Opportunistic Infections and Associated Factors among HIV Infected Patients on Anti-Retroviral Treatment at Bombo Hospital in Tanga Region, Tanzania

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Summary

BACKGROUND

A substantive number of People Living with HIV (PLHIV) develop Opportunistic Infections (OIs). The introduction of Anti-Retroviral Therapy (ART) in Tanzania led to a significant decline in opportunistic infections and a slower progression to AIDS, but OIs are still prevalent. This study was set to determine the magnitude of OIs and associated factors among HIV/AIDS patients on Anti-Retroviral Therapy (ART) attending care and treatment clinic at Bombo Regional Referral hospital, Tanga region.

MATERIALS AND METHODS

A cross-sectional descriptive study was conducted on HIV/AIDS patients on ART attending Bombo Hospital in Tanga from July to October 2019. A non-probability, consecutive sampling technique was employed to obtain study participants. Data were collected using available data obtained from the patients' files, hospital record books and interviews of study participants by using semi-structured questionnaires. Data were entered into the computer using Excel 2013, cleaned and analysed using Epi Info version 7.2.2.6. Any p-value of < 0.05, at a 95% confidence interval was regarded as statistically significant.

RESULTS

The study showed that out of the 360 participants, 126 cases (35.0%) of OIs were reported. Pulmonary Tuberculosis had the highest prevalence of 18.0% among PLHIV while other opportunistic Infections altogether contributed 17.0%. Late ART initiation (OR=10.9, 95% CI: 6.5 – 18.3, *p-value* <0.001), Poor drug adherence (OR=19, 95% CI: 9.0 – 39.7, *p-value* <0.001), female gender (69% vs. 31%), which was however, not statistically significant (*p-value* – 0.904), Informal and Primary School education (OR = 1.6, 95% CI: 1.1 – 1.6, *p-value* 0.04) being married (OR=2.1, 95% CI: 1.3 – 3.4, *p – value* 0.004) and widowed/widower (OR=7.7, 95% CI: 1.7 – 33.7, *p – value* 0.007) respectively were found to be associated with OIs to PLHIV.

CONCLUSION

The rate of OIs still high among PLHIV, Pulmonary Tuberculosis is the leading disease with 18.0% of all OIs symptomatic patients. Delay in ART initiation after positive test results, poor drug adherence and moderate malnutrition have been identified as major risk factors affecting 66.0%, 70.0%, 71%of PLWHA with OIs.

We recommend early initiation of ART, Education on ART adherence and refilling of large quantities of ARV drugs to individuals working far from their homes.

Keywords: *Opportunistic Infections, Early initiation of ART.*

[*Afr. J. Health Sci*. 2022 35(3): 252 - 262]

Introduction

Globally more than 70 million people have been infected with HIV and about 35 million people have died of HIV/AIDS. However, 36.9 million people were living with HIV at the end of 2017, where 69.7% of them in sub–Saharan Africa. The WHO African region remains most severely affected, with nearly 1 in every 25 adults (4.1%) living with HIV and accounting for nearly two-thirds of the people living with HIV worldwide, that is 69.7% (1)

According to UNAIDS, adult HIV prevalence in Tanzania is estimated at 4.7% in 2015, with HIV prevalence ranging from 0.2% (Kaskazini Unguja, Zanzibar) to 15.4% (Njombe). UNAIDS estimates indicate a total of 1.4 million Tanzanians living with HIV in 2015, out of a total population of 51,254,746. An estimated 54,000 new infections and 36,000 AIDS-related deaths occur in Tanzania annually (1). The latest estimates indicate that 1.7 million people acquired HIV in 2019, which is three times the 2020 target but being a 35% reduction of HIV infection since 2010. Moreover, 690,000 people lost their lives due to AIDS mainly due to opportunistic infections (2).

Opportunistic infections (OIs) which are associated with HIV remain the single main cause of ill-health and death in HIV/AIDS patients in resource-poor settings. Opportunistic infections lower the quality of life of HIV-infected persons, speed up the rate of progression to full-blown AIDS and reduce patients' response to antiretroviral treatment especially when HIV-positive patients are co-infected with tuberculosis (3).

Opportunistic infections (OIs) were the first clinical manifestations that alerted clinicians to the occurrence of acquired immunodeficiency syndrome (AIDS). Pneumocystis carinii pneumonia (PCP), toxoplasma encephalitis, cytomegalovirus (CMV) retinitis, cryptococcal meningitis, tuberculosis, disseminated Mycobacterium avium complex (MAC) disease, and pneumococcal respiratory disease, as well as certain cancers such as Kaposi sarcoma and central nervous system non-Hodgkin lymphoma, have been hallmarks of AIDS (4). These OIs and a few more, usually occurred, on average 7 to 10 years after infection with HIV. Until effective antiretroviral therapy (ART) was developed, patients generally survived only 1 to 2 years after the initial manifestation of AIDS (4). Regarding morbidity and mortality among PLHIV, it is estimated that 90% of HIV-related deaths are caused by opportunistic infections, compared to 7% due to cancers and 3% from other related causes (5)

Since the introduction of Anti-Retroviral Therapy (ART), a significant decline in opportunistic infections and a slow AIDS progression were observed. Also observed was a clear reduction of new HIV infections by 35%, plus a decline in AIDS-related mortality by 70%. However, the prevalence of opportunistic infections in HIV/AIDS patients is still 37.5% according to the Tanzania HIV impact survey of 2017.

Of note is that ART does not provide a cure for HIV, but drastically reduces immune depletion, which is responsible for the occurrence of Opportunistic infections (5). It is because of this fact that ART is not a cure, that there is still a palpable magnitude of opportunistic infections. The other reason is that viral suppression is not yet totally achieved. According to CDC, about 40% of Americans with HIV are not virally suppressed, and not all

infectious agents are diagnosed early, hence by the time they are diagnosed they are already immuno-suppressed, leading to the persistence of opportunistic infections (4,5).

The occurrence of opportunistic infection in all circumstances depends on exposure to infectious agents, and in those countries still having big magnitudes of bacterial and fungal infections the patterns differ from those places where infectious diseases are minimal (5).

Studies on the types and magnitude of opportunistic infections have been conducted in some East African countries, namely Ethiopia, Kenya and Uganda, and other countries like Nigeria and China. The prevalence of opportunistic infections in Ethiopia ranged from 18 to 60% and the latest recorded magnitude in October 2020 was 62% (9—12). The most recorded infections in Ethiopia were, in descending order: Oral Candidiasis, Tuberculosis, and Herpes Zoster; followed by chronic diarrhoea, and bacterial pneumonia. Cryptococcus meningitis and pneumocystis pneumonia were reported but did not feature prominently (9—12). The studies in Ethiopia (about nine) also looked at associated factors to opportunistic infections where old age, WHO disease stage and non-adherence to ART were leading determinants. The other East African states of Uganda and Kenya recorded very few studies.

In a study by Chepkondol and others in Kenya (2020), it was recorded that the main opportunistic infections were Pulmonary Tuberculosis (35%), Herpes Zoster (15.4%), and oral Candida (8%). The main deterging factors were long years of infection, low economic status, unskilled labour, low education level and low CD4+ count (14). One study in Uganda conducted on the frequency and Distribution of OIs indicated that late initiation of ART was associated with geohelminthic infections (32.4%) and infectious diarrhoea (25.6%). Other opportunistic infections noted were Oral candidiasis (34%) and Tuberculosis (17.7%) (15).

In Nigeria, a total of 354 patients, 109 (30.8%) males and 245 (69.2%) females participated in the study. Tuberculosis (TB) was the most common diagnosis on admission as well as the leading cause of death. The overall prevalence of opportunistic infections was 22.4%, and the types of infections were Candidiasis (8.6%) Tuberculosis (7.7%) and Dermatitis (5.6%). The independent risk factors in this study were identified as household income, advanced WHO stage at the time of initiation of ART, and low haemoglobin levels. Far from the African continent, similar studies were conducted like the one by Pang and co-authors in Sichuan, China. An investigation among 945 cases of PLHIV showed that the top five OIs were Bacterial pneumonia (25.8%), Candida infection (18.3%), Pneumocystis jiroveci pneumonia (11.9) Tuberculosis (11.4%) and Infectious diarrhoea (9.3%).

In Tanzania, the most recorded (routinely) OIs are Tuberculosis, Cryptosporidiosis, Cryptococcal meningitis, Toxoplasmodiasis, Pneumocystis jiroveci Pneumonia and Candidiasis (oral, pharyngeal, pulmonary). (6) Very few studies were directed at the magnitude of single disease units like tuberculosis and oral candidiasis (18).

However, precise data about the prevalence of opportunistic infections among HIV/AIDS patients in Tanzania is scarce and therefore the paucity hinders the effective measures to be taken in the diagnosis, management, and control measures of these infections. This study aimed to determine the prevalence of these opportunistic infections among patients on Anti-Retroviral Therapy (ART) and the association between ART initiation time and disease progression.

Materials and Methods

Study area

The study was conducted at Bombo Regional Referral hospital located in the Tanga region, Tanzania. Tanga Region is one of the 31 administrative regions of Tanzania. It is bordered by Kenya and Kilimanjaro Region to the north; Manyara Region to the west; and Morogoro and Coast regions to the south. Its eastern border is formed by the Indian Ocean. It has a population of about two million. Tanga city is the headquarters of the region, with a population of 273,332 in the 2012 census. Bombo is a town in Tanga city with the region font code of Africa/Middle East. It is located at an elevation of 544 meters above sea level. Its coordinates are $4^0$51'0" S and $38^0$40'60" E.

Bombo Regional Hospital is the referral regional hospital in Tanga, Tanzania. They have an average of 1500 outpatients per day and 100 to 200 inpatients per day; it has an average number of 412 beds.

The study site was conveniently chosen because the majority of HIV/AIDS patients who are diagnosed from dispensaries and health centres are referred to Bombo Regional Referral Hospital, specifically to Care and Treatment Clinic, (CTC) for ART initiation, refills and ward admissions.

Study design, population and sampling

A cross-sectional descriptive study was conducted among adult HIV/AIDS patients on Anti-Retroviral Therapy (ART) at Bombo Hospital in Tanga from July to October 2019. A non-probability, consecutive sampling technique was employed, in which all HIV/AIDS patients attending CTC at the hospital, who met the inclusion criteria were selected until the required sample was obtained. The required sample was obtained by using a single proportion formula for minimum sample size:

$n = Z^2 p(1-p)/ e^2$

Whereby

n = the required minimum sample size

e = margin of error (5%)

p = estimated proportion of 37.5%: Prevalence of OIs in PLWHA by UNAIDS, 2017(1)

Z = standard normal deviate corresponding to 95% confidence level=1.96

Therefore;

$n = (1.96)^2 \times (0.375) \times (1- 0.375) / (0.05)^2$

Hence, the minimum required sample size for the research study was 360 participants. A non-probability, consecutive sampling technique was employed to obtain study participants.

Pretest of data collection tools

During the Elective period for undergraduate medical students the data collection tools, particularly a checklist to gather available data and 25 questionnaires were tested at Mwananyamala hospital. The willingness of respondents to answer questions plus the availability of data were tested. The questionnaire was back-translated to English and the instrument was streamlined.

Data collection, management and analysis

The data were collected from the study participants, first by use of secondary data obtained from the patients' files and hospital record books. Information was obtained regarding dates for reporting to CTC, dates for initiation of ART and data on initial clinical examination. Primary data were obtained from interviews between the researchers and the participants as guided by semi-structured questionnaires. The questionnaire contained both open and closed-ended questions, which had hitherto been translated into the Swahili language. In this regard demographic and lifestyle data were collected and recorded. From

all patients, the study took the weight and height of each individual to calculate the body-mass index (BMI).

Data were entered into the computer using Excel 2013, cleaned and analysed using Epi Info version 7.2.2.6. Categorical variables were summarized as whole numbers and percentages. Descriptive statistics were used to analyse the general characteristics of the study population, namely demographics. The Chi-square test was used to determine the association between the outcome variable and predictor variables.

The predictors with a p-value of less than 0.05 were considered statistically significant and a 95% confidence interval was determined.

Ethical considerations

Permission to conduct the study was sought and received from the Institutional Research Ethics Committee of the University (IREC – HKMU) ethical clearance No. HKMU/IREC/27.10/123. Moreover, a letter requesting permission to conduct the study at Bombo Regional Referral hospital was written to the hospital authority before the research activity. All participants were elucidated on the aim of the study and verbal informed consent was obtained from each individual to voluntarily participate in the study. The respondents' names were not included on the questionnaires to ensure confidentiality and they were assured that the information collected was only to be used for purpose of the study.

Results

A total of 360 individuals were enrolled in the study, of these 250 (69.4%) were female while110 (30.6%) were male. The distribution of study participants shows further that the majority, 73.0% of these belonged to ages between 25 and 55 years. Almost half 156 (43.3%) of study participants had informal education. Moreover, almost 50% of 172 (47.9%) participants were single while only 23 (6.4%) were Widower/widowed, see table 1.

The study also found out that of the 360 people living with HIV/AIDS attending Bomb Hospital, 126 individuals had OIs which makes a prevalence of 35%. The individuals suffering from Pulmonary Tuberculosis were 65 with the highest prevalence of 18.0% followed by Herpes Zoster were 30 individuals which make up 8% of the study population. Other types of OIs were less than 5%. Significantly, the majority of the study population (65%) had no opportunistic infection, whatsoever.

However, the results show that individuals who had delayed for some time after positive test results had the highest frequency of OIs 83 (65.8%) while those who started taking medications immediately after positive test results had fewer cases of OIs were 43 (34.0%). Figure 1 below depicts the types of opportunistic infections, overall.

Table 2 below shows the factors associated with Opportunistic infections among PLWHA attending CTC at Bombo Referral Hospital. ART initiation time was significantly associated with opportunistic infections, Individuals with late ART initiation were almost 11 times high odds of having OIs (OR=10.9, 95% CI: 6.5 – 18.3*p – value* <0.001) than their counterparts (Individuals with immediate ART initiation).

The proportion of females with Opportunistic Infections after ART initiation was higher than males (69% vs. 31%) however it was not statistically significant (*p-value* – 0.904). Participants with Informal and Primary School education had almost twice the odds (OR = 1.6, 95% CI: 1.1 – 1.6, *p-value* 0.04) for having Opportunistic Infections after ART initiation than participants with Secondary and Tertiary education.

Compared to single or never-married women, married and widowed/widower were

almost two to eight times higher odds for Opportunistic Infections after ART initiation (OR=2.1, 95% CI: 1.3 – 3.4, *p-value* 0.004) and (OR=7.7, 95% CI: 1.7 – 33.7, *p-value* 0.007), respectfully.

Individuals with very poor drug adherence were at 19 times higher risk for Opportunistic Infections after ART initiation (OR=19, 95% CI: 9.0 – 39.7, *p-value* <0.001) than individuals with good drug adherence. All these associations were found to be statistically significant. However, no association was noted between opportunistic infection and age, occupation, socioeconomic and nutritional status of participants.

Table 1:
Socio-Demographic Characteristics of PLWHA CTC attending Bombo Referral Hospital (N=360)

Variables	Frequency	Per cent (%)
Level of education:		
Informal	156	43.3
Primary education	84	23.3
Secondary education	81	22.5
College/University	39	10.8
Age:		
15-25	29	8.1
26-35	74	20.6
36-45	75	20.8
46-55	116	32.2
56+	66	18.3
Marital Status:		
Single	172	47.9
Married	56	15.6
Cohabiting	67	18.7
Divorced/separated	41	11.4
Widower/widowed	23	6.4
Nutritional Status:		
Severe malnutrition	10	2.8
Moderate malnutrition	90	25.0
Normal weight for height	260	72.2
Occupation:		
Peasant/farmer	160	44.4
Employed	58	16.1
Self-employed	84	23.3
Unemployed	58	16.1
Sex:		
Male	110	30.6
Female	250	69.4
OIs After ART initiation:		
Yes	126	35.0
No	234	65.0
ART initiation time:		
Later after diagnosis	118	32.8
Immediate after diagnosis	242	67.2

Nutritional status

The overall prevalence of malnutrition in this study was 100 (27.8%) while severe malnutrition, BMI <16 was 10 (2.8%). Participants with moderate malnutrition (BMI=16—18.5) were 90 (25%) while the majority, 260(72.2%) had normal nutrition. A significant number of respondents 160 (44.4%) were peasants/farmers.

Discussion

The distribution of the study population by age shows that the majority (73.0%) were between ages 25 and 55 years, the sexually active group in the population. Regarding gender, the participants were divided into 30.6% (110/360) male and 69.4% (250/360) female.

This disparity can be attributed to the fact that while the prevalence of HIV infection was recorded as 5.0% in Tanzania (6), the rate of infection was 6.5% in females and 3.5% in males. The study found that out of the 360 people living with HIV/AIDS attending a clinic at Bombo Hospital, 126 individuals had OIs which makes a prevalence of 35.0%. Study participants aged 46-55 years had the highest frequency of opportunistic infections making a total of 116 (44.6%).

Pulmonary Tuberculosis had the highest prevalence of 18.0% among PLHIV. Other opportunistic Infections, namely Herpes Zoster, Oral and Oesophageal Candidiasis, Cryptosporidiosis, Cryptococcal Meningitis, Pneumocystis jiroveci Pneumonia and Kaposi Sarcoma had a prevalence of 8.0%, 1.0%, 2.0%, 1.0%, 4.0%, and 1.0% respectively.

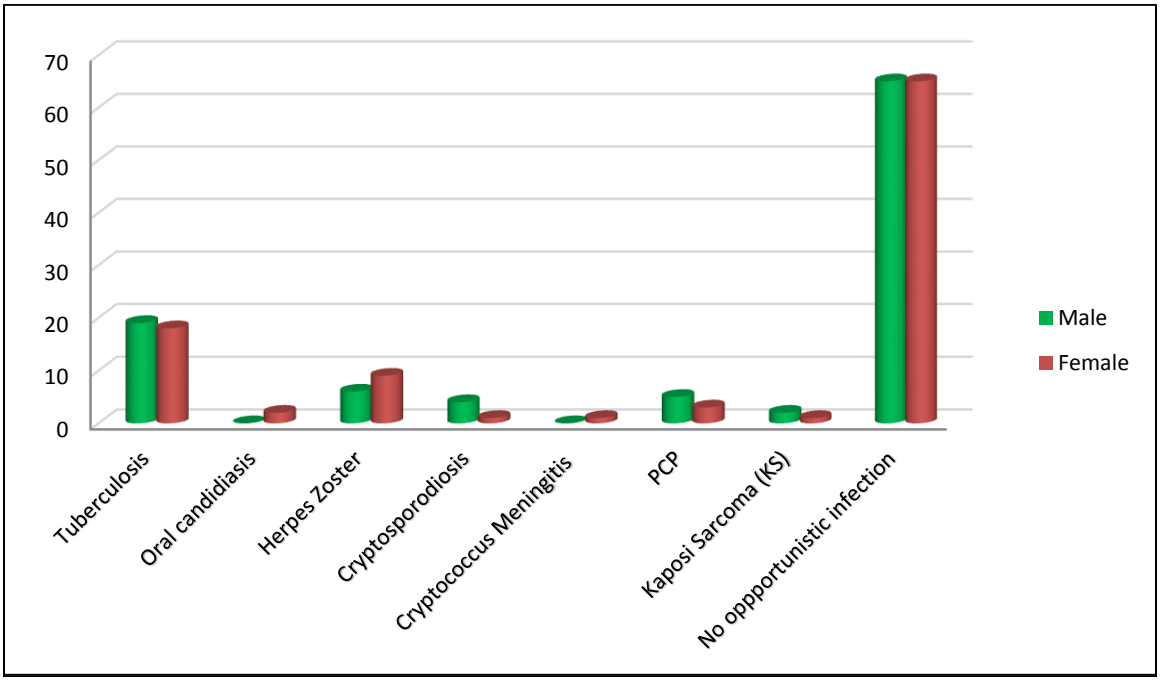

Figure 1:
Types of Opportunistic Infections among PLHIV attending CTC at Bombo hospital (n=360)

This rate of opportunistic infections (35.0%) in Tanzania compares well with most of those reported from other East African countries, between 2016 and 2018 which ranged from 24.5 to 42.8% (8,11,14), but it was higher than the ones recorded in China,25.0% (21) and Nigeria,22.4% (16)

However, the prevalence of Opportunistic Infections in Tanzania seems to be much lower compared with recordings in 2018-2020 by Waldereagawi 55.3% (9), Urgessa F., 52.4% (12), Chepkondol G. 78.8% (13) Fite B,62.0% (20). These results differ very much from the findings of this study, which may be because the present study used a small sample of 360 persons only.

Table 2:
Factors Associated with Opportunistic Infections among PLWHA attending CTC at Bombo Referral Hospital (N=360)

		Opportunistic Infections						
	Variables	**Yes**		**No**		**Crude OR**		
		Freq	**(%)**	**Freq**	**(%)**	**OR (95% CI)**		***P-Value***
ART initiation time:	**Later after diagnosis**	86	70.4	35	29.6	10.96.5 – 18.3		**<0.001**
	Immediate after diagnosis	43	17.8	199	82.2	1.0		
Gender:	**Female**	87	34.8	163	65.2	0.9	0.6 – 1.6	0.904
	Male	39	35.5	71	64.5	1.0		
Mother's Education level:	**Informal & Primary Sch**	64	41.0	92	59.0	1.6	1.1 – 2.5	**0.04**
	Secondary& Tertiary	82	78.9	22	21.1	1.0		
Marital Status:	**Single**	73	42.2	100	57.0	1.0		
	Married	32	26.0	91	74.0	2.1	1.3 – 3.4	**0.004**
	Divorced	19	46.3	22	53.7	0.0	0.4 – 1.7	0.63
	Widowed	2	8.7	21	91.3	7.7	1.7 – 33.7	**0.007**
Age:	**15-25**	10	34.5	19	65.5	1.0		
	26-35	27	36.5	47	63.5	0.9	0.3 – 2.3	0.84
	36-45	29	38.7	46	61.3	0.8	0.3 – 2.0	0.69
	46-55	40	34.5	76	65.5	1.0	0.4 -2.3	1.00
	56+	20	30.3	46	69.7	1.2	0.4 – 3.0	0.68
Occupation:	**Peasant/farmer**	66	41.3	94	58.7	1.0		
	Employed	17	29.3	41	70.7	1.6	0.9 – 3.2	0.11
	Self-employed	27	32.1	57	67.9	1.5	0.8 – 2.6	0.16
	Unemployed	16	27.6	42	72.4	1.8	0.9 – 3.5	0.06
Socioeconomic Status:	**Low class**	10	33.3	20	66.7			
	Middle class	96	35.6	174	64.4	0.9	0.4 – 2.0	0.81
	Upper class	20	33.3	40	66.7	1.0	0.4 – 2.5	1.00
Drug Adherence:	**Very Poor**	89	53.9	76	46.1			
	Poor	28	70.0	12	30.0	0.5	0.2 – 1.0	0.07
	Good	9	5.8	146	94.2	19	9.0 – 39.7	**<0.001**
Nutritional Status:	**Severe Malnutrition**	10	100.0	0	0.0			
	Moderate Malnutrition	90	100.0	0	0.0			
	Normal Weight	26	10.0	234	90.0			

Significantly, the majority of the study population (65%) had no opportunistic infection, whatsoever. This finding might justify the difference between the present study results and those described above. Another difference is that oral candidiasis, bacterial pneumonia and helminthic infections which are featured in other studies were not prominent in this study.

One of the most prominent findings of this study is that ART initiation time was significantly associated with opportunistic infections. Individuals with late ART initiation were almost 11 times high odds (OR=10.9, 95% CI: 6.5 – 18.3*p – value* <0.001) than their counterparts (Individuals with immediate ART initiation).

The finding on ART initiation period since diagnosis, as a risk factor is being reported here for the first time compared to many other previous studies. Other factors of significant association in this study were drug adherence and education level which were reported in similar studies.

Limitations of the Study

The first limitation was time resources, which forced us to conduct an observational study in one tertiary health facility which had one care and treatment centre (CTC). We could do better with a follow-up study or retrospective cohort study in all health facilities with CTCs, in the Tanga region to establish the association between OIs and ART initiation time (early/late).

The other is that the sample size was limited to 360 participants only, also emanating from the first limitation above.

Conclusion

Despite the introduction of ART to people living with HIV/AIDS, opportunistic infections still contribute to morbidity and mortality of PLWHA on ART with a prevalence of 35% whereby Pulmonary Tuberculosis is the leading opportunistic infection with a prevalence of 18.0%. Moreover, the delay in ART Initiation after positive test results, poor nutritional status and poor drug adherence have been identified as major risk factors affecting the target population.

Recommendations

The study has shown that delay in ART initiation after positive test results, poor drug adherence and moderate malnutrition were the major risk factors of OIs among PLWHA. We recommend early initiation of ART to PLHIV by physicians after positive test results since it confers a survival benefit to PLHIV and reduces the risk for OIs. We also recommend education by health workers on adherence to ART including refilling large quantities of ARV drugs to individuals working far from their homes.

Authors' contributions

All authors contributed equally to proposal writing, data collection, data analysis and writing of the manuscript.

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Sources of Funding - None

Conflict of interests

The authors declare that they have no competing interests.

Acknowledgements

The authors are grateful to all who participated in the preparation of this manuscript. The authors acknowledge all participants who participated in this study and all individuals who delivered and collected questionnaires.

References

1. **UNAIDS** Global AIDS Report.2018
2. **Ministry of Health**, Community Development, Gender, Elderly and Children. National AIDS Control Programme.

National Guidelines for the Management of HIV and AIDS. April 2019.

3. **WHO** case definitions of HIV for Surveillance and revised clinical staging and immunological classification of HIV related disease in adults. Geneva. World Health Organisation, 2007 (www.who.int//hiv/pub/guidelins/hivstaging 150307.pdf).
4. **Panel on Opportunistic infections in Adults and Adolescents with HIV**. Guidelines for prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV: recommendations from Centres for Disease Control, National Institute of Health, and the HIV Medicine Association of the Infectious Diseases of America.*AIDSinfo2019; 1-5.Available at http://aidsinfo.nih.gov/lvguidelines/adult_oi. pdf. Accessed 22April, 2021*.
5. **Centers for Disease Control and Prevention**, 2014. HIV/AIDS basic statistics. *Online at http://www. CDC. gov/HIV/basics/statistics. html. Accessed July, 2018.*
6. **Tanzania Commission for AIDS** (TACAIDS), Zanzibar AIDS Commission (ZAC), Tanzania HIV impact Survey (THIS)- REPORTS 2016-2017
7. **Ministry of Health Community Development Gender, Elderly and Children. National AIDS Control Programme.** National Guidelines for the Management of HIV and AIDS in Tanzania 7th Edition. April, 2019
8. **Solomon B., *et al.*** Spectrum of opportunistic infections and associated factors among PLHIV in the era of HAART in Dawro Zone Hospital, Ethiopia: a retrospective study. *BMC research notes.2018; 11(1): 604*
9. **Wardearegawi T, GerenseaH, Berth H *et al***. The Magnitude of opportunistic infections and Associated Factors in HIV-infected Adults on Anti-retroviral Therapy in Southern Zone Tigray, Ethiopia: a cross sectional study. *Pan Afr Med J.2020; 35:126*
10. **Arefaine G, Abebe S, Bekele E *et al.*** Incidence and predictors of HIV related of HIV Opportunistic Infections after Initiation of HAART at Hyder Hospital, Mekele, Ethiopia: a retrospective single centred study. *Plos one, 2020; 15(4): e0229757*
11. **Masur, H., Brooks, J.T., Benson, C.A., Holmes, K.K., Pau, A.K. and Kaplan, J.E., 2014**. Prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: Updated Guidelines from the Centers for Disease Control and Prevention, National Institutes of Health, and HIV Medicine Association of the Infectious Diseases Society of America. *Clinical Infectious Diseases*, *58*(9), pp.1308-1311.
12. **Urgessa, F., Ararsa, A. and Ataro, Z**., 2018. Prevalence and Associated Risk Factors of Opportunistic Infections among Anti-Retro Viral Treatment Naïve HIV/AIDS Infected Patients. *J AIDS Clin Res*, *9*(763), p.2.
13. **Chepkondol G, Jolly P, Yatich N, Mbowe O, and Jaoko W.** Types and Prevalence of Opportunistic infections/conditions Among HIV-positive patients attending Kenyatta Hospital in Nairobi, Kenya. *Afri Heath Sci. 2020; 20(20):615-624 https://doi./org/10.4314/abs v 20i*
14. **Rubaihayo J, Tumwesige N, Konde-LuluJ *et al***. Frequency and Distribution patterns of Opportunistic Infections Associated with HIV/AIDS in Uganda. *BMC Res Notes,2016; 9:501*
15. **Weissberg D, Mubiru F, Kambugu A, Fehr J, Kirraga A, von Braun A *et al.*** Incidence Patterns and Risk Factors of Opportunistic Infections
16. **Iroezindu, M.O., Ofondu, E.O., Hausler, H. and Van Wyk, B.,** 2013. Prevalence and risk factors for opportunistic infections in HIV patients receiving antiretroviral therapy

in a resource-limited setting in Nigeria. *J AIDS Clin Res*. 2013: *3*, p.002.

17. **Ngasala G, Mgabo M, Mrema J, *et al***. Oral candida infection Among HIV patients Kilimanjaro Christian Medical Centre in Northern Tanzania. *Tanzania Journal of Health Research*. Vol 18 number1, January 2016
18. **World Health Organization**, 2018. World health statistics 2018: monitoring health for the SDGs, sustainable development goals.
19. **Moges N. and Kassa G.** Prevalence of Opportunistic Infections and Associated Factors Among Patients Taking Anti-retroviral therapy (ART) in debre Marcos Referral hospital, Northern Ethiopia. *J AIDS Clin Res 2014; 5:5. DOI:10.4172/2155s-6113*
20. **Fite B. Aga DJ.** Spectrum of Opportunistic Infections and Associated Factors among Patients Attending Antiretroviral Therapy clinic at Nekemte Specialised Hospital, Western Ethiopia. *Available on internet: DOI: https://doi.0rg/10.21203/rs.3.rs-8323239. Accessed 20 April, 2021*.
21. **Pang W, Shang P, Li Q, CSU J, *et al.*** Prevalence of Opportunistic Infections and Causes of Death among Hospitalized HIV-infected Patients in Sichuan, China. *Tohoku J Exp Med.,2018; 244:231-242*