Cross-sectional Study

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Magnitude of opportunistic infections and associated factors among adult people living with human immune deficient virus on art at selected public hospital, mogadishu somalia: cross-sectional study

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Introduction: Opportunistic infections (OIs) remain the leading cause of death among people living with Human immune deficient virus and OIs-related mortality in Africa is estimated at 310 000 cases. Besides, Somalia has scant data about OIs since a high burden of tuberculosis and HIV co-infection has been reported. Hence, up-to-date information is vital for better treatment and interventions and may support national and international HIV strategies and eradication programs. Therefore, this study aims to estimate the magnitude of OIs and determine factors associated with among people living with HIV/AIDs on anti-retroviral therapy (ART) in a selected public hospital in Mogadishu, Somalia.

Materials and methods: A hospital-based cross-sectional study was conducted between 1 June and 30 August 2022 by interviewing HIV patients and reviewing case record files using a validated questionnaire containing sociodemographic, clinical, OIs history, behavioural and environmental characteristics. Logistic regression was used to determine factors associated with OIs at the significance level of a = 0.05.

Result: The magnitude of OIs among people living with HIV was 37.1% (95% CI = 31.6–42.2); major identified OIs were pulmonary tuberculosis 8.2%, Diarrhoea 7.9%, and Pneumonia 4.3%. Based on Multivariable logistic regression drinking non-sterilized water [adjusted odds ratio (AOR) = 2.395, 95% CI: 2.010–4.168], living with domestic animals (AOR = 4.012, 95% CI: 1.651–4.123), Co-morbidity of chronic disease (AOR = 2.910, 95% CI: 1.761–3.450), and poor ART adherence (AOR = 3.121, 95% CI: 1.532–6.309) were factors associated with OIs.

Conclusion: Human immune deficient virus patients in Mogadishu, Somalia, suffer from OIs. The OIs reduction strategies should improve drinking water sanitation, provide special consideration for those living with domestic animals and those with a co-morbid chronic disease, and improve ART adherence.

Keywords: factors associated, HIV/AIDs, mogadishu, opportunistic infections, prevalence, somalia

Introduction

HIV is a virus that attacks the body's immune system leading to immunosuppression with recurrent opportunistic infections (OIs) and immunological illnesses[1]. Globally, over 38 million patients are living with HIV/AIDs and caused almost 650 thousand deaths in 2021[2]. Africa still suffers a tremendous burden, with over 25 million people living with HIV[3]. Around 43% of new African HIV cases were in East and Southern counties, including Somalia[4]. OIs remain the leading cause of morbidity and

HIGHLIGHTS

- The magnitude of opportunistic infections (OIs) among people living with HIV was 37.1% [95% CI = 31.6–42.2].
- Major identified OIs were pulmonary tuberculosis 8.2%, diarrhoea 7.9%, and pneumonia 4.3%.
- Factors associated with OIs were drinking non-sterilized water [adjusted odds ratio (AOR) = 2.395, 95% CI: 2.010–4.168], living with domestic animals [AOR = 4.012, 95% CI: 1.651–4.123], co-morbidity of chronic disease [AOR = 2.910, 95% CI: 1.761–3.450], and poor anti-retroviral therapy adherence [AOR = 3.121, 95% CI: 1.532–6.309].

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mortality among people living with HIV (PLWHI), accounting for around 90%, opportunistic cancers were 7%, and only 3% may associate with other causes[5]. OIs-related death in Africa has an estimated 310 thousand cases[6–8].

However, high-active anti-retroviral therapy (ART) reduces the risk of OIs, reducing viral load by suppressing the virus and restoring the immune system[9–13]. Enhancing ART uptake and access is highly recommended[10,14,15]. PLWHI in poor settings may have poor ART access with significant immune suppression and may associate with a high risk of OIs. The prevalence may differ over time in different geographical locations[7]. OIs reduce the quality of life, enhance stigma with life opportunity restriction, and increase poverty by enhancing treatment costs and affecting SDG attainment in poor settings[16].

The OIs' magnitude and most common types differ in geographical locations[14,17–19]. In the US, oesophageal candidiasis, tuberculosis (TB), herpes simplex virus, and cryptosporidiosis declined while pneumonia increased[14]. OIs magnitude is higher in US-born Latin than in Central America-born[20]. The prevalence of fungal OIs increased[21]. In Spain, oesophageal candidiasis and TB significantly decreased while the Mycobacterium avium complex increased[22]. In Brazil, OIs magnitude declined between 1980 and 1999. OIs prevalence variations may associate with the patient's profile and risk behaviours, such as education level, sex, resident region, occupation, hygiene, and nutritional status as well. Brazil showed a high incidence of TB and toxoplasmosis in low-education people[5].

In Africa, over 310 000 OIs-related deaths have been reported[23,24]. The most significant causative pathogenic organism is *Mycobacterium tuberculosis* which causes pulmonary and non-pulmonary TB. TB incidence is less than 10% in the general population, while it is over 10% per year for PLWHI[25]. Visceral leishmaniasis has a greater risk of relapse with polyparasitic nature, unusual manifestation, poor restorative outcomes, and impaired healthcare access for PLWHI in limited resource settings[26]. Opportunistic respiratory tract, gastrointestinal, central nervous system, genital, and skin infections also had a significant burden[27–33]. Numerous factors are associated with OIs, such as older age, low haemoglobin (HB), chronic comorbid disease, late HIV-clinical stage, poor hygiene, low CD4, poor ART adherence, and use of substances[25,34].

There is scant data about HIV opportunistic infections in Somalia, especially in Mogadishu, the most populated city. Besides, OIs magnitude and predictors were not reported in Somalia since TB clinics showed a high burden of TB and HIV coinfection[35–38] with high mortality[39]. HIV healthcare coverage in Somalia is insufficient and PLWHI is downhearted due to discrimination with restricted life opportunities that may impact ART uptake and enhance OIs magnitude[35,36]. Moreover, around 43% of new African HIV cases were in East and Southern counties, including Somalia[4]. A 75% OIs recurrence was reported in Ethiopia East Africa[40]. Up-to-date information regarding OIs magnitude and predictors in Somalia is vital for better treatment and interventions and may support national and international HIV strategies and eradication programs. Therefore, the study aims to estimate the magnitude of opportunistic infections and determine factors associated with among HIV/AIDs adult patients on ART treatment in a selected public hospital in Mogadishu, Somalia.

Materials and methods

Study design

A hospital-based cross-sectional study was implemented to evaluate the magnitude of OIs and determine factors associated with among people living with HIV/AIDs on ART undergoing ART unit in the study hospital in Mogadishu, Somalia, during the data collection period between 1 June and 30 August 2022.

Study setting

This study was implemented in the Mogadishu, Banadir region of Somalia. It is the most populated region with the capital city and consists of 17 districts with an estimated population of over 3 million[38]. The study hospital is one of the two public hospitals in the region and is a public teaching and referral hospital administrated by the Somalia Ministry of Health. The hospital had the largest ART centre in south and central Somalia, with over 70% of people living with HIV attendants, and had record files.

Study population, inclusion, and exclusion criteria

The study population was HIV/AIDs adult patients who had evidence of HIV/AIDS infection on ART in the ART unit of the study hospital. Adult people living with HIV/AIDs who had evidence of HIV/AIDS infection on ART and had a patient record file in the study hospital were included after excluding those who did not verbally communicate or did not hear, those who had incomplete file baseline information (HIV-clinical stage, CD4 cell count, HB, OIs diagnosis), those who were not mentally fit, and those who in ICU or had severe medical conditions.

Sample size calculation

The sample size was calculated based on the standard formula of cross-sectional studies[41] $n = Z^2_{a/2}P^*(1-P)/d2$, where $Z^2_{a/2}$ was 1.96 level of confidence, P is the estimated proportion of prevalence which was 26.4%[42] and D is the desired level of precision which set at 0.05. The total sample size study required was 329, including an additional 10% to avoid errors. A systematic sampling technique was used to select the study participants.

Research tool and variables

A well-structured validated questionnaire was developed based on the literature reviewed[5–8,12,14–19,42] and discussed by three experts. The dependent variable was the magnitude of OIs among people living with HIV on ART. A senior medical doctor diagnosed the OIs based on the patient's medical history, clinical features, and laboratory investigation. Those who had at least one OIs were considered infected, while those who did not have anyone were judged non-infected cases.

The independent study variables were sociodemographic-related characteristics (age, sex, marital status, education level, occupation, monthly income, parenting status, accommodation status, and residential area), clinical characteristics (CD4 cell count, HB level, chronic co-morbid diseases status, WHO HIV stage, regiment line, and ART adherence), behavioural and environmental related characteristics (living with a domestic animal, the floor of the living house, privet latrine availability, sanitation drinking water, cigarette smoking, chewing khat, and physical activities).

The number of pills from the prescribed drugs remembered last month was calculated to measure ART adherence. Those who remembered greater than or equal to 95% recognized good adherence, while those who remembered less than 95% recognized poor adherence[43]. Those who drink water from nationally water-licensed companies that passed national water quality control were recognized as sterilized water drinkers, while those drinking pipe water or similar sources recognized non-sterilized water drinkers.

The questionnaire was primarily developed in English, and language experts did forward-backward translations to verify the consistency. Three external experts (An infectious disease specialist, a Tropical medicine physician, and a clinical researcher) did content validity using the item objective congruence method[44]. Subsequently, a 30-respondent pilot study was conducted in the study hospital an accepted Cronbach's alpha of 0.81 was achieved.

Process of data collection

Well-trained data collectors implemented a face-to-face interview and reviewed patient case record files lasting 30 min individually following the study tool in a private room after the hospital director approved accessing patient record files. Senior medical researchers reviewed and monitored collected data daily to identify biases and errors earlier to correct them.

Statistical analysis

Data were cleaned, coded, entered, and kept on the speeded sheet, then imported into the SPSS version 20 (SPSS) for analysis. Descriptive statistics were used for general characteristics by presenting frequency with percentages because all data were categorical. The magnitude of OIs reported as a percentage with a 95% CI from the bootstrap analysis. Logistic regression in univariate and multivariate models was used to determine factors associated with Opportunistic infections. Variables with a *P* value less than 0.25 in Univariate logistic regression model were candidates for multivariate logistic regression following Bursac *et al.*[45] suggestion. The Hosmer–Lemeshow goodness of fit test was used to indicate the final model goodness of fit[46]. In multivariate logistic regression, variables having a *P* value less than 0.05 was considered statistically significant. Data were presented in tables and figures, and this work report aligns with the STROCSS criteria[47]. This study registered researchregistry.com with UIN research-registry (https://www.researchregistry.com/register-now#user-researchregistry/researchregistry___).

Results

Sociodemographic characteristics

A total of 329 people living with HIV/AIDs participated in the study, 54.4% were male, 52.9% were married, 44.7% were youth between 30 and 45 years old, 47.1% were illiterate, 59.9% were employed, 53.8% had more than 200 USD monthly income, 87.2% were parents, 89.1% live in rural areas, and 77.8% live rental accommodations (Table 1).

Table 1
Socio-demographic characteristics.

Characteristics	*n* (%) 329 (100.0)
Sex	
Male	179 (54.4)
Male	150 (45.6)
Marital status	
Single	14 (4.3)
Married	174 (52.8)
Divorced	98 (29.8)
Widowed	43 (13.1)
Age (year)	
18–29	127 (38.6)
30–45	147 (44.7)
> 45	55 (16.7)
Education	
Illiterate	155 (47.1)
Primary	125 (38.0)
Secondary	49 (14.9)
Occupation	
Employed	197 (59.9)
Jobless	132 (40.1)
Monthly income $US	
≤ 200	152 (46.2)
> 200	177 (53.8)
Parenting status	
Yes	287 (87.2)
No	42 (12.8)
Residential area	
Rural	36 (10.9)
Urban	293 (89.1)
Accommodation status	
Rent	256 (77.8)
Owner	73 (22.2)

Clinical, psychosocial, behavioural, and environmental characteristics

Around half (59.0%) of the study participant's CD4 is greater than 500 cell count, 73.9% live with domestic animals, 78.7% haemoglobin level is less than or equal to 10, 59.9% of the participants' floor house is corrugated iron, 64.7% does not have privet latrine, 75.1% drink pipe water, and 50.8% had a co-morbid chronic disease. Over two-thirds (70.5%) live with HIV for 1 to 3 years, 84.8% had stage I/II, 87.2% used the first regiment line, 77.8% had poor ART adherence, 93.0% disclosure their HIV status, 36.2% were cigarette smokers, 30.7% chewing khat, 33.1% had regular physical activities (Table 2).

Magnitude and types of Opportunistic infections

The magnitude of opportunistic infection among HIV/AIDs adult patients on ART was 37.1% (95% CI = 31.6–42.2) (Table 3).

The most common OIs were pulmonary TB 8.2%, followed by diarrhoea 7.9%, bacterial pneumonia 4.3%, toxoplasmosis 3.6%, *Cryptococcus meningitis* 3.3%, *Herpes zoster* 2.7%, *OEsophageal candidiasis* 2.7%, cryptosporidiosis 1.5%, extrapulmonary TB 1.5%, and recurrent mycosis 1.5% (Fig. 1).

Table 2

Clinical, psychosocial, behavioural, and environmental characteristics.

Characteristics	*n* (%) 329 (100.0)
CD4	
< 350	62 (18.8)
350–500	73 (22.2)
> 500	194 (59.0)
Living with a domestic animal	
No	86 (26.1)
Yes	243 (73.9)
Haemoglobin (HB)	
≤ 10	259 (78.7)
> 10	70 (21.3)
The floor of the house	
Corrugate iron	197 (59.9)
Cement	93 (28.3)
Wood	31 (9.4)
Other	8 (2.4)
Privet latrine availability	
Yes	116 (35.3)
No	213 (64.7)
Drinking water	
Sterilized	247 (75.1)
Non-sterilized	82 (24.9)
Co-morbid disease	
No	162 (49.2)
Yes	167 (50.8)
Years with HIV	
< 1	45 (13.7)
1–3	232 (70.5)
> 3	52 (15.8)
HIV stage	
Stage I/II	279 (84.8)
Stage III/IV	50 (15.2)
Type of regiment	
First line	287 (87.2)
Second line	42 (12.8)
ART adherence	
Poor	256 (77.8)
Good	73 (22.2)
HIV status disclosure	
Disclosure	306 (93.0)
Hide	23 (7.9)
Smoking	
Yes	109 (36.2)
No	210 (63.8)
Chewing khat	
Yes	101 (30.7)
No	228 (69.3)
Physical activities	
Yes	109 (33.1)
No	220 (66.9)

ART, anti-retroviral therapy.

Factors associated with opportunistic infections among

In the Bivariate logistic regression analytical model, 11 factors were found to be associated with having opportunistic infections: Age, parenting status, accommodation status, residential area, living with domestic animals, co-morbidity of chronic diseases, WHO HIV stage, regiment line, ART adherence, and HIV status disclosure. These variables were candidates for multivariable logistic regression and four factors were found to be associated with opportunistic infections (OIs).

Table 3

Magnitude and types of opportunistic infections among HIV adult patients.

Characteristics	*n* = 331 (%)	95% CI
Magnitude of OIs		
No	207 (62.9)	57.8–68.4
Yes	122 (37.1)	31.6–42.2

OI, opportunistic infection.

The odds of OIs were 2.395 times greater [adjusted odds ratio (AOR) = 2.395; 95% CI; 2.010–4.168) for those who drink non-sterilized water compared to those who drink sterilized water.

Those living with domestic animals had 4.012 times (AOR = 4.012; 95% CI; 1.651–4.123) greater risk of developing OIs than those who do not live.

Those who have co-morbid chronic disease had 2.910 times (AOR = 2.910;95% CI; 1.761–3.450) greater risk of developing OIs than those who did not have it.

The Odds of OIs were 3.121 times (AOR = 3.121; 95% CI;1.532–6.309) greater for those who had poor ART adherence than those who had good adherence (Table 4).

Discussion

People living with HIV/AIDs in Mogadishu, Somalia, suffer from OIs, particularly those living with domestic animals, those with a chronic co-morbid disease, those who drink non-sterilized water, and those had poor ART adherence. Moreover, the most common OIs in this cohort was pulmonary TB. The magnitude of OIs in this study is higher than similar studies done in south Ethiopia[42], Addis Ababa Ethiopia[48], Nigeria[49], and Southern Ethiopia[50], while alternatively is lower than in Vietnam [51], Tigray region of Ethiopia[52], and northwest[40], and south Ethiopia[53] as well. This disparity may be due to different patient factors, geographical location, drug resistance, infection exposure, microbial agents, sociodemographic or economic variables, nutritional and immunity status, and sample size differences.

This study reported that those who had poor ART adherence had a three times greater risk of developing OIs than those who had good adherence. ART is a powerful instrument against OIs due to its action to reduce HIV mortality and morbidity mainly associated with OIs; without a patient's perfect adherence, it is hard to become effective. Poor ART adherence was described as taking less than 95% of prescribed medications[44]. It may be related to adverse outcomes, including treatment failure, viral mutation or non-suppression, drug resistance, HIV progress to the AIDs, and recurrent OIs since patients have limited second or third-line treatment options[54]. Developing effective programs that retain patients to ART is highly required in Sub-Saharan Africa, particularly in the study area. Similar studies were inline[55–57].

This study reported that the risk of OIs is two-time greater for those who drink non-sterilized water than for those who drink sterilized water. Poor hygiene or improper human or animal excretion distribution can lead to drinking water and food contamination, particularly in low-income settings like Somalia. The

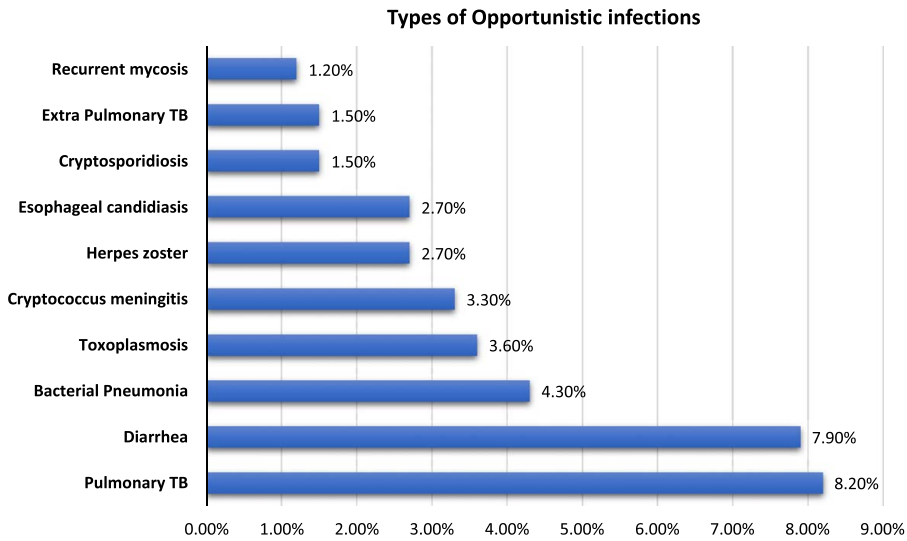

Figure 1. Most common types of opportunistic infections among PLWHI. PLWHI, people living with HIV; TB, tuberculosis.

Table 4

Factors association with the magnitude of OIs among HIV adult patients.

	Opportunistic infections				
Variables	**Yes (%)**	**No (%)**	**OR (95% CI)**	**AOR (95% CI)**	***P***
Age					
18–30	43 (33.9)	84 (66.1)	1	1	
30–45	62 (42.2)	85 (57.8)	0.702 (0.429–1.148)	0.547 (0.303–1.089)	0.057
> 45	17(30.9)	38 (69.1)	1.144 (0.580–2.258)	0.871 (0.401–1.892)	0.727
Having children					
Yes	102 (35.5)	185 (64.5)	1.649 (0.859–3.165)	1.832 (0.853–3.935)	0.120
No	20 (47.6)	22 (52.4)	1		
Accommodation status					
Rent	90 (35.2)	166 (64.8)	1440 (0.848–2.443)	0.946 (0.458–1.950)	0.879
Owner	32 (43.8)	41 (56.2)	1	1	
Residential area					
Rural	22 (61.1)	14 (38.9)	1	1	
Urban	100 (34.1)	193 (65.9)	3.033 (1.488–6.183)	2.311 (0.799–6.690)	0.122
Drinking water					
Sterilized	98 (39.7)	149 (60.3)	1	1	
Non-sterilized	24 (29.3)	58 (70.7)	1.589 (0.927–2.727)	2.395 (2.010–4.168)	0.034*
Living with a domestic animal					
No	50 (58.1)	36 (41.9)	1	1	
Yes	72 (29.6)	171 (70.4)	3.299 (1.982–5.489)	4.012 (1.651–4.123)	0.001*
Co-morbid disease					
No	66 (40.7)	96 (59.3)	1	1	
Yes	56 (33.5)	111 (66.5)	1.363 (0.870–2.135)	2.910 (1.761–3.450)	0.041*
HIV stage					
Stage I/II	82 (29.4)	197 (70.6)	1		
Stage III/IV	40 (80.0)	10 (20.0)	0.104 (0.050–0.218)	1.390 (0.629–2.687)	0.081
Regiment line					
First line	92 (32.1)	195 (67.9)	5.299 (2.595–10.820)	1.187 (0.323–4.367)	0.797
Second line	30 (71.4)	12 (28.6)	1	1	
ART adherence					
Poor	81 (31.6)	175 (68.4)	2.768 (1.626–4.713)	3.121 (1.532–6.309)	0.002*
Good	41 (56.2)	32 (43.8)	1	1	
HIV disclosure					
Disclosure	110 (35.9)	196 (64.1)	1	1	
Hide	12 (52.2)	11 (47.8)	1.944 (0.830–4.551)	0.924 (0.322–2.646)	0.882

AOR, adjusted odds ratio; ART, anti-retroviral therapy; OI, opportunistic infection; OR, odds ratio.
*Significant level at *P* value <0.05.

second most common OIs in this study is diarrhoea. The most common causes are enteric bacteria (*Shigella flexneri*, *Salmonella enteritidis*, *Campylobacter jejuni*) or intestinal parasites (helminths or protozoa) that can transmit through contaminated water and food. People living with HIV are more susceptible to OIs intestinal parasites and bacteria due to immunocompromise, and 80% of AIDs people die from OIs rather than HIV itself[58,59]. The rate of HIV/AIDs and enteric bacteria or intestinal parasites co-infection is remarkably high in sub-Saharan African countries poverty and malnutrition may exacerbate[56]. Waterborne pathogens are a significant risk of recurrent diarrhoea in people living with HIV resulting in reduced nutrition and treatment absorption, loss of nutrition and elements into diarrhoea, and high viral load with low CD4 counts, ultimately leading to poor quality of life and high mortality rate. Similar studies are in line[56,58].

Those who have Co-morbid chronic disease had two times greater risk of developing OIs than those who did not have it. Also, chronic diseases are multifactorial, but HIV chronic inflammation and its medications' side effects may interlink metabolic abnormalities such as dyslipidemia, diabetes mellitus (DM) with insulin resistance, and systematic inflammation. Some ART medications have direct effects, such as protease inheritors affecting lipid metabolism and nucleoside reverse transcriptase inheritors affecting mitochondrial function with subcutaneous fat loss and gaining central adiposity that may place HIV patients at additional risk of cardiovascular disease[60]. Moreover, pulmonary and extrapulmonary TB is the most common OIs in this study, and DM has multiple mechanisms to enhance TB susceptibility. It's hyperglycaemia and cellular insulinogenic had direct effects on macrophages and lymphocytes, reducing immunity's ability to fight TB. Furthermore, DM reduces chemotaxis and phagocytosis activities of monocytes, and antigen presentation leads to an immune reduction that may predispose to the risk of infections. HIV and DM co-morbidity may become a greater risk of developing numerous OIs because both have a similar combined effect on the immune system. HIV and chronic disease co-morbidity may affect the natural history of HIV infection with implications in diagnosis, susceptibility, and unusual clinical manifestation that may enhance HIV progress to AIDs. Previous studies support this[61–63].

Those who live with domestic animals have a four times greater risk of developing OIs than those who do not live. People living with HIV are more susceptible to direct, and indirect exposure to countless microbial organisms from zoonotic the most common include *Toxoplasma gondii*, *Mycobacterium bovis*, Cryptosporidium, Microsporidia, Salmonella, and several other enteric bacteria, viral and parasitic infections that cause most OIs including diarrhoea, TB, and others. In addition, animal bites or scratches may result in tissue damage with infection-induced and may also participate in disease transition. Living with domestic animals is an additional risk of infection exposure, particularly in a limited resource setting. Similar studies are line[64,65].

Conclusion

The magnitude of OIs among people living with HIV/AIDS in Mogadishu, Somalia, is high and having chronic co-morbid disease, drinking non-sterilized water, living with domestic animals, and poor ART adherence were factors associated with compared to counterparts. The most common OIs was pulmonary TB. Hence further generalized research targeting a high population with a long-term period is highly required to identify a cause-and-effect relationship. In addition, healthcare workers should emphasize OIs early diagnosis with effective timely treatments to reduce HIV progress to AIDs and improve quality of life.

Study limitations

Firstly, the cause-and-effect relationship between OIs and predictive variables cannot be estimated due to the nature of the cross-sectional study. The study was hospital-based by targeting HIV patients on ART so the finding may differ from the general population.

Ethical statements and consent to participate

This study was conducted following the rules and regulations of the World Medical Association's declaration of Helsinki. Ethical clearance was obtained from the study hospital review board. The hospital's ethical review board approved the process with approval number: IRB Ref no:-2022/03/BH0045. Eligible respondents directly explained the study objectives or through legal guardians for illiterate respondents without influence or coercion on their decision. Agreed participants gave written informed consent to sign or fingerprint for illiterate participants, and only agreed participants were included in the study. Moreover, all participants were informed that they had a full right to participate or discontinue the interview at any time, confidentiality was kept, questionnaires were anonymous, and data were only present as a general number without reflecting individual information.

Consent

Not applicable.

Source of funding

Not applicable.

Author contribution

All authors developed the study design, reviewed the literature, and data collection tools. O.A.A. collected data. A.K.M. had research ideas, analyzed data, write a report, drafted a manuscript, and formulate a timeframe. All authors read and approved the final manuscript.

Conflicts of interest disclosure

All authors declare that they don't have any conflicts of interest.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

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Data availability

All datasets generated and/or analyzed during the current study are included in this article

Provenance and peer review

Not commissioned, externally peer-reviewed.

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