following information was supplied regarding the data availability:

The raw data measurements and codes are provided in the data Data S1.

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The following things have not been addressed
Co-morbid conditions\
History of substance use
History of medication use/pill burden
Duration of illiness, ART use
Methodology is not sufficient:
- (sampling ,data management, quality control??)
-objectives (specific)