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Causes and predictors of hospitalization and in-hospital mortality among HIV/AIDS patients on highly active antiretroviral therapy in secondary and tertiary care hospitals in Oromia Regional State: multi-center cross-sectional study

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Abstract

Introduction: Highly active antiretroviral therapies (HAART) decrease the incidence, morbidity, and mortality of acquired immunodeficiency syndrome (AIDS) dramatically. However, current research reported an increased hospitalization rate among AIDS patients. Therefore, this study aimed to determine causes and predictors of hospital admission as well as in-hospital mortality amongst human immunodeficiency virus (HIV)/AIDS-infected patients on HAART.

Material and methods: This was a multi-center cross-sectional study, and included HIV/AIDS patients who were admitted to secondary and tertiary care hospitals in Oromia Regional State from May 1, 2017, to August 30, 2017. Data were collected from hospitalized HIV/AIDS patients using structured checklist and interview. Results were analyzed with Statistical Package for Social Sciences (SPSS) software, version 22. Bivariate and multivariable logistic regression analysis were performed to evaluate association, and p-value < 0.05 was used to determine relationship between dependent and independent variables.

Results: Out of 171 participants enrolled, 105 (61%) were hospitalized due to opportunistic infections. Age ranged from 40 to 49 (AOR = 0.30; 95% CI: 0.09-0.98%) vs. 18-29, females (AOR = 2.41; 95% CI: 1.11-5.24%), CD4+ count less than 200 (AOR = 10.32; 95% CI: 3.49-30.52%), and poor adhered (AOR = 2.78; 95% CI: 1.21-6.41%) were significantly related to hospitalization with opportunistic infections (AIDS-related illnesses). Among admitted patients, 20 (11.7%) died in hospital. Poorly adherent patients and those who spent 9 days or more in hospital were more exposed to in-hospital death, with AOR = 3.093; 95% CI: 1.012-9.453% and AOR = 4.533; 95% CI: 1.371-14.985%, respectively.

Conclusions: The major causes of hospitalization were HIV/AIDS-related illnesses. Adherence to the HIV drug regimen is warranted to minimize hospitalization with opportunistic infections and HIV/AIDS mortality.

Introduction

Human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) are a foremost public health difficulty with the worldwide new cases of 2.1 million and 1.1 million deaths, out of which about 42.7% was in Eastern and South African region [1]. Highly active antiretroviral therapy (HAART), a combination of three and more HIV repressing drugs, has appreciably enhanced the immunological standing of infected people, making HIV a controllable illness [2]. Thriving antiretroviral treatment contains viral reproduction [3]. CD4+ T cell lymphocyte count is one of the main significant predictive factors for worsening of HIV infection, and the root for suggestion in the initiation of antiretroviral management and prophylaxis [4].

HAART could decrease the incidence [5], morbidity [5, 6], and mortality [5-7] of AIDS dramatically. However, current studies reported an increased rate of hospitalization among AIDS patients, which was up to 26.6% [8] regardless of remarkable worldwide increase of HAART treatment [1]. Furthermore, the rate and length of hospitalization was higher in these patients than wide-ranging population [9].

This in turn was accompanied with a bigger danger of death larger than about 20%, as revealed in studies from Brazil, Iran, and Uganda, showing death rate of 44.8%, 25.7%, and 21% among hospitalized AIDS patients, respectively [10-12].

Limited studies were performed evaluating causes of hospitalization and in-hospital mortality among general cohorts of AIDS patients during HAART. Moreover, these studies had various limitations. First, almost all of them were retrospective in nature using card review or secondary data collection, which might elevate a problem of incompleteness, such as clinical characteristics and a few of laboratory investigations (e.g., CD4+ count level) missing [13-15]. The second limitation included lack of representativeness, as majority of them were done in a single university or teaching hospital, which might not represent the whole picture of health setting [12-14, 16]. The third and final limitation was they had no uniformity in reporting the cause for hospitalization and in-hospital mortality. Some reported an increased risk of mortality with AIDS-related illness in the recent era of HAART, due to late presentation and being HAART naïve [6, 8]. On the contrary, others found non-AIDS-related illness, like cardiovascular, malignancy, non-AIDS-related infections, and drug toxicity as the major causes of mortality in this group of patients [17, 18].

In order to fill-up the above-mentioned gaps with previously published works, the present multi-center cross-sectional study aimed to determine causes of hospital admission, predictors of admission with opportunistic infection, and in-hospital mortality among HIV/AIDS-infected individuals on HAART in secondary and tertiary hospitals in Oromia Regional State.

Material and methods

Study setting, time, and design

A hospital-based cross-sectional study design was employed from May 1, 2017, to August 30, 2017, in Oromia Regional State, Ethiopia. In Oromia, there are nearly 36 hospitals (32 general hospitals and 4 referral hospitals), out of which 12 hospitals were selected using a lottery method. In total, 10 hospitals were included in the present study, 2 excluded because of unwillingness (i.e., Fiche Hospital, Shashamene Hospital). 1/3rd of the hospitals were chosen to ensure representativeness of the data. The names of hospitals included Nekemte Referral Hospital, Ambo General Hospital, Bishoftu General Hospital, Adama Hospital Medical College, Jimma University Medical Center, St. Lukas Hospital, Mettukarl Hospital, Chiro Hospital, Goba General Hospital, and Assella Hospital. These hospitals provide a wide range of services, such as voluntary counseling and testing (VCT), prevention of mother-to-child transmission, antiretroviral therapy, treatment of opportunistic infections, and other curative services. Medical wards were considered and patients admitted there were included in the present study, since HIV/AIDS patients are mainly managed in these departments.

Study population

All HIV/AIDS patients on HAART who were admitted to a medical ward at a period of data acquisition were involved in the present study. Those patients who were on HAART for less than 6 months and were re-admitted after first discharge with an improvement were excluded.

Sampling amount and sampling procedures

General and referral hospitals in Oromia Regional State were considered as the study hospitals and were chosen using a lottery method. Therefore, all the consecutive participants who fulfilled the inclusion criteria were enrolled into 4 months study. Pre-tested and standardized questionnaire were adapted from different literature and modified to fit the local context [14-22]. Data were collected by ten nurses, with two clinical pharmacists as supervisors. The questionnaires contained independent variables, such as demography (age, gender, body mass index (BMI), employment status), CD4+ count, adherence level, prophylaxis (cotrimoxazole prevention therapy [CPT], isoniazid prevention therapy [IPT]), and length of hospitalization. Adherence was measured using patient self-report, and dependent variables included cause of hospital admission and in-hospital mortality.

Causes of hospitalization were categorized based on diagnoses of disease conditions that lead to a hospitalization. If a patient had multiple diagnoses during hospitalization, one underlying cause of hospitalization would be determined by applying the following priority order: (1) WHO stage 4

Table 1. Socio-demographic and clinical characteristics of the study participants from Oromia Regional State hospitals, Ethiopia

Factor	n (%)
Age, years	
18-29	42 (26.6)
30-39	61 (35.7)
40-49	40 (23.4)
≥ 50	28 (16.3)
Sex	
Male	74 (43.3)
Female	97 (56.7)
Employment status	
Employed	123 (71.9)
Not employed	48 (28.1)
Body mass index	
Malnutrition	60 (35.1)
Normal range	103 (60.2)
Overweight	8 (4.7)
Current CD4+ count level	
Greater than 200	52 (30.4)
Less than 200	119 (69.6)
Isoniazid prevention therapy	
Yes	102 (59.6)
No	69 (40.4)
Cotrimoxazole prevention therapy	
Yes	155 (90.6)
No	16 (9.4)
Time on HAART	
Less than 5 years	99 (57.9)
Greater than 5 years	72 (42.1)
Adherence level	
Good	64 (62.6)
Poor	107 (37.4)

opportunistic disease; (2) WHO stage 3 opportunistic disease; (3) other infection; (4) other cancer; (5) other disease. Finally, the underlying causes of hospitalization were grouped into two broad categories, such as HIV/AIDS and non-HIV/AIDS reason of admission.

Data handling and investigation

Firstly, data was applied into Epi-data version 4.4 and transferred to Statistical Package for Social Sciences software, version 22.0, for data analysis. The descriptive data analysis was performed and presented as frequency, summary statistics, and table. Bivariate and multiple variable logistic regressions were done to identify associated factors. Both crude and adjusted odds ratios with 95% confidence interval were computed, and statistical importance was confirmed at p-value < 0.05.

Consideration of ethics

Research ethical clearance letter was initially attained from the Jimma University Institute of Health Science Researches' ethical board, No. IHRPGC/348/2017. Then, the ethical clearance together with a support letter from the Jimma University was given to ethical review committee of Oromia Regional Health Bureau (ORHB) for a revision. The final support letter written to respective hospitals was obtained from ORHB. Then, a written consent was secured from chief executive officer (CEO) of the selected hospitals and provided to a ward senior or responsible person to get a permission. Finally, data collectors informed the patients about the study's main objectives and any unclear point related to the study, after which, an informed consent was taken from each individual. To ensure confidentiality of respondents, their names were excluded from the questionnaire.

Results

From 12 hospitals selected to be included in this study, only 10 hospitals had shown their willingness to contribute. A total of 171 participants were enrolled for over 4 months period from 10 hospitals. The age of study participants ranged from 18 to 70 years. The mean age of the participants was 36.66 ± 11.8. The higher proportion, 61 (35.7%) were in the age range of 30 to 39 years, and the majority, 97 (56.7%) of enrolled were females. About 123 (71.9%) of the individuals were employed. The majority of the participants, 103 (60.2%), had normal body mass index, and greater than two-third of the patients had greater than 200 CD4+ count. Nine-tenth and three-fifth of the study participants were taken prophylaxes of cotrimoxazole and isoniazid prevention therapy to prevent opportunistic infections, respectively. Greater than half, 99 (57.9%) of the study participants were less than five years' time on HAART. The majority, 107 (62.6) of them had a good adherent to their HAART medication (Table 1).

Causes for hospital admission among the study participants

105 (61%) out of 171 participants hospitalization was caused by AIDS-related illness, while 66 patients (39%) were admitted as a result of non-AIDS-related illnesses.

Predictors of hospital admission with opportunistic infection among the study participants

In the bivariate analysis, variables, such as the age category of 40 to 49 years, males, current CD4+ count less than 200, less than 5 years on HAART, and poor adherence level

Table 2. Bivariate and multivariate logistic regression to determine predictors of causes of hospital admission among HIV/AIDS patients on highly active antiretroviral therapies (HAART)

Variables	Admission with AIDS-related illness		COR (95% CI)	p-value	AOR (95% CI)	p-value
	Yes	No				
Age in completed years						
18-29	12	30	1.00		1.00	
30-39	26	35	0.54 (0.23-1.25)	0.149	0.81 (0.27-2.41)	0.707
40-49	19	21	0.44 (0.18-1.10)	0.080	0.30 (0.09-0.98)	0.046
≥ 50	9	19	0.84 (0.30-2.38)	0.750	0.93 (0.24-3.55)	0.911
Sex						
Male	22	52	1.96 (1.04-3.72)	0.039	2.41 (1.11-5.24)	0.026
Female	44	53	1.00		1.00	
Employment status						
Yes	50	73	1.00	0.378	1.00	0.463
No	16	32	1.37 (0.68-2.76)		1.45 (0.54-5.87)	
Nutrition status						
Malnutrition	22	46	1.56 (0.82-2.96)	0.174	1.16 (0.53-2.54)	0.710
Normal	44	59	1.00		1.00	
Current CD						
Greater than 200	5	47	9.89 (3.68-26.59)	0.000	10.32 (3.49-30.52)	0.000
Less than 200	61	58	1.00		1.00	
Isoniazid prevention therapy						
No	25	44	1.18 (0.63-2.22)	0.602	1.19 (0.52-2.71)	0.681
Yes	41	61	1.00		1.00	
Cotrimoxazole prevention therapy						
No	6	10	1.05 (0.36-3.05)	0.925	1.24 (0.32-4.88)	0.758
Yes	60	95	1.00		1.00	
Time on HAART						
Less than 5 years	31	68	2.08 (1.11-3.89)	0.023	1.73 (0.80-3.71)	0.161
Greater than 5 years	35	37	1.00		1.00	
Adherence level						
Good	15	49	2.98 (1.49-5.94)	0.002	2.78 (1.21-6.41)	0.016
Poor	51	56	1.00		1.00	

were the factors significantly associated with admission of patients with AIDS-related illnesses (opportunistic infections), and time on HAART for less than 5 years was adjusted in multiple variables.

In multiple variables logistic regression analysis, the odds with the age range of 40 to 49 years were about 30% more likely admitted with AIDS-related illness than the age range between 18 to 29 years (AOR = 0.30; 95% CI: 0.09-0.98%). Females were twice more likely to be admitted with AIDS-related illness compared to males (AOR = 2.41; 95% CI: 1.11-5.24%). The likelihood of current CD4+ count less than 200 was ten times more likely predictor of admission with AIDS-related illness compared to those with CD4+ count greater than 200

Table 3. Incidence of death among admitted HIV/AIDS patients on highly active antiretroviral therapies in Oromia Regional State, Ethiopia, 2017

In-hospital death	n (%)
No	151 (88.3)
Yes	20 (11.7)
Total	171 (100)

(AOR = 10.32; 95% CI: 3.49-30.52%). Those poorly adhered to their treatment regimen were three times more likely to be admitted as a result of AIDS-related illness than those with good adherent (AOR = 2.78; 95% CI: 1.21-6.41%) (Table 2).

Table 4. Bivariate and multivariate logistic regression to determine predictors of causes of hospital admission among HIV/AIDS patients on highly active antiretroviral therapies (HAART)

Variables	In-hospital mortality		COR (95% CI)	p-value	AOR (95% CI)	p-value
	No	Yes				
Reason for admission						
AIDS (opportunistic infection)	61	5	1.00	0.747		0.678
Non-AIDS-related	90	15	0.983 (0.221-4.377)	0.982	0.747 (0.188-2.960)	
Age in completed years						
18-29	34	8	1.00	0.099	1.00	0.134
30-39	61	0	0.00	0.00	0.00	0.997
40-49	36	4	0.229 (0.037-1.431)	0.115	0.399 (0.100-1.589)	0.193
≥ 50	20	28	1.938 (0.429-8.756)	0.390	2.398 (0.668-8.616)	0.180
Sex						
Males	63	11	1.00	0.336	1.00	0.241
Females	88	9	0.554 (0.166-1.845)		0.504 (0.160-1.586)	
Unemployment status						
Yes	41	7	1.00	0.755		0.703
No	110	13	1.275 (0.277-5.871)		1.333 (0.304-5.846)	
Nutrition status						
Normal	95	8	1.00	0.034	1.00	0.057
Malnutrition	56	12	3.735 (1.103-12.647)		2.961 (0.969-9.045)	
Current CD4+ count						
Greater than 200	45	7	1.00	0.300		0.200
Less than 200	106	13	1.981 (0.544-7.210)		2.219 (0.655-6.186)	
Isoniazid prevention therapy						
Yes	91	11	1.00	0.172		0.223
No	60	9	2.433 (0.679-8.720)		2.011 (0.654-6.186)	
Cotrimoxazole prevention therapy						
Yes	137	18	1.00	0.869		0.828
No	14	2	0.829 (0.090-7.621)		0.787 (0.091-6.811)	
Time on HAART						
Less than 5 years	89	10	1.00	0.743	1.00	0.728
Greater than 5 years	62	10	1.218 (0.375-3.956)		1.226 (0.388-3.880)	
Adherence level						
Good	53	11	1.00	0.049	1.00	0.048
Poor	98	9	3.832 (1.007-14.588)		3.093 (1.012-9.453)	
Length of hospitalization						
< 9 days	85	5	1.00	0.021	1.00	0.013
≥ 9 days	66	15	4.918 (1.266-19.110)		4.533 (1.371-14.985)	

Incidence of death among the study participants

The incidence of death in this study was 11.7% (20 cases), and 88.3% (151 cases) of patients were discharged.

Mortality and its associates

As presented in the following table using bivariate analysis, nutrition status, level of adherence, and length of hospital stay have shown a significant association with hospital

mortality at *p*-value of 0.034, 0.049, and 0.21, respectively. Upon backward stepwise logistic regression, poor adherence and prolonged hospital stay (i.e., greater than 9 days) were found to have a significant association with in-hospital mortality. Accordingly, those individuals who were poorly adherent to their medications were 3 times more likely to die in hospital than those with good adherence (AOR = 3.093; 95% CI: 1.012-9.453%). Similarly, the patients who spent 9 days and more in hospital were 4.5 times more likely to die in hospital than those who spent less than 9 days (AOR = 4.533; 95% CI: 1.371-14.985%) (Table 4).

Discussion

This present study was carried out in Oromia Regional State hospitals to assess predictors for hospitalization with opportunistic infection among HIV-infected patients receiving HAART. We found that three-fifth of the study participants were hospitalized with AIDS-related illnesses. This result was similar to a study from India [19], which indicated a low adherence to treatment among the study participants. It is obvious that non-adherence increases the risk of hospitalization. Most of the studies show that the most common causes of hospitalization were opportunistic infections [19, 20]. Similarly in our study, majority of the study participants were hospitalized with opportunistic infections. However, this result was greater than that reported in studies from Iran and Uganda [12, 20]. On the other hand, our study result was lower than a research conducted in Thailand [13].

In this study, the patients in age category from 40 to 49 years were significantly associated with opportunistic infections as a cause of hospitalization. This might be due to a decrease in immunity as age increases [21, 22].

Our study revealed that females were significantly associated with opportunistic infections' hospitalization. Comparably, a study performed in the USA showed females having 51% of higher rates than males [8]. This is probably because of variation of treatment adherence between the two sexes, which would later result in a difference in the cause of hospitalization [23].

Here, we found that lower CD4+ count was significantly associated with opportunistic infection as a cause of hospitalization. This was similar to a study conducted in Australia, which observed that higher CD4+ cell count was significantly associated with a decreased risk of hospitalization [9]. Deaths are more common in population with CD4+ count less than 200/ μL at the time of admission. As the level of CD4+ count increases, the patient recovers from HIV-related illness and the immunity of individual increases [14].

In our study, poor adherence was associated with opportunistic infection as the cause of hospitalization. Poor adherence is a known factor that contributes to HIV/ AIDS-related infections. Most of the patients were uneducated, with little knowledge about medication adherence, and saturated information about their treatment and continuous follow-up during HAART [24, 25]. Due to discontinuation of their treatment, they are at high-risk for HIV-related illness hospitalization. Common challenge in many health systems in Ethiopia is termination of treatments' regimens by patients themselves, which leads to poor treatment outcomes and hospitalization [26].

This study investigated the incidence of in-hospital mortality among HIV-infected patients receiving HAART in hospitals of Oromia Regional State. The incidence of death reported with in current study was lower than that stated in studies done in Brazil, Uganda, and West Africa [11, 12, 27]. This might be because of advancement in treatment and counseling of patients with trends of time, as there was a difference in time among the studies. However, it was greater than studies from Thailand and Barbados [13, 28]. These differences were related to study's different setting, period, populations, and design. Poor adherence and prolonged hospital stay have significant association with in-hospital mortality. Both of them were known to contribute to different kinds of infections, apart from prolonged hospital stay that, in particular, would cause hospital's acquired infections, and ultimately would result in hospital death [29].

This study had limitation in a resource constraint of laboratory investigation. Even if there were other laboratory parameters, which could affect the outcome, the study could not show them, as laboratory tests were not done for the majority of patients due to financial difficulties of the participants.

Conclusions

This study had revealed that HIV/ AIDS-related illnesses are the major causes for hospitalization among patients on HAART. Moreover, poor adherence, low CD4+ count, male sex, and age range from 40 to 49 years were related with opportunist infections (AIDS-related illnesses) as the causes of hospitalization. This research highlights that an appropriate treatment, prevention, and continuous monitoring of HIV/AIDS illness are needed to decrease hospitalization rate due to opportunistic infections. Working to improve adherence to HAART, to prevent AIDS hospitalization, and minimize the risk of opportunistic infections is strongly recommended.

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Conflict of interest

The authors have no conflict of interest.

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