



The Open Public Health Journal

Content list available at: www.benthamopen.com/TOPHJ/

DOI: 10.2174/1874944501710010208



RESEARCH ARTICLE

Nutritional Status of HIV Clients Receiving HAART: Its Implication on Occurrence of Opportunistic Infection

Sadikalmahdi Hussien^{1,*}, Tefera Belachew² and Nezif Hussein³

¹Department of Pharmacology and Clinical Pharmacy, School of Pharmacy, Addis Ababa University, Addis Ababa, Ethiopia

²Human Nutrition Department, Jimma University, Jimma, Ethiopia

³Clinical Pharmacy Department, School of Pharmacy, Jimma University, Jimma, Ethiopia

Received: July 28, 2017

Revised: August 01, 2017

Accepted: September 29, 2017

Abstract:

Purposes:

We aimed to assess the effects of nutritional status on occurrences of opportunistic infection in HIV/AIDS patients using antiretroviral therapy at Jimma University Specialized Hospital.

Methods:

We conducted a retrospective study on 340 adults who were taking antiretroviral therapy and the patients were followed for 2 years after they commence treatment. Medical Chart review was done from January 30 to February 28, 2014. SPSS for windows version 21 was used to analyze the data. The data was analyzed by SPSS for windows version 21. Time to occurrence of opportunistic infection was estimated by Kaplan-Meier analysis and Cox-proportional Hazard model was used to identify predictors of opportunistic infections.

Results:

Eighty three [24.4%] patients developed opportunistic infection after initiation of highly active anti-retroviral therapy. Fifty five [66.3%] patients were from malnourished group. Malnutrition, Stavudine based regimen, Zidovudine based regimen and taking isoniazid prophylaxis were associated with greater hazard of developing opportunistic infections.

Conclusions:

Malnutrition was significant predictor of opportunistic infections. Malnourished patients were associated with high risk and early development of opportunistic infections.

Keywords: Malnutrition, Opportunistic infections, Survival, Ethiopia.

1. INTRODUCTION

The impact of HIV infection on nutritional status of patients was identified during the early times of HIV epidemic [1]. Wasting is the commonest sign of malnutrition in patients with HIV/AIDS especially as patients progress to severe disease states [1]. Increasing energy requirements, reducing food intake, and adversely affecting nutrient absorption and metabolism is the mechanism by which HIV affects nutritional status [2]. If nutritional needs of the patient are not met, the patient may have decreased immunity and increased opportunistic infections (OIs), which may further lead to malnutrition.

* Address correspondence to this author at the Department of Pharmacology and Clinical Pharmacy, School of Pharmacy, Addis Ababa University, Addis Ababa, Ethiopia; Tel: 0911545735; E-mail: sadhussen@yahoo.com

Disease progression, increases morbidity, and reduces survival time are the outcome of poor nutritional status in PLHWA [3].

Highly active antiretroviral therapy (ART) decreases death, increases CD4 lymphocyte counts and decreases occurrences of opportunistic infections [4, 5]. Immunologic recovery differs from person to persons. It is slow in some patients, leading to incomplete recovery of immune function which in turn leads to greater risk of developing opportunistic infections and death compared to those who have fast immune recovery [6]. Some patients may die even with sufficient CD4 count and low viral load [5]. Therefore, adjunctive treatments might be important in promoting CD4 recovery and promoting survival in patients taking HAART.

Studies confirmed malnutrition was major determinant of death and poor immunologic recovery in patients taking HAART [7 - 11]. However, only few studies examined the effect of malnutrition on occurrence of opportunistic infections globally. Studies are lacking in developing countries including Ethiopia.

Malnutrition may negatively affect immunologic recovery to HAART, increase risk of opportunistic infections and shortens survival. Therefore, Malnutrition might be potential risk factor for increased mortality in patients initiating ART.

2. METHODS

2.1. Study Design and Participants

Retrospective cohort was done at Jimma University Hospital ART Clinic. The Hospital has a bed capacity of 450 and is the only referral and teaching hospital in western part of Ethiopia. The Hospital serves around 80,000 outpatients and 9000 inpatients each fiscal year. The Hospital ART clinic started service in 2002. The Clinic is serving 3700 patients [11]. The primary data was filled by assigned health professionals between September 11, 2006 and September 10, 2011. We extracted the data from the medical charts of the patients from January 30 to February 28, 2014. Single proportion formula was used to calculate the sample size, which assumes proportion of mortality [common measure of treatment outcome] in malnourished group to be 61.8% and proportion of mortality in well-nourished group to be 46.8. The final calculated sample size was 340 patients; one hundred seventy (170) patients in both groups. We isolated medical charts of all adult patients who started ART between September 2006 and September 2011 was isolated. We categorized the charts into malnourished and well-nourished groups based on their BMI at the beginning of HAART. Malnutrition was defined as a BMI <18.5, while BMI \geq 18.5 was defined as a well-nourished. Patients with incomplete data on weight, height and outcome variables, transferred-out during follow-up, pregnant women's (BMI and nutrient metabolism vary during pregnancy), were excluded from the study. Clinically trained health professionals were used for collecting the data. The endpoint of this study was occurrence of opportunistic infections.

We followed the patients till occurrence of event (opportunistic infection/s) or 2 years (end of study). We excluded those who did not develop opportunistic infections at the end of the 2nd years. Patients who did not develop opportunistic infection/s at the end of study were also excluded. The survival time was calculated in days using date of starting treatment and date of an event or date excluded.

2.2. Statistical Methods

Epi data version 3.1 was used to edit, clean and complete the data. The data was then exported to SPSS for windows version 21 for statistical analysis. We did survival analysis. Variables with p value of <0.25 in bivariate analysis and BMI were selected and exported to multivariable cox-proportional analysis model to identify predictors of opportunistic infection/s. Survival time was estimated by Kaplan–Meier survival analysis. Cox proportional hazard model was used to identify predictors of opportunistic infection/s over a period of time t. The level of significance was set at p value less than 0.05 and 95% confidence intervals (CI) were used throughout. We checked multi-collinearity.

3. RESULTS

3.1. Baseline Characteristics

All patients were followed for 2 years. Eighty three patients developed opportunistic infections. Fifty five (66.26%) patients were from malnourished group. The median baseline CD4 count was 144.5 [IQR 89–209] cells/mm³. The mean age of the participants and the median age were 34 [IQR 26–38] years and 30 years respectively. Two hundred (58.8%) patients were females. Mean baseline BMI was 1.50 [IQR 1.0–2.00] kg/m² (Tables 1, 2).

Table 1. Baseline demographic characteristics and associated mortality and opportunistic infections of 340 HIV-infected patients in Jimma University specialized hospital, from January 2006 to December 2011.

Characteristics	Number of patients [%]	Number of deaths[%]	Number of OI [%]
Sex			
Male	140[41.2]	19[45.2]	38[45.8]
Female	200[58.8]	23[54.8]	45[54.2]
BMI			
<18.5	170[50]	25[59.5]	55[66.3]
≥18.5	170[50]	17[40.5]	28[33.7]
Religion			
Orthodox	203[59.7]	29[69]	44[53]
Muslim	100[29.4]	13[31]	26[31.3]
Protestant	31[9.1]	0	11[13.3]
Catholic	2[0.6]	0	1[1.2]
Others	2[0.6]	0	0
Age(years)			
<30	174[51.2]	21[50.0]	46[55.4]
30-39	94[27.6]	11[26.2]	21[25.3]
40-49	57[16.8]	6[14.3]	12[14.5]
>50	15[4.4]	4[9.5]	4[4.8]
Marital status			
Single	43[12.6]	7[16.7]	10[12.0]
Married	116[34.1]	16[38.1]	36[43.4]
Widowed	22[6.5]	1[2.4]	5[6.0]
Divorced	44[12.9]	8[19.0]	9[10.8]
Occupation			
Gov't employee	98[28.8]	14[33.3]	19[22.9]
Merchant	5[1.5]	0[0]	2[2.4]
Unemployed	189[55.6]	25[59.5]	51[61.4]
Private org	37[10.9]	2[4.8]	10[12.0]
NGO's	5[1.5]	1[2.4]	0[0]
Educational status			
Not educated	69[20.3]	4[9.5]	24[28.9]
Primary	122[35.9]	17[40.5]	25[30.1]
Secondary	106[31.2]	14[33.3]	21[25.3]
Tertiary	42[12.4]	7[1.7]	12[14.4]

Table 2. Baseline clinical characteristics and associated mortality and opportunistic infections of HIV-infected patients in Jimma University specialized Hospital, between January 2006 to December 2011.

Characteristics	Number of patients[%]	Number of deaths[%]	Number of OI[%]
WHO clinical stage			
Stage I	65[19.1]	6[14.3]	15[18.1]
Stage II	95[27.9]	9[21.4]	15[18.1]
Stage III	144[42.4]	17[40.5]	44[53.0]
Stage IV	36[10.6]	10[23.8]	9[10.8]
HAART regimen			
Stavudine based	219[64.4]	19[45.2]	60[72.3]
Zidovudine based	72[21.2]	12[28.6]	18[21.7]
Tenofovir based	49[14.4]	11[26.2]	5[6.0]
Base line CD4			
>350	5[1.5]	0[0.0]	2[2.4]
200-350	94[27.6]	7[16.7]	19[22.9]
100-199	139[40.9]	15[35.7]	37[44.6]

(Table 2) contd.....

Characteristics	Number of patients[%]	Number of deaths[%]	Number of OI[%]
<100	102[30.0]	20[47.6]	25[30.1]
Risky behaviour			
Yes	120[35.3]	14[33.3]	58[69.9]
No	220[64.7]	28[67.7]	25[30.1]
Cotrimoxazole Prophylaxis			
Yes	330[97.1]	42[100.0]	81[97.6]
No	10[2.9]	0[0.0]	2[2.4]
Fluconazole Prophylaxis			
Yes	20[5.9]	8[19.1]	5[6.0]
No	320[94.1]	34[80.9]	78[94.0]
INH prophylaxis			
Yes	62[18.2]	7[16.7]	20[24.1]
No	278[81.8]	35[83.3]	63[75.9]

3.2. Occurrence of Opportunistic Infections

In Kaplan-Meier bivariate cox-proportional analysis, there was statistically significant difference in time of opportunistic infection/s occurrence between malnourished and well-nourished group [p=0.001]. Malnourished patients at the start of HAART develop opportunistic infections early in the course of treatment compared to well-nourished group (Fig. 1). In bivariate cox-proportional hazard model baseline nutritional status and HAART regimen were significantly associated with time of opportunistic infection/s occurrence (Table 3).

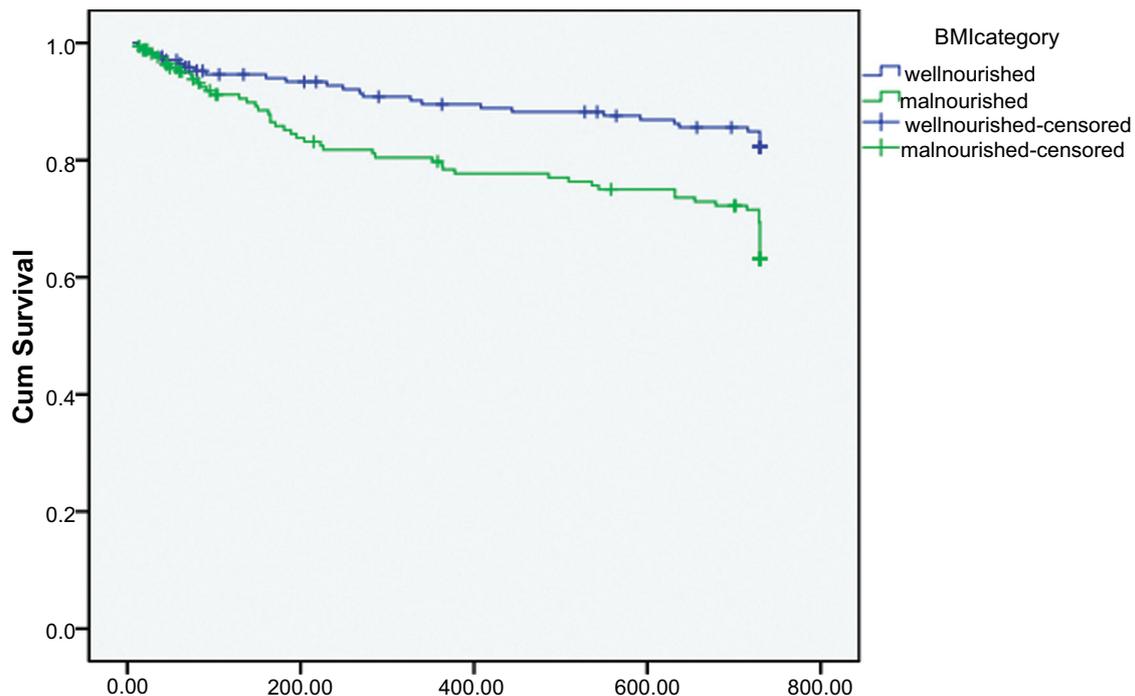


Fig. (1). Survival functions stratified according to nutritional status in HIV infected individuals in cohort of patients at Jimma university specialized hospital, January 2006 to December 2011.

Table 3. Kaplan-Meier analysis of factors associated with opportunistic infections in HIV-infected individuals at Jimma University Specialized Hospital, January 2006 to December 2011.

Variables	Number of OI	Mean survival time in days [95 %CI]	P	
Age group (yrs)	< 30	46	620.93[585.173,656.685]	0.757
	30-39	21	632.70[587.857,677.550]	
	40-49	12	652.22[599.260,705.175]	
	≥50	4	601.58[491.012,712.155]	

(Table 5) contd.....

Variables		Number of OI	Mean survival time in days [95 %CI]	P
Sex	Female	45	634.09[603.441,664.735]	0.329
	Male	38	621.39[582.296,660.479]	
BMI	< 18.5	55	594.27[555.615,632.922]	0.001
	≥ 18.5	28	661.52[632.772,690.278]	
Marital status	Single	10	631.97[562.164,701.775]	0.615
	Married	36	592.67[546.266,639.070]	
	Widowed	5	643.37[574.149,712.584]	
	Separated	9	612.30[580.625,643.97]	
Educational level	Not Educated	24	566.89[503.064,630.719]	0.089
	Primary	25	651.11[614.903,687.324]	
	Secondary	21	655.27[615.672,694.875]	
	Tertiary	12	610.26[535.895,684.626]	
CD4 count	< 100	25	629.11[583.779,674.431]	0.521
	100-199	37	617.88[578.817,656.949]	
	200-350	19	651.09[609.222,692.964]	
	> 350	2	511.40[263.608,759.192]	
Risky behaviors	Yes	25	647.35[608.379,686.314]	0.241
	No	58	618.54[587.838,649.236]	
Baseline comorbidity	Yes	3	675.28[587.677,762.878]	0.313
	No	80	626.02[600.930,651.113]	
Baseline OI	Yes	62	624.29[595.897,652.684]	0.818
	No	21	642.80[597.438,688.167]	
Cotrimoxazole prophylaxis	Yes	81	629.56[605.258,653.856]	0.676
	No	2	609.00[458.693,759.307]	
Fluconazole Prophylaxis	Yes	5	544.00[410.554,677.446]	0.389
	No	78	632.73[608.431,657.035]	
INH prophylaxis	Yes	42	577.50[512.176,642.833]	0.083
	No	41	640.46[615.170,665.833]	
Baseline HAART	D4T based	60	614.44[583.314,645.574]	0.051
	AZT based	18	617.08[558.409,675.759]	
	TDF based	5	628.86[604.828,652.887]	
Baseline WHO	Stage I	15	649.68[598.913,700.445]	0.066
	Stage II	15	666.86[628.711,705.013]	
	Stage III	44	598.24[556.866,639.611]	
	Stage IV	9	609.18[530.651,687.706]	

Variables with Hazard ratio less than 0.25 in bivariate cox-proportional hazard model were fitted to multivariable cox-proportional hazard model. BMI [HR=2.27, 95% CI: 1.416, 3.625, p=0.001], Stavudine based regimen [HR=2.93, 95% CI: 1.178, 7.309, p=0.021], Zidovudine based regimen [HR=3.15, 95% CI: 1.155, 8.583, p=0.025] were found to be predictors of OI in multivariable cox-proportional hazard model. Patients who took isoniazid prophylaxis were 1.69 times at hazard of developing OI [HR=1.69, 95% CI: 1.016, 2.830, p=0.043] (Table 4).

Table 4. Multivariable Cox-proportional model to isolate predictors of opportunistic in HIV-infected individuals at Jimma University specialized hospital, January 2006 to December 2011.

Variable		Number of OI	HR [95% CI]	P
BMI	< 18.5	55	2.27[1.416,3.625]	0.001
	≥ 18.5	18	1	
Educational level	Not educated	24	1	0.114
	Elementary	25	0.635[0.361,1.115]	0.086
	Secondary	21	0.596[0.330,1.076]	0.786
	Tertiary	12	1.103[0.542,2.247]	
Baseline HAART	D4T based	68	2.93[1.178,7.309]	0.021
	AZT based	18	3.15[1.155,8.583]	0.025
	TDF based	5	1	
INH Prophylaxis	No	41	1	0.043
	Yes	42	1.695[1.016,2.830]	

4. DISCUSSION

Malnutrition at the start of HAART was predictor of opportunistic infections [HR=2.93, 95% CI, 0.416, 3.625, p=0.001]. This finding is in line with reports by Simone and his colleague which shows BMI of less than 18.5 kg/m² was

strongly associated with increased risk of disease progression [12]. Moreover, the study was comparable with findings reported by Zhou and his colleague which showed that lower BMI was associated with developing new AIDS defining illness [13]. Furthermore, it is consistent with finding from study conducted at South Africa where patients with low BMI, irrespective of OC, at ART initiation showed a decrease in hemoglobin, increase in AST and increase in TB at ART initiation compared to those with normal BMI (≥ 18.5 kg/m²) [14]. Likewise, this finding is comparable with findings from Nigeria which showed that low BMI was determinant of opportunistic infections [15]. Another study done by Yoann and his colleague confirmed that Patients with baseline BMI less than 18.5 were two times at higher risk of having opportunistic infections ($p=0.016$.) [16].

We identified that patients who were on Zidovudine based regimen had high risk of developing opportunistic infections compared to those patients who started their treatment by Tenofovir based regimen. This finding was in line with the study conducted in India which shows higher OI was seen in patients receiving AZT based regimen (46% vs. 31%, $p=0.22$) [17]. A study by Samuel and his colleagues [18] in Kenya showed that patients started on TDF based regimen had better survival than AZT based regimen (61 vs. 56.5 months) respectively. In addition, one extra opportunistic infection was prevented every 14 patients treated using this TDF/3TC/EFV regimen ($p=0.026$). On the contrary, AZT/3TC/EFV was the least protective regimen used in this set-up, where one patient will experience 9 episodes extra of opportunistic infections with similar course of treatment ($p=0.049$) [17].

In our study, patients who took prophylaxis for opportunistic infections were at high risk of developing opportunistic infections. This finding is in contrast to the study from Addis Ababa, Ethiopia which shows that Isoniazid has protective effect against development of Opportunistic infections. The difference could be due to small sample size and we looked at the development of all opportunistic infection. However, study done in Addis Ababa focused on the development of Tuberculosis alone.

CONCLUSION

Nutritional status at the commencement of HAART significantly predicts development of opportunistic infections in HIV patients receiving HAART.

Patients who started on Zidovudine based regimen, Stavudine based regimen were at high risk of developing opportunistic infection compared to patients who started on Tenofovir based regimen.

Isoniazid Prophylaxis contributes in the development of opportunistic infections.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by Institutional Review Board (IRB) of Jimma University.

HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the *Helsinki Declaration* of 1975, as revised in 2008 (<http://www.wma.net/en/20activities/10ethics/10helsinki/>).

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

- [1] Trujillo EB, Borlase BC, Bell SJ, *et al.* Assessment of nutritional status, nutrient intake, and nutrition support in AIDS patients. *J Am Diet Assoc* 1992; 92(4): 477-8. [PMID: 1556349]
- [2] World Health Organization. Nutrient requirements for people living with HIV/AIDS: Report of a technical consultation Geneva, Switzerland .

- 2003.
- [3] Hsu JW, Pencharz PB, Macallan D, Tomkins A. *Macronutrients and HIV/AIDS: A Review of Current Evidence in Consultation on Nutrition and HIV/AIDS in Africa: Evidence, Lessons and Recommendations for Action*. Durban, South Africa: WHO, Department of Nutrition for Health and Development 2005.
- [4] Palella FJ Jr, Delaney KM, Moorman AC, *et al.* HIV Outpatient Study Investigators. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. *N Engl J Med* 1998; 338(13): 853-60. [<http://dx.doi.org/10.1056/NEJM199803263381301>] [PMID: 9516219]
- [5] Valdez H, Chowdhry TK, Asaad R, *et al.* Changing spectrum of mortality due to human immunodeficiency virus: Analysis of 260 deaths during 1995–1999. *Clin Infect Dis* 2001; 32: 1487-93.
- [6] Floridia M, Fragola V, Galluzzo CM, *et al.* HIV-related morbidity and mortality in patients starting protease inhibitors in very advanced HIV disease (CD4 count of < 50 cells/microL): an analysis of 338 clinical events from a randomized clinical trial. *HIV Med* 2002; 3(2): 75-84. [<http://dx.doi.org/10.1046/j.1468-1293.2002.00104.x>] [PMID: 12010353]
- [7] Feldman JG, Burns DN, Gange SJ, *et al.* Serum albumin as a predictor of survival in HIV-infected women in the Women's Interagency HIV study. *AIDS* 2000; 14(7): 863-70. [<http://dx.doi.org/10.1097/00002030-200005050-00013>] [PMID: 10839595]
- [8] Feldman JG, Gange SJ, Bacchetti P, *et al.* Serum albumin is a powerful predictor of survival among HIV-1-infected women. *J Acquir Immune Defic Syndr* 2003; 33(1): 66-73. [<http://dx.doi.org/10.1097/00126334-200305010-00010>] [PMID: 12792357]
- [9] Jerene D, Endale A, Hailu Y, Lindtjorn B. Predictors of early death in a cohort of Ethiopian patients treated with HAART. *BMC Infect Dis* 2006; 6: 136. [<http://dx.doi.org/10.1186/1471-2334-6-136>] [PMID: 16948852]
- [10] Johannessen A, Naman E, Ngowi BJ, *et al.* Predictors of mortality in HIV-infected patients starting antiretroviral therapy in a rural hospital in Tanzania. *BMC Infect Dis* 2008; 8: 52. [<http://dx.doi.org/10.1186/1471-2334-8-52>] [PMID: 18430196]
- [11] Tang AM, Forrester J, Spiegelman D, Knox TA, Tchetgen E, Gorbach SL. Weight loss and survival in HIV-positive patients in the era of highly active antiretroviral therapy. *J Acquir Immune Defic Syndr* 2002; 31(2): 230-6. [<http://dx.doi.org/10.1097/00126334-200210010-00014>] [PMID: 12394802]
- [12] Simone E, Langford JA, David A, Cooper. Predictors of disease progression in HIV infection. *AIDS Res Ther* 2007; 4(11): 4-11. [<http://dx.doi.org/10.1186/1742-6405-4-11>] [PMID: 17502001]
- [13] Zhou NIP J, R Ditangco. AIDS-defining illness diagnosed within 90 days after starting highly active antiretroviral therapy among patients from the TREAT Asia HIV Observational Database. *Int J STD AIDS* 2007; 18(7): 7. [PMID: 17326854]
- [14] Grobler L, Siegfried N, Visser ME, Mahlangu SS, Volmink J. Nutritional interventions for reducing morbidity and mortality in people with HIV. *Cochrane Database Syst Rev* 2013; 2(2): CD004536. [PMID: 23450554]
- [15] Michael O, Iroezindu EOO, Harry Hausler, Brian Van Wyk. 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; S3(002) [<http://dx.doi.org/10.4172/2155-6113.S3-002>]
- [16] Madec Y, Laureillard D, Pinoges L, *et al.* Response to highly active antiretroviral therapy among severely immuno-compromised HIV-infected patients in Cambodia. *AIDS* 2007; 21(3): 351-9. [<http://dx.doi.org/10.1097/QAD.0b013e328012c54f>] [PMID: 17255742]
- [17] Kassa NA. Prevalence of opportunistic infections and associated factors among HIV positive patients taking anti-retroviral therapy in debreMarkos referral hospital, Northwest Ethiopia. *J AIDS Clin Res* 2014; 05(05): 1-6.
- [18] Muhula SO, Peter M, Sibhatu B, Ndirangu Meshack KL. Effects of highly active antiretroviral therapy on the survival of HIV-infected adult patients in urban slums of Kenya. *PA J* 2015; 20(63): 1-9.