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Full Length Research Paper

Human papillomavirus (HPV) infection and abnormal cervical cytopathology among human immuno-deficiency virus (HIV) positive women in Northern India

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Human immune deficiency virus (HIV) infection is associated with a higher risk of human papillomavirus (HPV) positivity and cervical intraepithelial neoplasia (CIN) which may progress to cancer. Hence, it is important to screen all HIV positive women for this cancer which is amenable to cure in early stages. A cross sectional case-control study was conducted on 100 HIV seropositive women and matched seronegative controls attending Lok Nayak Hospital, New Delhi to study the prevalence of HPV infection and abnormal cervical cytopathology. A detailed cervical evaluation including a per-speculum examination, pap smear, cervical scrape for HPV DNA polymerase chain reaction (PCR), visual inspection of cervix with acetic acid, colposcopy and guided biopsy were done. Abnormal pap smears were found in 63% women of which 10% were squamous intraepithelial lesions. Biopsy revealed cervical intraepithelial neoplasia in 2% of all cases (5.6% of all patients biopsied). Prevalence of HPV in HIV positives was 24% compared to 4% in controls (p value 0.001), also bearing a significant correlation with CIN, thus placing HIV positives at a higher risk for cervical dysplasias and cancer. The sensitivity of HPV DNA test for detection of cervical dysplasias was 86.3% and specificity 64.2%. HIV positivity predisposes to invasive cervical cancer on account of immunosuppression and co-existing HPV infection, thereby the need for aggressive screening for cervical intraepithelial lesions. Both HPV DNA PCR and pap smear are optimal screening tools in these women.

Key words: Human immune deficiency virus (HIV), cervical human papillomavirus (HPV) infection, cervical intraepithelial neoplasia, pap smear, human papillomavirus (HPV) DNA polymerase chain reaction (PCR).

INTRODUCTION

India is one of the most populous countries in the world with more than one billion inhabitants. Of this number, it is estimated that about 2.4 million Indians are living with human immune deficiency virus (HIV), the national audit prevalence being 0.36%. The proportion contributed by women is 39%. Both HIV serotypes exist in India and HIV1-C is the most predominant. In a setting of expanding feminization of the HIV epidemic, Indian women are overburdened with a high morbidity and mortality and limited access to health care. HIV positivity and cervical neoplasia are both prevalent health problems in India, the latter being the most common genital tract cancers in women in India, with a significant prevalence of precursor intraepithelial lesions in the reproductive age group. This

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is thus one of the few cancers which can be subject to primary prevention by screening tests. Cervical screening tests should be available to the general population, and especially to HIV positive women, who are at an increased risk of developing cervical cancer. It is well accepted that women with AIDS show a high prevalence for cervical cancer. Cervical cancer has been since long accepted as an AIDS defining diagnosis by CDC on account of the high prevalence (Centers for Disease Control and Prevention, 1993).

HIV infection is associated with a higher risk of human papillomavirus (HPV) positivity and consequent cervical intraepithelial lesions (CIN) which may progress to cervical cancer. Papillomaviruses are small non-enveloped double stranded DNA viruses. Their genome includes two important genes, E6 and E7, which produce proteins that can attach themselves to Rb and p53 tumor suppressor genes and abrogate their functions. The high risk HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68) which are responsible for cervical neoplasias have cytologic effects ranging from mild form of the disease, condylomatous atypia or koilocytic atypia to severe dysplasias. HPV 16 has been found to be the most common type and appears to begin progression earlier and more consistently than the other subtypes. This is further compounded by the immunosuppression in HIV positive women resulting in chronic persistent HPV infection especially with several strains simultaneously, which is more likely to progress to invasive cancer.

In developed countries, on account of this high rate of dysplasia, a comprehensive gynecologic examination including a pap smear has been indicated at the initial evaluation and at subsequent visits. In view of the dual burden of HIV infection and cervical cancers in India, locally feasible screening guidelines need to be developed based on accurate data on prevalence of cervical abnormalities and HPV infection among HIV positive women. This will help to diagnose the maximum possible HIV positive women in early stages of CIN and reducing morbidity on account of CIN and cancer in this group of patients.

MATERIALS AND METHODS

Recruitment of the study population

This was a cross-sectional case control study conducted in the Department of Obstetrics and Gynecology, Maulana Azad Medical College and associated Lok Nayak Hospital, New Delhi from September, 2007 to February, 2009. One hundred HIV seropositive women attending the antiretroviral therapy (ART) Clinic at Lok Nayak Hospital and an equal number of healthy HIV seronegative women, matched for age and parity, taken as controls, were recruited. Patients with a surgically or congenitally absent cervix, known cervical malignancy, or an associated pregnancy were excluded from the study. A written informed consent to participate in the study was solicited following which the cases were subjected to a complete general physical examination, a local genital examination and a per speculum examination.

Screening and sample collection

A pap smear was taken for cytological examination using the wooden Ayre's spatula, was stained by the Papanicolaou's method and graded according to the modified Bethesda system. The same end of the Ayre's spatula was preserved in phosphate buffer saline (PBS 7.2) at -40°C for DNA extraction and HPV genotyping for types 6, 11, 16, 18 (the most common types genotypes) by polymerase chain reaction (PCR) using MY09/MY11 consensus primer (Milutin Gasperov et al., 2008). The cervix was visualized after liberal application of 5% acetic acid (VIA). Any whitening of the original pinkish color of a normal cervix was considered VIA positive whereas absence of the same was considered VIA negative. All subjects were then subjected to a colposcopic examination, the findings of which were noted according to the International Colposcopic nomenclature and scoring was done using modified Reid's index. A cervical biopsy was taken from suspicious areas, fixed in 10% formalin and sent for histopathological examination.

Statistical analysis

All data was compiled in terms of counts (percentage) under different categorical variables. The correlation between two categorical variables was determined using Chi square test or Fischer's exact test. The sensitivity, specificity, positive predictive value, negative predictive value were calculated for HPV DNA taking cervical biopsy as the standard reference.

RESULTS

Socio-demographic characteristics of the study population

The women in the study belonged to the reproductive age group. The mean age was 30.98 ± 5.8 standard deviation (SD) years for cases and 30.69 ± 3.1 SD years for controls. The mean parity of cases was found to be 2.41 ± 0.9, compared to 2.79 ± 0.8 in the control group. The most common mode of transmission of HIV infection amongst the study group was the heterosexual route (90%). None of the HIV seropositive women gave history of multiple sexual partners, though a history of promiscuity was elicited from their husbands. Most of the women studied (41%) were in World Health Organization (WHO) stage I and the mean CD4 cell count was 383.89/µl. Fifty five percent were already on anti-retroviral treatment at the time of the study.

Cervical cancer screening

On per-speculum examination, the cervix was found to be abnormal in 43% of the HIV positive women as compared to 8% of controls ($p < 0.001$). The most common finding was cervical erosion seen in 20% of cases followed by vaginal discharge in 13%. HIV positive women were found to have a significantly greater percentage of abnormal pap smears ($p < 0.01$) (Table 1). A statistical significance was found between abnormal pap smear findings and advancing WHO stage ($p < 0.015$) and lower

Table 1. Results of cytological examination (Pap smear).

Pap test report	Cases (%)	Controls (%)
Normal	37	89
Inflammation	28	10
Inflammation with TV/ *Candida*/ HSV/ *B. vaginosis*	11	0
Inflammation with HPV	14	1
ASCUS	2	0
LSIL	0	0
LSIL with HPV	4	0
HSIL	2	0
Inadequate	2	0

TV- Trichomonas vaginalis, HSV- herpes simples virus, ASCUS- atypical cells of undetermined significance, LSIL- low grade squamous intraepithelial neoplasia, HSIL- high grade squamous intraepithelial neoplasia, HPV- human papillomavirus.

CD4 cell counts ($p < 0.016$). On application of 5% acetic acid to the cervix, 33% were VIA positive compared to only 3% controls ($p < 0.001$). Colposcopy was found to be abnormal in 36% of HIV seropositive patients and 1% of seronegative controls ($p < 0.001$) and majority (52.7%) had a Reid score of 3 to 5. A colposcopy guided biopsy was indicated in 36 cases whereas none of the controls were eligible for a cervical biopsy by virtue of normal colposcopic examination. The most common finding was the presence of condylomatous changes (suggestive of HPV) infection in 55.6% of cases. High grade lesions (CINIII) were seen in 5.6% of the patients biopsied, that is, 2% of the total cases.

Cervical HPV positivity in HIV positive women

HPV positivity on cervical smear was seen in 24% of HIV seropositive women compared to 4% of controls (Tables 2 and 3). Most of the HIV positive subjects who tested positive for HPV were almost equally distributed among WHO stages I, II, and III. There was no significant correlation between the WHO stage of HIV and HPV infection ($p = 0.184$). A statistical significance was found between HPV positivity and low CD4 counts ($p = 0.001$). Eighty seven percent of HPV positive cases were VIA positive compared to 15.8% of HPV negative cases (p 0.001). Most (66.7%) of the HPV positive cases had a Reid score between 3 to 5 while 80% of HPV negative cases revealed a normal colposcopic examination ($p < 0.001$) (Table 4). The sensitivity of HPV DNA test for detection of cervical dysplasias in HIV positive women was 86.3% and specificity 64.2%. The positive predictive value was 79.1% and negative predictive value 75%.

DISCUSSION

Acquired immune deficiency syndrome (AIDS) in our country is most prevalent among sexually active younger population groups. The majority of HIV infection (87.7%) afflicts women between 15 to 44 years of age. The cervix was found to be grossly unhealthy on per-speculum examination in 43% cases and only 8% controls. Amongst HIV positive women, cervical erosion was the most prevalent finding (20%), followed by the presence of vaginal discharge (13%), and a suspicious looking cervix (10%). Thus, in the present study, HIV seropositive women showed a higher incidence of sexually transmitted infections (STIs) manifesting as cervical erosion and vaginal discharge. Out of them, 45% showed inflammatory pap smears and 10% showed squamous intraepithelial neoplasia (SIL) and only 20% were normal smears. Infection and erosion heal by a process of squamous metaplasia, and it is this area, that is the transformation zone which is most susceptible to dysplastic changes, thus making these patients predisposed to development of CIN. Sixty six percent of HIV positive patients with an unhealthy cervix had SIL on cytology and CIN on histopathology. Hence, an abnormal cervix on per-speculum examination is likely to harbor an underlying cervical intraepithelial abnormality.

In our study, 63% of cases had an abnormal pap smear as compared to 11% of controls. Fourteen percent of smears showed koilocytic changes suggestive of HPV infection. Two percent of pap smears had atypical cells of undetermined significance (ASCUS). The percentage of cases with SIL was 6%, 4% being low grade squamous intraepithelial neoplasia (LSIL) with HPV, and 2% high grade squamous intraepithelial neoplasia (HSIL).

In the present study, the percentage of HIV positive women with CIN on histopathology was 2%. The histopathological examination of both patients revealed CIN III with condylomatous changes. Of the remaining cases, 20% were found to have condylomatous changes. A biopsy was not indicated in any of the controls and thus a statistical significance could not be determined. Thus, the percentage of CIN in HIV positive women was found to be higher, comparing with data in studies conducted in the general Indian population where the prevalence of

Table 2. Results of HPV DNA PCR test.

Parameter	Negative (%)	Positive (%) (HPV type)				
		6	11	16	18	Total HPV positives
Cases (n=100)	76	1	0	22	1	24
Controls (n=100)	96	0	0	4	0	4

Presence of HPV DNA in HIV positive women was found to be statistically significant (p = 0.001). Most common type was HPV 16

Table 3. Association of HPV infection with Pap smear results in HIV positive women.

Parameter	Normal [N (%)]	Inflammation [N (%)]	Inflammation with HPV [N (%)]	ASCUS [N (%)]	LSIL [N (%)]	LSIL with HPV [[N (%)]	HSIL [N (%)]
HPV positive (n=24)	2 (8.3)	5 (20.5)	10 (41.7)	1 (4.2)	0 (0)	4 (16.7)	2 (8.3)
HPV negative (n=76)	36 (47.4)	34 (46.1)	4 (5.3)	1 (1.3)	0	0	0

Of the 24 HPV positive cases, 25% showed dysplastic cells and 41.7% showed inflammation with HPV on Pap smear. The association of HPV positivity with abnormal Pap smear was found to be significant (p < 0.001)

Table 4. Association of CIN with HPV positivity in HIV positive cases.

Parameter	HPV positive (%)	HPV negative (%)
Chr. Cervicitis (n=14)	4 (28.5)	10 (71.5)
Condylomatous changes (n=20)	17 (85)	3 (15)
CIN I (n=0)	0	0
CIN II (n=0)	0	0
CIN III (n=2)	2 (10)	0

Total number of cervical biopsies taken = 36. 85% patients with condylomatous changes were positive for HPV DNA whereas all patients with CIN III were harbouring HPV.

CIN was found to range from 0.47 to 1.3% (Mulay et al., 2009). No cases with invasive cervical cancer were detected in our study. This could be explained by the fact that cervical cancer is a disease mainly of elderly groups and the mean age of cases in our study was 30.98 years.

Studies in various regions of the world have shown that women infected with HIV are at an increased risk for cervical cancer precursor lesions. The percentage of HIV positive patients with CIN is variable but has been reported to be as high as 30% in African studies where the prevalence of HIV itself is quite high (Christopher et al., 2007). Weissborn et al. (2003) found HIV infection to be associated with significantly high HPV loads and cervical dysplasia, with the highest load in advanced disease. Massad et al. (2005) conducted a large prospective multicenter cohort study and found at least one abnormal smear during follow-up of 73% of HIV positive women and 42% seronegatives (Luthra et al., 1987). The lower percentage in our study could be attributed to small sample size and the lower prevalence of HIV amongst the population covered in the study. This may also be explained by most patients belonging to WHO stage I of HIV disease and others were already on antiretroviral therapy (ART). The development of CIN in HIV positive patients may also be influenced by other factors like parity, nutritional status, hygiene, ART, immediate treatment after diagnosis of HIV, and presence of other STIs. The patients with CIN III in our study were planned for a cone biopsy and further follow-up. A significant correlation was found between the prevalence of CIN and clinical WHO stage or the degree of immunosuppression (CD4 cell count). Advanced HIV related disease which is associated with immunosuppression favors persistence of high loads of cervical oncogenic type HPV infection and clinical expression in HIV positive women.

A greater prevalence of HPV infection has been found in HIV positive women. The prevalence ranges from 30% to as high as 65% (Maria et al., 2008; Danny et al., 2008). In our study, 24% of HIV infected women were positive for HPV as compared to 4% of controls. While we did not find any association of HPV infection with WHO stage of disease, there was a significant correlation with lower CD4 counts. In a study conducted by National AIDS Research Institute (NARI), Pune in 2003, pap smear abnormalities were found in 6.3% of the 287 HIV

Table 5. Comparison of sensitivity and specificity of high risk HPV for screening CIN.

Study	Number	Sensitivity (%)	Specificity (%)
Kaufman et al. (1997)	462	52	-
Infantlolino et al. (2000)	314	86	41.3
Cuzick et al. (1995)	2009	75	-
Gaffikin et al. (2003)	2199	80	61
Present study	100	86.3	64.2

positive women screened while 33% were positive for HPV 16/18 (Joshi et al., 2005). Greater HPV positivity in HIV positive women is attributed to various factors including chronic immunosuppression and consequent chronic HPV infection, infection with strains which are more likely to cause cancer, HPV in both the cervix and anus, infection with several strains of HPV virus simultaneously, reactivated HPV infections which were previously under control and HPV that poorly responds to other therapies-multiple treatments using different methods may be needed.

HIV infected women with co-existing HPV were analyzed and a significantly greater prevalence of abnormal cervical cytology was found. Of the 24 HPV positive cases in our study, 25% showed dysplastic cells on pap smear (LSIL with HPV, HSIL). Forty two percent revealed inflammation and HPV, and the remainder comprised of normal and simple inflammatory smears. Abnormal pap smears and colposcopy, and VIA positivity were common in HPV positive cervical smears. Screening for HPV infection and CIN in HIV positive women using VIA and colposcopy should be an early adjunct to pap smear considering the high risk of cervical dysplasias in HIV positive women.

The validity of an HPV test (to screen for cervical dysplasias in HIV positive women) calculated in our study was comparable with that in previous studies where the sensitivity ranges from 50 to 80% and specificity is 40 to 60% (Table 5). Combining the HPV DNA test with pap smear examination increases the negative predictive value to nearly 99%.

Conclusions

It is evident from the present study that HIV positive women are overwhelmingly burdened with a greater risk of cervical neoplasia. Higher rates of HPV infection with a greater persistence and severity of sequelae are evidence for an early diagnosis and interruption of the infectious pathology conducive to cervical cancer. Detection of HPV infection can be employed as a primary preventive measure for cervical cancer by direct PCR or indirect tools for example, pap smear, VIA, colposcopy, either singly or as combined integrated tests. The prevalence of CIN and high risk HPV infection in HIV seropositive women is high enough to warrant a routine gynecological evaluation and cervical cytological screening in these patients. However, larger and longitudinal studies are needed to evaluate the progression and effects of antiretroviral therapy on these abnormalities as well as to choose the best screening tool in HIV seropositive women.

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ABBREVIATIONS

ART, Anti-retroviral therapy; **ASCUS,** atypical squamous cells of undetermined significance; **AIDS,** acquired immunodeficiency syndrome; **CDC,** Center for Disease Control; **CIN,** cervical intraepithelial neoplaisa; **DNA,** deoxyribonucleic acid; **HIV,** human immunodeficiency virus; **HPV,** human papilloma virus; **SIL,** squamous intraepithelial neoplasia; **LSIL,** low grade squamous intraepithelial neoplasia; **HSIL,** high grade squamous intraepithelial neoplasia; **HSV,** herpes simplex virus; **NARI,** National AIDS Research Institute; **PCR,** polymerase chain reaction; **STI,** sexually transmitted infections; **TV,** trichomonas vaginalis; **VIA,** visualisation with acetic acid; **WHO,** World Health Organisation.

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Full Length Research Paper

Youth attitude to some human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) preventive measures in some institutions of higher education in Nigeria

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Youth attitude to some human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) is a world-wide epidemic that has given governments around the world sleepless nights. The case of sub-Sahara Africa is particularly worrisome. More than half the world cases are believed to be in this region. Nigeria as one of the countries in this region is not speared the devastating spread of the virus and young people are particularly vulnerable. This research focused on attitudes of young people towards some preventive measures of HIV/AIDS transmission in some tertiary institutions in the southern part of Nigeria. Samples of size 50 were randomly taken from four institutions and the data obtained were tabulated and analyzed using the chi-square test. It was discovered that response to these measures is poor. Majority of the youths are aware of the preventive measures but they appear to be indifferent to them.

Key words: Attitude, preventive measures, Youth attitude to some human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS), institutions of higher learning.

INTRODUCTION

Acquired immune deficiency syndrome (AIDS) is a viral disease caused by human immunodeficiency virus (HIV) that is usually found in body fluids like blood, semen, vagina fluid, and breast milk of infected persons (Arinola and Adekunjo, 2012). The virus can be transferred from one infected person to another, mostly through sexual intercourse and sharing of unsterilized instruments like blades, knives, and syringes which had once been used by infected persons (Olaleye, 2003). Since it was first discovered in the early 1980s, scientists have been struggling to find a cure for the disease without success. The best that have been achieved so far is management of the infection to prolong the lives of infected persons. This management entails regular intake of anti-retroviral drugs to boost the immunity of infected persons against other diseases referred to as opportunistic infections. According to Arinola and Adekunjo (2012), HIV/AIDS is an extraordinary kind of crisis; it is both an emergency and a long-term development issue. Tumer and Unal (2000), as quoted by Arinola and Adekunjo (2012), assert that HIV/AIDS is one of the most complex health problems of the 21st century. Despite increased funding, political commitments and progress in expanding access to HIV treatment, the AIDS epidemic continues to outpace every global response. It is estimated that about 24.7 million people are living with HIV/AIDS in sub Saharan Africa. It is among the leading causes of death in this region (Arinola and Adekunjo, 2012).

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The mode of transmission of the disease makes it all the more dangerous. It is transmitted through sexual intercourse with infected people, sharing sharp objects, blood transfusion, etc., thereby impacting seriously on our mode of social interactions. People have to adjust their lifestyles and the manner of their social interactions. As a result many issues are involved in the control of the infection. It is a well known fact that awareness of these issues, especially among the most vulnerable group in the populace which is the youth, can enhance efforts to control the spread of the virus.

The issue of HIV/AIDS has become the concern of governments across the world. As the spread of the disease does not recognize national boundaries, all countries of the world are involved in bringing the scourge under control. Funds that would otherwise have been spent on control and treatment of other common diseases like malaria as in the case of sub-Sahara African countries and childhood killer diseases are now being over stretched to include the control of HIV/AIDS. This has brought considerable pressure on the finances of most African countries. Nigeria's effort at bringing the spread of the virus under control in the country is coordinated by National Action Committee on AIDS (NACA). At the state level, State Action Committee on AIDS (SACA) was formed to complement the activities of NACA at the Federal level. When the epidemic was first reported in Nigeria, the government did not respond with decisive action until 1999 when a democratic government came into power. NACA was formed by the government in 2001 and in spite of the efforts of the agency, about 1,000 fresh cases of HIV infections, mostly among the youths, are recorded everyday in Nigeria (NACA, 2010). As a result many research works tend to focus on young people. Ruma (2009) carried out a cross sectional study to determine the knowledge and awareness of HIV/AIDS among senior secondary schools in some parts of the north. The study revealed that the majority knows what HIV/AIDS is and they are aware that the disease has no cure. Also a high percentage knows that the disease can kill. Fawole et al. (2011) examined the level of awareness of HIV/AIDS and sexual behavior of tertiary institution students and found that in spite of high level of awareness among the students, they were still found to engage in risky sexual practices. Momoh et al. (2006) examined the issue of school age girls' awareness in Nigeria. They found that female undergraduates show a moderate level of awareness but among divorced students, as a sub-variable of marital status, there was poor awareness of HIV/AIDS issues.

HIV/AIDS AND YOUNG PEOPLE

Young people are the most affected group in any society. United Nations AIDS Programme (UNAIDS) has estimated that every minute of every day, five young women and men become newly infected with HIV. Worldwide, nearly half of all new HIV infections today are in young people aged 10 to 25 years, and in the worst affected countries, the proportion is even greater, exceeding 60% in some places. In 1999, UNAIDS estimated that one third of all infected individuals were youths, ages 15 to 24, and half of all new infections occur in youths of the same age (UNAIDS, 1999). They also estimated that about half of the world's total new adolescent HIV infections occur in sub-Saharan Africa (UNAIDS, 1999) and in fact nearly 70% of people living with HIV/AIDS live in sub-Saharan Africa, and over 80% of AIDS deaths have occurred there. HIV/AIDS has had a devastating effect on African youths who often lack access to sexual health information and services.

Higher institutions of learning have a good concentration of young people who interact on a daily basis. They are a very susceptible environment for transmission of the virus. It is therefore, very important that students in higher institutions of learning have the right attitude towards issues of HIV/AIDS. A good attitude can greatly reduce the spread among the students and contribute to the control effort nationally. Awareness programs are not in short supply in Nigerian universities. They come in the form of seminars, symposium, bills, leaflets and one-on-one discussion (Onyene et al., 2010). Inspite of various campaigns about HIV/AIDS, there is a conception that the prevalence rate of the scourge is high among the students in tertiary institutions (Fawole et al., 2011). Among researchers who have questioned the effectiveness of the various awareness programmes are Ibe (2005) and Magnus and Gbakeji (2009). On the other hand, Onyene et al. (2010), Omoregie (2002), and Adedimeji (2003), are of the opinion that the problem might not be awareness as there is usually high level of awareness among the students. The problem might be attitudinal. Many of them simply do not care or are indifferent to the risk associated with unsafe sexual practices.

VOLUNTARY COUNSELING AND TESTING (VCT)

One of the ways by which young people can be more responsive to the issues of HIV is through voluntary counseling and testing. By voluntarily submitting themselves for counseling and testing, the point is being made that the message of HIV awareness is getting across to them. VCT is an opportunity for people to receive counseling and at the same time, be tested for the virus. This process prepares people for the outcome of the test, whether positive or negative. For people who are negative, it encourages them to adopt preventive measures while for those who tested positive, VCT will encourage them to show a sense of responsibility in society by not spreading the virus to other people. It will also allow them to make informed decisions concerning

marriage, child-bearing, etc. According to USAID Project Search (Task Order No. 2), VCT allows individuals to learn their HIV status through pre-and post-test counseling and an HIV test. VCT is client-initiated, as opposed to provider-initiated testing and counseling (PITC) when health care providers initiate discussion of HIV testing with clients who are seeking health care for other reasons.

By combining personalized counseling with knowledge of one's HIV status, VCT is designed to motivate people to change their behaviors to prevent the acquisition and transmission of HIV, reduce anxiety over possible infections, facilitate safe disclosure of infection status and future planning, and improve access to HIV prevention and treatment services.

According to UNFPA, some countries have introduced mandatory testing for certain categories of individuals which includes prospective students applying to enter university (Ecuador), new military recruits (China), first time antenatal attendants, refugees, those in institutionalized care like orphanages, detention centers, prisons, etc. UNFPA identified a common feature of mandatory testing as the lack of counseling and supportive services offered after testing. The concept of mandatory testing should not be encouraged as it does not ensure that individuals and couples are provided with all the information necessary to make an informed decision as to whether or not to test, and the enabling environment to cope with the outcome/results of the test. It does not also ensure that people are voluntarily complying with awareness and preventive measures being promoted by society.

Nigeria does not have a policy of mandatory testing and counseling as this will be considered to violate people's right to self-determination or freedom of choice. However, patronage at VCT centers is not common. People do not voluntarily go for counseling and testing but they may submit themselves for testing if required as part of service delivery by a health service provider. This is as a result of stigmatization suffered by carriers of HIV in the society. Unless it is absolutely necessary, people will not go for test. Majority of tests carried out in Nigeria will fall into the category of PITC. This work examines, among other things, patronage of VCTC by students and their attitude towards the services. The work also examines sentiments, particularly religious sentiments, and how it affects their attitudes towards VCT. It also looked at such habits as smoking, condom use and the practice of safe sex.

METHOD OF DATA COLLECTION

Questionnaires were used to collect data. Four institutions were sampled and data were obtained from 50 randomly selected students from each of the four institutions, making a total of 200 respondents. Where a respondent declined to answer the questions, the researcher randomly interviewed another student to make up the number. The questions provided options for the students to choose from while in some cases, the questions were left open for answers to be provided by the respondents. The questions were straight to the point and did not request respondents to give unnecessary information about themselves. This helped to build confidence in the respondents and they were able to answer the questions as freely as they could.

RESULTS AND DISCUSSION

Statistical Package for Social Sciences (SPSS) was used to analyze the data. Preliminary analysis shows that 85% of the respondents were below the age of 30 years and over 30% were in the age bracket of 20 to 24 years. About 46% of the sampled students were single, 30.5% were married, 13% were co-habiting and 10.5 were divorced. The age group 20 to 24 years has the highest percentage of married students which stands at 43%, while 47% were single and 6% were co-habiting. Only 3% were divorced. Next to this age group in terms of the number of married students is the 'above 30 years' age group which has 34.5% married students. About 19.2% of them were single, 10.3% cohabiting and 37.7% divorced. The age group '15 to 19 years' has the highest percentage of single students which stands at 77.4% and second highest percentage of co-habiting students (16.1%) (Table 1).

The data also revealed that 58.7% of singles have unprotected sex, 96.2% of those cohabiting have unprotected sex and 95.2% of divorced students also have unprotected sex. The percentage of those who use protected (safe) sex was even higher (9.8%) among married students than those cohabiting (6.38%), and those divorced (4.83%) students. This is worrisome because these two groups fall into the groups that are more likely to have multiple sexual partners (Table 2).

Concerning students that have undergone HIV/AIDS test, divorced students had the highest percentage of 81%, followed by co-habiting students with a percentage of 76.9%. Married students had a percentage of 68% and singles students had 46.7%. Majority of single students have never had an HIV/AIDS test (Table 3).

The percentages of the students that have visited the VCT centre stood at 31% for single students, 18.5% for married students, 10% for co-habiting students and 6% for divorced students.

Investigation was made as to the impact of religious sentiment on VCT, unprotected sex and HIV/AIDS test. A chi-square test was carried out and it was found that the null hypothesis of independence between religion and each of the control measures were rejected for HIV/AIDS test with a probability of 0.015, not rejected for VCTC with a probability of 0.078 and rejected for unprotected sex with a probability of 0.002. This means that decision to visit a VCT centre is not influence by religion. Having HIV/AIDS test and practice of safe sex are influenced by religion sentiments. Smoking habit was also examined to see how it relates to the control measures for HIV/AIDS.

Table 1. Distribution of respondents by age and marital status.

Age		Marital status				Total
		Single	Married	Cohabiting	Divorce	
15-19	Count	24	2	5	0	31
	% within age	77.4	6.5	16.1	0.0	100.0
	% within marital status	26.1	3.3	19.2	0.0	15.5
	% of total	12.0	1.0	2.5	0.0	15.5
20-24	Count	39	36	5	3	83
	% within age	47.0	43.4	6.0	3.6	100.0
	% within marital status	42.4	59.0	19.2	14.3	41.5
	% of total	19.5	18.0	2.5	1.5	41.5
25-29	Count	24	13	13	7	57
	% within age	42.1	22.8	22.8	12.3	100.0
	% within marital status	26.1	21.3	50.0	33.3	28.5
	% of total	12.0	6.5	6.5	3.5	28.5
30-Above	Count	5	10	3	11	29
	% within age	17.2	34.5	10.3	37.9	100.0
	% within marital status	5.4	16.4	11.5	52.4	14.5
	% of total	2.5	5.0	1.5	5.5	14.5
Total	Count	92	61	26	21	200
	% within age	46.0	30.5	13.0	10.5	100.0
	% within marital status	100.0	100.0	100.0	100.0	100.0
	% of total	46.0	30.5	13.0	10.5	100.0

Table 2. Students' marital status and practice of safe sex.

Marital status		Unprotected sex		Total
		Yes	No	
Single	Count	54	38	92
	% within marital status	58.7	41.3	100.0
	% within unprotected sex	35.1	82.6	46.0
Married	Count	55	6	61
	% within marital status	90.2	9.8	100.0
	% within unprotected sex	35.7	13.0	30.5
Cohabiting	Count	25	1	26
	% within marital status	96.2	3.8	100.0
	% within unprotected sex	16.2	2.2	13.0
Divorce	Count	20	1	21
	% within marital status	95.2	4.8	100.0
	% within unprotected sex	13.0	2.2	10.5
Total	Count	154	46	200
	% within marital status	77.0	23.0	100.0
	% within unprotected sex	100.0	100.0	100.0

Table 3. Distribution of HIV test by marital status.

Marital status		HIV test		Total
		Yes	No	
Single	Count	43	49	92
	% within marital status	46.7	53.3	100.0
	% of Total	21.5	24.5	46.0
Married	Count	42	19	61
	% within marital status	68.9	31.1	100.0
	% of Total	21.0	9.5	30.5
Cohabiting	Count	20	6	26
	% within marital status	76.9	23.1	100.0
	% of Total	10.0	3.0	13.0
Divorce	Count	17	4	21
	% within marital status	81.0	19.0	100.0
	% of Total	8.5	2.0	10.5
Total	Count	122	78	200
	% within marital status	61.0	39.0	100.0
	% of Total	61.0	39.0	100.0

It was found that the hypothesis of independence is rejected at .007 level of significant for unprotected sex which means the practice of safe sex can be influenced by students who have a habit, particularly smoking habit. The hypothesis of independence between smoking habit and HIV test is upheld at 0.158 level of significance. It can therefore be said that smoking habit does not affect a student's decision to have HIV test. Also the hypothesis of independence between smoking habits and VCT is upheld at 0.402 level of significance, which means smoking habit does not affect student's decision to visit a VCT centre. Other habits like drinking and taking hard drugs were not examined.

Conclusion

Not many researches have been done on the impact of the promotion of behavioral change interventions aimed at reducing the spread of the virus. Such behavioral changes include abstinence, delaying the onset of first sexual intercourse, use of condoms, reducing the number of sexual partners and so on (Michielsen 2012).

Additionally, they aim to increase knowledge, change attitudes, improve access to services and to reduce stigma or address other mediators as self-esteem and self efficacy. But it is generally observed that the interventions have had little or no effect on people's behavior in sub-Sahara Africa, especially among young people. Michielsen (2012) found that interventions have had little or no positive effects on sexual behavior, and 'condom use at last sex' only increased marginally among males but remained at a low level.

The results of this analysis tend to point in this direction. Level of safe sex is low, particularly among single students. Only about 41% practice safe sex in spite of the measures being used by various government agencies, non-governmental agencies and other concerned organizations to educate the youths about the need for safe sex. Majority of the students do not go for voluntary HIV test. The percentage of those that have VCT is as low as 31% among the singles students.

Habits and sentiments also play some roles in the attitude of students towards these intervention measures. Smoking habit influences safe-sex practice. Those who smoke are more likely to have unprotected sex. Religion sentiment among the students is strong and has influence on student's decision to have HIV test.

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Full Length Research Paper

HIV and AIDS in Africa: Questioning the validity and the efficacy of the HDI measures

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This paper poses methodological and ethical questions on the measures adopted by the human development index (HDI) data in assessing development in Africa, with particular emphasis on human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS). It is a well-known fact that these measures are great indicators of development or otherwise. The central position of the paper is that given the difficulty in collecting data reports on Africa, how accurate and reliable are the HDI standards in measuring the spread of HIV and AIDS in Africa? Perhaps a medical research report in Nigeria has come up with a figure that over 7 million Nigerians have been medically proven to live with HIV while close to 5 million have been suspected to be positive to HIV. But these people have not come out boldly to either be tested for HIV or treated due to the myths and misconceptions surrounding the infection (Akingbade, 2013). The paper however held that there is a need for further research in determining the validity of HIV/AIDS prevalence in Africa. It concluded with adequate recommendations.

Key words: Human development index (HDI), Africa, human immunodeficiency virus/acquired immune deficiency syndrome.

INTRODUCTION

The measures adopted by the human development index (HDI) over the years have been studied by scholars. Most scholars, like Chowdhury (1991) and Noorbakhsh (1998), emphasized on the limitations of the arbitrariness of the qualitative and quantitative measures such as ranking and the assignment of weights which are used as the indices for assessment. The measurement of HIV and AIDS falls under the life expectancy variable of the HDI which is compiled by the United Nations Development Program and published as the Human Development Report on an annual basis. The measurement thus serves as a global benchmark for assessing sustainable development, by examining the impact of gross domestic product (GDP), education and life expectancy to ascertain ascertain the relationship among variables. The HDI basically collects its data on human immunodeficiency virus (HIV) and acquired immune deficiency syndrome(AIDS) in African countries using primary sources such as the Joint UN Program and Updates on HIV and AIDS, the Report on the Global HIV/AIDS Epidemic, and a joint publication of UNAIDS and the World Health Organization. On an annual basis, various regional centers provide update reports based on investigations, national data findings, data findings from governments, international organizations, non-governmental organizations and private sector organizations (such as employers, insurers and hospitals) (HDR, 2004). These reports are compiled, and states are assigned

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numerical assigned numerical values based on the quantity of the HIV/AIDS causalities recorded annually.

Statement of the problem

This research is motivated by certain underlining problems in the area of research on HIV and AIDS in Africa. Briefly, the common problems will be highlighted:

i) Generally in Africa there is a lack of an adequate demographic and socioeconomic data.
ii) This has led to an obvious problem of access and use of valid data in policy making.
iii) There is insufficient data or insufficient demand and use of data, its application by policy makers and key stake holders both at National and international level.
iv) The general notion that a wrong data would ultimately lead to the application of the wrong policy.
v) Finally the central position of this research as well as the most eminent problem is that given the difficulty in collecting data reports on Africa as mentioned, how certain are the HDI standards in measuring the spread of HIV and Aids in Africa? If the HDI assigns the Western countries low scores especially the United States merely because of their technological advancement in controlling this epidemic, then should the measurement be based on the number of the carriers of this disease or the amount of death that result from it or the sophistication of the control measures?

More also, given the unprecedented increase in teenage pregnancies in the west how certain are the generalizations made by the HDI on the prevalence of HIV and AIDS in Africa. Based on available evidence, according to the United states Center for Diseases Control and Prevention (CDC) 2012, result shows that out of 79% of teens that are teenage mothers, 80% of these pregnancies occurred accidentally. The teen pregnancy rate in the United States of America is twice as that of Canada, four times that of Germany and France, and eight times that of Japan. Given this evidence, the research questions the efficacy of the HDI reports on the prevalence of HIV and AIDS in Africa. More also, given the cultural inclination of most African societies contrasted with a Western Laissez-faire life style characterize by the portrayal of sex through the mass media which results in an inappropriate and rather careless approach about the concept of sex, the HDI measures deserves thorough and critical investigation.

In this paper, the emphasis is on the social, political, technological and cultural limitations of the HDI, regarding the assessment of HIV and AIDS in Africa. In particular, the study will focus on the limitations and the backdrops of data collection in Africa. it will examine the growing trend of HIV and AIDS over the years in Africa as reported by the HDI, as well as the means of data collection which is used as the basis of assessment; secondly, it will offer constructive criticism of these assessment measures with specific reference to their political, social and technological limitations; thirdly, the paper questions the low scores accorded to developed countries or high-income countries based on their GDP as well as the technological sophistication; and finally, the research offers suggestions on what the United Nations Development Programme (UNDP) can do to improve the quality of data collection and assessment of HIV and AIDS in Africa.

THE HUMAN DEVELOPMENT INDEX AND HIV/AIDS IN AFRICA

The HDI has provided a benchmark for the assessment of sustainable development in Africa. One of its measures for assessing life expectancy among countries is the degree and spread of HIV and AIDS in a country at any particular point in time (Escosura, 2011). In Africa, particularly sub-Saharan Africa, the report of the HDI indicates a rapid and escalating growth of HIV infections; this in effect determines life expectancy and the level of development in the African region. According to the records, between 1990 and 2011 there was a continuous growth in the number of the carriers of HIV and AIDS infections in Africa, totaling about 39 million. By 2011, it reported that there were 34.0 million people in the world who had HIV/AIDS, Sub-Saharan Africa having a total of 23.5 million. Meanwhile, North America and Western and Central Europe had a total of 2.0 million and 1.0 million people infected at rather low annual death rates of 28,000 and 7,500, respectively, according to the HDI record (UNAIDS, 2012).

WHY IS THIS STUDY IMPORTANT?

In an attempt to solve the problem of HIV and AIDS in Africa, cultural solutions must be taken into cognizance (Müller and Moyo, 2011; Airhihenbuwa and Webster, 2004). While scholars have noted this stated fact, they however have not examined the nexus between the effect of African culture (bad governance and poor state of infrastructure) and the assumed predominance of HIV/AIDS in Africa. Why is culture a necessity for explaining the limited assumption of the prevalence of HIV/AIDS Africa? In extant literature, the emphasis has been on the need to place culture at the praxis of any development ideas, prescriptions solution and generalizations (Robert, 1994). Unfortunately, the researchers have largely deemphasized this concept, in the long run. Take for instance while there are plethora of debates on the origin of HIV and AIDS, its rather popular correlation with underdevelopment is largely questionable. The popular perception among scholars is that Africa is backward and that HIV and AIDS hinder development, or

they are indicators of underdevelopment. But the case of Botswana appears to question this scholarly contention, thus underscoring the need to study development and underdevelopment in relation to cultural realities, where development and underdevelopment are predetermined by HIV/AIDS.

First, with Botswana's improving GDP praised by the international community, in 2007, the country's HIV/AIDS records were still on the high side (Hans, 2013). This displaces the whole idea of development to be facilitated by absence of HIV and AIDS predominance. It is on this instance that to totally displace the peculiarity of Africa's culture when it comes to the study of HIV/AIDS predominance will be intellectually incapacitating. Indeed, there are reasons one should be skeptical about the predominance of HIV/AIDS in Africa, because of certain features inherent in African culture. On the positive side there is a strong moral, cultural and communal discipline in most African societies. On the negative side the society is complicated by state shoddiness and adynamia which are asymmetrically opposed to modernization and development. On the negative side you have factors such as technological constraints and political corruptions which are all broadly endemic features in the African society, necessitated by weak governance which complicates the process of data collection, and limits the validity of quantitative findings used as benchmark for generalizations by most international agencies, particularly the UNDP's HDI. These various weaknesses will be considered in the next phase of this paper.

EXPECTED BENEFITS TO THE DEVELOPING AND DEVELOPED STATES

This paper is expected to contribute to the broader discourse on the challenges and solutions to Africa's development. As it relates to the issue of HIV and AIDS, it is expected that if the United Nations Development Program will tackle the perceived and unclear prevalence of HIV/AIDS in Africa, it must be certain about the number of the carriers of this disease in the continent. The aim is not solely to criticize the findings of the UNDP but also to proffer adequate solution on what can be done to achieve proper documentation which will not only have positive implication on the society in terms of transparency and goal oriented policy application, but will also be beneficial to the developed societies such as the United States, Canada, France, Great Britain who contribute a substantial amount of their wealth to the actualization of the goals of UNDP. As the global economic domain becomes more challenging, it will be wise on the part of the developed countries that run these institutions to device a more strategic approach towards the actualization of its goals.

Unregistered hospitals and clinics

In examining the validity of an adequate HDI-generated data, furthermore, an issue that must not be left out also is the existence of many health care centers that are not approved by the governments and thus will not want to affiliate with any agency of any sort in most African states. As mentioned earlier, the adequacy of any data-gathering methodology is dependent on its coverage within the involved polity (Rolfe, 2006). The issue of unregistered clinics is further aggravated by government legislations. In Kenya, while one may applaud the passage of the Health Care Record bill in 2006, which demanded that Kenyans register with government acknowledged and approved hospitals, the national hospital insurance funds of civil servants awarded medical insurance to unregistered clinics and health care outlets in April, 2012 (Wabala, 2012). What this simply means is that there are no existing legislations governing the modus operandi of the health care sector in Kenya (Wabala, 2012). So, how can reliable data be collected and made available in the health facilities?

In September, 2012, the Lagos State government in Nigeria shut down 15 clinics and hospitals which had been operating illegally for years in the urban society. With Lagos being one of the metropolitan cities in the country, how well can it be argued that the annual HDI and UNDP surveys have been able to obtain the accurate and adequate records they need to compare HIV epidemic with that in other countries (Akinsanmi, 2012)? The implication of this is that given the dormant approach of most African government towards the adequate regulation of the health care system, accuracy in data collection is highly limited.

CORRUPTION IN THE HEALTH SECTOR

Corruption is an endemic phenomenon in Africa affecting every aspect and context of the society. Corruption goes beyond embezzlement of government funds or direct stealing of government monies in the areas of contract awards, budgetary allocations and during implementation of policies. Corruption comes with a lot of complexities and complications which threaten the viability of the health care industry in terms of health care accessibility, equity and outcome (Vian, 2007). In a qualitative comparative study of Armania, Bulgaria, Albania, Armenia, Azerbaijan, Republic of Georgia, Mozambique and Carpe Verde, Vian found out that the Presidents Emergency Plan for AIDS Relief (PEPFAR), the Global Fund for AIDS, TB and Malaria, and other development partners, contributing hundreds of millions of dollars per year, created pressure to increasingly spend funds, and increased the risk of corruption by requiring hasty decisions with limited and falsified, and sometimes unavailable data (Vian, 2007). From the foregoing, the tendency to inflate the number of carriers of HIV and AIDS in African countries due to perceived aid benefits from external donors remains a questionable issue and deserves further studies and thorough investigation,

especially given the fact that virtually all the governments in Africa are corrupt.

DOES AID INCREASE HIV/AIDS?

Studies have queried the prevalence of HIV/AIDs in Africa in donor-dependent countries. Particularly in the case of Uganda, the rationale behind the acceptance of the prevalence of HIV and AIDS in Uganda by the incumbent president has been linked to the government's total dependence on aids (Tumushabe, 2006). To a large extent, Museveni's government has been totally dependent on aid from non-governmental organizations, international donors, and others. With a constant huge yearly pay by late 1999 and early 2000 to 2005, Uganda was heavily externally financed to the tune of 600 million dollars per year (Tumushabe, 2006). In reality, the early assistance was vital for the government's delivery of basic social services and amenities, reduce the prevalent high costs of basic services, goods and remuneration of its public servants, which owed to the harsh economic situation suffered in the country after the long years of despotic military leadership under the Idi Amin and Obote regimes (Tumushabe, 2006).

Accordingly, considering the economic devastation and financial apocalypse of the Museveni-led Ugandan government, as well as its corrupt tendencies, how justifiable is that the government did not embrace the prevalence of HIV and AIDS as a premise to attract financial largess? Tumushabe (2006) has argued that the Museveni government in its attempt to claim the success of HIV/AIDS eradication monopolized the press, and has given the international community a positive impression.

LOCATION OF TESTING AND GLOBAL PERCEPTION OF AFRICA

The location of testing when it comes to HIV and AIDS largely can influence the outcomes. Given the prevalent deteriorated health care systems, biological evidences have contradicted most study results in Africa. According to research, there are 70 diseases or conditions that can possibly cause false-positive reactions on HIV results in Western and non-western blocs by Johnson (2001). Many of these conditions are quite prevalent in Africa, including tuberculosis, malaria, leprosy, Q-fever, tapeworms or other parasites, and leishmaniasis. In order for tests for the conditions to work properly, it must be true that a protein (also called an antigen) will react only with the antibody that matches it. Antigen-antibody reactions are non-specific. Antibodies cross-react with antigens other than the ones that originally elicit them (Johnson, 2001). Scientists routinely ignore this well-known factor when it comes to HIV antibody tests. This questions the reason how in most cases individuals in Africa test positive and at some point test negative (Johnson, 2001). From the fore-going the argument is made that given the already destabilized health status in Africa, the HIV status of individuals may further be complicated resulting to false or wrong judgment of HIV status. This uncertainty is further worsened with the low testing ratio of some African countries. For instance, Zimbabwe government emphasized the importance of voluntary counseling and testing for HIV (VCT) in its National AIDS Policy in 1999. Between 2005 and 2010, the total number of health facilities offering HIV testing and counseling increased from 3,951,218 but still only 20% of the population knew their status in 2009 (IHAC Report, 2013).

DISCRIMINATION AGAINST HIV/AIDS PATIENTS

Another important factor to be considered as a limitation to the adequacy and accuracy of the HDI data on Africa is the staggering rate of discrimination against HIV and AIDS patients in the continent. Due to the fact that most individuals with HIV and AIDS are discriminated against, the burden of health care as well as health provisions are left on the shoulders of the family members and friends (IHAC, 2013). This to a large extent could limit hospital documentation of HIV and AIDS cases in most African societies. Given the great divide between the health care system and patients in Africa, getting adequate data from hospitals or even private clinics might be difficult, accordingly complicating the whole process of obtaining very reliable information on HIV and AIDS patients in Africa. And it is a fact that only the few rich and the well-to-do can afford hospital bills and medical care in the African continent (Mbele, 2005).

TECHNOLOGICAL CONSTRAINTS

The effectiveness of any study both for academic and development purposes is hinged on the methodology of data collection (Rolfe, 2006). To a large extent, the validity and trustworthiness of a data depends on the wideness of its coverage, its all-encompassing approach, and not on narrow estimates. In Africa, getting adequate and up-to-date records in hospitals and maternal homes is an increasing challenge. How can the HDI obtain adequate result in Africa when the health care sector is in shambles, lacking adequate finance, space, electricity and modern computer to save health records of patients? In Nigeria for instance, according to a study by Idowu et al. (2003) on the use of information technology in three government-owned health care institutions, it was found out that none of the hospitals had ever been connected to the internet. So, how can it be argued that the HDI assessment and measures are not inadequate? The study by Abdulkadir et al. (2011) indicates that the update and accuracy of medical records in Nigeria is questionable.

Similarly, in their study, where medical records handling and archiving were assessed by examining the unit record books of Radiology and other departments in six regional hospitals, they accounted thus:

“In all centres, there were variable non-documentation of patients’ age and sex, hospital number, doctors’ names and date of request. The names of patients and consultants in charge were commonly indicated. Unit record books generally suffered mutilations and in 27.2 to 33.2% of the requests, clinical information was inadequate or not provided. Radiological requests information provision and handling in our tertiary hospitals were inadequate”.

To further illustrate the weakness of HIV/AIDS reports in Africa particularly in Nigeria, according to a new revelation made known to the media:

“A medical research report in Nigeria has come up with a figure that over 7 million Nigerians have been medically proven to live with HIV while close to 5 million have been suspected to be positive to HIV. But these people have not come out boldly to either be tested for HIV or treated due to the myths and misconceptions surrounding the infection (Akingbade, 2013)”

Having identified these weaknesses based on available evidence it is in the position of this paper to go beyond mere criticisms. The next phase identifies what can be done to ensure an adequate data gathering process as it concerns HIV/AIDS in Africa.

HOW CAN HDI IMPROVE DATA COLLECTION ON HIV AND AIDS IN AFRICA?

Solution 1: Adequate and comprehensive researches.

If the HDI will tackle the perceived and unclear prevalence of HIV/AIDS in Africa, it must be certain about the number of the carriers of this disease in the continent. It is the position of this paper that the HDI under the umbrella of the UNDP must spend more on research. Adequate data-gathering techniques in Africa will not take merely a year to build but decades. UNDP must invest and develop a more adequate and sophisticated data-gathering mechanism in collaboration with the various bureaus of statistics. In doing this, if the HDI is sincere, it must work with the government agencies, adequately financing and mobilizing its activities during this period. This is because any project left in the hands of African governments is due to be “compromised”, given the kakistocratic system that has ravaged the political and social spheres in Africa.

Solution 2: Integrated electronic health record systems

The HDI must invest wisely together with the collaboration of the various national governments at the development of an adequate health care system, which will connect various government-registered clinics and hospitals together in a database at the national level and at the continental level. The integrated electronic health record system is operational in most developed societies like the United States, Canada and United Kingdom. The information contained in this database is organized primarily to support enduring, efficient and quality health care. And the database will help in sharing information about patients within the nation or across the continent. The implication this will have on the African states is not only a radical change in the health care delivery system, but also a radical improvement in recognizing the prevalent diseases that mostly result in mortality in the continent. Malaria, tuberculosis and typhoid are even more deadly diseases that kill sporadically, than HIV/AIDS.

Without an adequate health care system, diseases are further complicated by giving the wrong medications for the wrong diseases. Thus, there must be an adequate, interconnected data system managed by the HDI; otherwise, the true position of HIV/AIDS prevalence in Africa will remain elusive. It is only when the accurate number of HIV/AIDS infection is known that the adequate approach towards prevention can be devised.

Solution 3: Partner with educational institutions

There is a need for adequate partnership between research institutions in Africa and the UNDP in generating adequate data for its policy purposes. This will not only ensure for accuracy in terms of numbers but transparency in the end product of the research conducted. More also, datas generated and compiled by these institutions will not only improve the validity of adequate methodology in the research conducted on HIV/AIDS across the continent but will also contribute immensely in institutionalization of adequate research culture in the continent of Africa. This is important because one discouraging fact in conducting research on HIV/AIDS and other related health and social issues is the lack of adequate and reliable data. More also government policies across the continent is highly skewed due to this stated fact. In other to improve an adequate research culture, transparency in data collection which contributes immensely to policy making, there is a need to partner with educational institutions in the continent.

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Predictors of mortality among HIV positive adults on antiretroviral therapy in Debremarkos Referral Hospital, Northwest Ethiopia

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Globally, human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) reduces life expectancy by seven years. Mortality is high among non-treated patients in Ethiopia with about 58.1/100 person years of observation. However, the predictors of mortality have not been adequately studied. Hence, the main objective of the study was to determine predictors of mortality among HIV positive adults on antiretroviral treatment in Debremarkos Referral Hospital, Northwest Ethiopia. A facility-based retrospective cohort study design was conducted from September to February, 2013. Data were collected from 640 patients who were enrolled for treatment in Debremarkos Referral Hospital from 2005 to 2013. Proportional hazards Cox model was used to show the independent predictors of the risk of mortality. A total of 261 patients died during the follow up period. Baseline hemoglobin level of < 10 g/mm^3 (Adjusted Hazard Ratio (AHR) = 1.86, 95% CI: 1.39 to 2.64), baseline ambulatory functional status (AHR = 2.72, 95% CI: 1.90 to 3.90), bedridden functional status (AHR = 2.38, 95% CI: 1.32 to 4.27), baseline World Health Organization (WHO) staging III and IV (AHR = 2.16, 95% CI: 1.10 to 4.25), recent antiretroviral therapy (ART) adherence (AHR: 2.16, 95% CI: 1.03 to 4.56) and fair adherence (AHR = 1.88, 95%CI: 1.08-3.29) were associated with increased mortality. The risk rate of patients with unexplained chronic diarrhea and without prophylaxis for tuberculosis was increased by 1.53 and 3.98 times compared to patients without diarrhea and treated with tuberculosis prophylaxis, respectively. The mortality rate was high during early phase of treatment especially within the first 6 and 12 months. Baseline hemoglobin < 10 g/mm^3, baseline functional status-ambulatory and bedridden functional status, baseline WHO staging (stage III and IV), poor recent antiretroviral therapy adherence, chronic diarrhea and absence of tuberculosis prophylaxis were all significant predictors of mortality. Therefore, patients with the aforementioned predictors should be followed closely and frequently.

Key words: Predictors, mortality, HIV positive adults, antiretroviral therapy, Ethiopia.

INTRODUCTION

Expanding access of treatment had been contributing by 19% decline of deaths among people who are living with human immunodeficiency virus (HIV) between 2004 and 2009 (Joint United Nations Programme on HIV/AIDS (UNAIDS), 2010). A review of 14 cohort studies in high income countries showed that there is still a large discrepancy between the life expectancy of the general population and an HIV-infected individual. The death rates remain higher in HIV-infected individuals than in un-infected individuals, even when successfully treated, and that

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both AIDS and several serious non-AIDS events are more common in those with a lower CD4 cell count (WHO, 2002; Hogg et al., 2008).

Life expectancy at age 20 is decreased to 18.3 and 11.4 year for men and women who are infected by HIV, respectively (Biadgilign et al., 2012). The overall estimated mortality rate in 12 months post-antiretroviral treatment (ART) initiation is 14%. In sub-Saharan Africa (SSA), most causes of death are tuberculosis (TB), acute sepsis, cryptococca meningitis, malignancies (especially Kaposi's sarcoma and chronic diarrhea or wasting syndrome (Gupta et al., 2011; Stephen et al., 2008; Johannessen et al., 2008).

In developed countries, there is early initiation of ART with well monitoring and evaluation of the drug effects as well as patient response. Although, in Ethiopia free based ART is practiced for eight years, there is no enough data on mortality predictors once they are enrolled to treatment. The effectiveness of highly-active antiretroviral therapy (HAART) could vary from region to region because of the difference in background disease burden (such as tuberculosis or intestinal parasites), viral subtypes and possible genetic differences in drug metabolism (Massaquoi et al., 2009).

In the Debremarkos hospital, there has not been a study on mortality predictors of HIV patients on ART since the commencement of the service. Therefore, this study was designed to identify predictors of mortality among HIV positive adults who were on ART in Debremarkos Referral Hospital, Northwest Ethiopia.

METHODOLOGY

Study design, area and period

A facility-based retrospective cohort study design was conducted in Debremarkos Referral Hospital from 30th September, 2013 to 30th February, 2013.

Study population

All HIV positive adults' record in Debre Markos Referral Hospital who were on antiretroviral therapy enrolled to treatment from 30th September, 2005 to 30th February, 2013 were the source population and selected HIV positive adults' record on care and support follow up who had started ART at the hospital within the same period were included in the study. All HIV positive adults' record who were on antiretroviral therapy enrolled for treatment from 30th September, 2005 to 30th February, 2013 in Debre Markos Referral Hospital were used for source population, and selected HIV positive adults' record on care and support follow up who had started ART at the hospital within the same period were included in the study.

Eligibility criteria

All adult (≥ 15 years old) HIV positive individuals on care and support follow up who had started ART and had at least one visit in Debre Markos Referral Hospital were included. Adults with incomplete registration cards during the review who started ART from other healthcare institutions, drop outs, lost and transfer were excluded from the study.

Sample size determination

As the investigation was a cohort study, the sample size required for achieving statistically significant results was determined using two population proportion formula. Therefore, sample size was calculated by taking into account the major exposure variables and using open epi version 3.04.04 statistical package (Biadgilign et al., 2012). Among exposure variables, WHO staging is chosen as the main exposure variable of non-accidental mortality during the 6 years of follow up since it was considered to give the optimal sample size and most significant result. In this regard, a 5% level of significance (two-sided), a power of 80% and a ratio of unexposed to exposed of 1:1, estimated proportion of mortality in Ethiopia was taken as 4.1% for non-exposed group (WHO stage I and II) and 10.1% for exposed group (WHO stage III and IV) (Tsegaye and Worku, 2011; Worku and San Sebastian, 2009; Jerene and Lindtjørn, 2005) (Table 1). However, in practice, getting 320 patients in their WHO stage I and II was difficult and the rest were from stage III and IV. Thus, the total sample size was 640.

Sampling technique

Simple random sampling technique was used to recruit predetermined sample size from the clinic computerized register. First registration number was identified and computer generated number was used to select study subjects among the eligible cards. In Debremarkos Referral hospital, there were a total of 8,412 HIV patients enrolled for care and treatment between the year 2005 and 2013. To follow the patient for at least a minimum of 6 years, we included patents enrolled between September, 2005 and January, 2008 which was a total of 5,122 patients. From these patients, 273 transfer in, 24 incomplete registration, 45 lost, 259 drop, 1 stop and 76 children less than 15 years were excluded from the study, resulting in 1,646 eligible patients. The samples of 640 patient registration cards were selected randomly.

Variables of the study

The dependent variable of this study was occurrence of death and independent variables included demographic factors and clinical conditions such as WHO staging, baseline CD^{+}_{4} counts, Hgb status, opportunistic infections, concomitant illness, diagnosis/functional status, cotrimoxazole prophylaxis and base line body weight.

Operational definition

1. Incomplete card: When one of the independent variable is not registered namely, CD_4^+ cells, Hgb, WHO stage, functional status and TB status
2. Lost to follow up: Not seen since ≥ 1 month < 3 months (Worku and San Sebastian, 2009; Jerene and Lindtjørn, 2005).
3. Drop: Lost to follow up for > 3 months.
4. Transfer out: A patient referred to another health facility for care evidenced by his/her document.
5. Transfer in: A patient who started treatment I in another health institution and continued in Debremarkos hospital as evidenced by his/her registration card.

Functional status

1. Working: Able to perform usual work in or out of the house;
2. Ambulatory: Able to perform activities of daily living;

Table 1. Sample size calculation of retrospective cohort study HIV patients on ART in Debremarkos referral hospital, Northwest Ethiopia, 2005 to 2013.

Assumption	Major exposure variable	Sample size by Fleiss with CC Formula	Total number of sample size
Two-sided significance level: 0.05 Power: 80 Ratio of sample size: 1:1 Percent of Unexposed with Outcome: 4.1 Percent of Exposed with Outcome: 10.1 Odds Ratio: 0.38 Relative risk: 0.41	WHO clinical HIV staging grouped (I, II non exposed; III, IV exposed)	Number of exposed=320 Number of non-exposed=320	640

3. Bedridden: not able to perform activities of daily living (Jerene and Lindtjorn, 2005).
4. Baseline: Start of ART initiation;
5. ART regimen: Types of first line, second line, change in regimen;
6. Follow up outcomes: Lost to follow up, transfer out, adherence;
7. Mortality: if patient was known to be dead as reported by treating clinicians or community health agents, neighbor and/or relatives other than accidental causes while on ART;
8. Adherence: adherence is defined as good if adherence is > 95% (< 2 doses of 30 doses or < 3 dose of 60 dose is missed) as documented by ART physician; fair if adherence is between 85 to 94% (3 to 5 doses of 30 doses or 3 to 9 dose of 60 dose is missed) as documented by ART physician; and poor if adherence is < 85% (> 6 doses of 30 doses or > 9 dose of 60 dose is missed) as documented by ART physician;
9. Side effect: As recorded by ART physician/nurse on the patient card.

Data collection procedure

Data collecting checklist was prepared based on routine data registration protocol using the standardized ART entry and follow up form employed by the ART clinic. The data collecting checklist was used by data collectors for recording information from patients' cards.

Data quality control

To ensure quality, data were collected by ART staff nurses working in the hospital after one day training on the techniques of data collection. The completeness of data was checked by two trained supervisors so as to provide feedback in registration process and to correct when necessary. Furthermore, every night, data collectors, supervisors and principal investigators used to discuss about documenting the findings and exchange of the information. Moreover, pre-test was done on registrations that were not included in the final study.

Data processing and analysis

The data were entered in Epi data version 3.1 computer program. Prior to the analysis, the whole data were cleaned and 20% of the data was double-entered. The completeness of the data was checked. Errors related to inconsistency were verified using cross tabulation and other data exploration methods. The data was exported to statistical package for social sciences (SPSS) version 16.0. Then recorded, categorized and sorted to facilitate analysis. Then analysis done using SPSS version 16.0. Univariate Cox-proportional Hazards model was used to assess the relationship between baseline variables and mortality and calculate hazard ratios. Those variables showed statistical significance in univariate analysis with p-value of < 0.25 (David Jr., 1999) were selected for multivariable analysis and declared as statistically significant when p-value < 0.05.

Ethical consideration

Ethical clearance was obtained from the Ethical Review Board of Debremarkos University, College of Health Sciences, Department of Public Health. Permission was obtained from Debremarkos Referral Hospital and ART clinic. Verbal informed consent was obtained from responsible bodies of the hospital and ART clinic prior to the review. Confidentiality and privacy of the information were assured and maintained.

RESULTS

Between 19th September, 2005 to 30th January, 2008, 5,122 HIV patients were enrolled in Debremarkos Referral Hospital, from which 2,604 were on ART. Eventhough, 5,122 HIV patients were enrolled between 19th September, 2005 to 30th January, 2008 in Debremarkos Referral Hospital, only 2604 patients were on ART.

Basic characteristics of the cohort

Cards of six hundred and forty (379 alive and 261 death) adult HIV infected individuals were included in the present study. Among the cohort, 53.10% were females and the mean age was 35.40 years (standard deviation (SD) ± 9.62). Five hundred ninety five (93.00%) of the study participants were followers of orthodox religion and 260 (40.80%) were married. Two hundred and thirty four (36.60%) of the study participants had primary education. The median weight at base line was 50.00 kg (Inter Quartile Range (IQR) = 44.00 to 55.00 kg). Base line mean hemoglobin was 12.23 (IQR = 10.60 to 14.00). The base line median CD4 count was 115.00 cells/µl (IQR = 63.25 to 164.75). About 399 (62.30%) were at WHO clinical stage III during the initiation of ART. Moreover, 415 (64.80%) of the participants were in working functional

Table 2. Socio-demographic characteristics of patients initiated ART at Debremarkos Referral Hospital, 2005-2013 (N=640).

Variable	Alive (n=379, %)	Death (n=261, %)
Sex		
Male	176 (46.40)	124 (47.50)
Female	203 (53.60)	137 (52.50)
Age (years)		
15-29	107 (16.70)	82 (12.80)
30-44	214 (33.40)	118 (18.40)
45-59	52 (8.10)	55 (8.60)
≥ 60	6 (0.90)	6 (0.90)
Residence		
Urban	275 (43.00)	181 (28.30)
Rural	104 (16.20)	80 (12.50)
Ethnicity		
Amhara	369 (57.70)	258 (40.30)
Oromo	5 (0.80)	1 (0.20)
Tigray	5 (0.80)	2 (0.30)
Marital status		
Married	168 (26.20)	93 (14.50)
Widowed	77 (12.00)	47 (7.30)
Never married	41 (6.40)	32 (5.00)
Divorced	77 (12.00)	71 (11.10)
Separated	16 (2.50)	18 (2.80)
Educational status		
Not educated	89 (13.90)	78 (12.20)
Primary	149 (23.30)	85 (13.30)
Secondary	94 (14.70)	66 (10.30)
Tertiary	47 (7.30)	32 (5.00)
Occupation status		
Merchant	87 (13.60)	38 (5.90)
NGO employee	10 (1.60)	7 (1.10)
Gov't employee	82 (12.80)	63 (9.80)
Day laborer	69 (10.80)	48 (7.50)
"Jobless"	27 (4.20)	13 (2.00)
Farmer	53 (8.3)	47 (7.30)
Others	51 (8.0)	45 (7.00)

functional status and 196 (30.60%) were ambulatory in the time of ART initiation (Tables 2 and 3).

Baseline opportunistic infections were recorded in the patient registration; 92 (14.38%), 6 (0.94%), 234 (36.56%), 203 (31.79%) and 381 (59.53%) had esophageal candidacies, Kaposi's sarcoma, oral recurrent candidacies, unexplained persistent diarrhea and fever, respectively. Twenty four patients (3.75%) had presumed diagnosis of pneumocystic carnii pneumonia (PCP). Patients with unexplained weight loss > 10% were 103 (16.09%) and with recurrent severe bacterial pneumonia, active TB, herpes simplex, recurrent upper respiratory tract infections and herpes zoster were 197 (30.78%), 89 (13.91%), 94 (1.68%), 192 (30%) and 101 (15.75%), respectively (Figure 1).

Predictors of mortality

This study tried to identify the predictors of mortality among adult HIV positive patients on ART. Accordingly, baseline hemoglobin level of < 10 g/mm^3 (AHR = 1.88, 95% CI: 1.39 to 2.64), baseline ambulatory functional status (AHR = 2.72, 95% CI: 1.90 to 3.90), bedridden functional status (AHR = 2.38, 95% CI: 1.32 to 4.27), baseline WHO stages III and IV (AHR = 2.16, 95% CI: 1.10 to 4.25), side effects of drug (AHR = 7.81, 95% CI: 4.58 to 13.31), recent ART adherence (AHR = 2.16, 95% CI: 1.03 to 4.56), fair adherence (AHR = 1.88, 95% CI: 1.08 to 3.29), unexplained persistent chronic diarrhea (AHR = 1.53, 95% CI: 1.09 to 2.15) and absence of TB prophylaxis (AHR = 3.98, 95% CI = 1.87, 8.44) were significant predictor of mortality among patients on ART (Tables 4 and 5).

DISCUSSION

In this retrospective cohort study, 261 patients died resulting in seven years overall mortality rate of 10.74/100 person-year observation (PYO). Meanwhile, the independent predictors of death were base line hemoglobin < 10 g/mm^3, ambulatory and bedridden functional status, advanced WHO clinical stage, patients with no recorded side effect of the drug, poor adherence for ART drug, presence of unexplained persistent diarrhea and absence of TB prophylaxis recently.

In this study, after initiation of the antiretroviral treatment, the incidence of mortality was 10.74/100 PYO. Many studies showed that mortality incidence among patients taking ART is decreasing since the discovery of the drug (Jerene and Lindtjørn, 2005; Jerene and Næss et al., 2006; Jerene et al., 2006; Ergete, 2011). Estimated mortality rate in ART+ group was 15.40/100 PYO and most of the death occurred during the first three months (Jerene and Lindtjørn, 2005). Mortality incidence in pre-HAART and HAART group was 58.1/100 PYO (Jerene et al., 2006) and 25.90/100 PYO (Tsegaye and Worku, 2011). In this regard, previous studies showed that mortality is declined by 65.00% in patients on HAART. This study revealed that mortality was decreased compared to the previous studies. This might be due to the relatively longer study period covering both early and recent phases of treatment. People's awareness has been increased so that they sought treatment in relatively less advanced disease stage. Moreover, treatment guidelines become more familiar to health professionals

Table 3. Baseline clinical and laboratory information of 640 patients initiated ART at Debremarkos Referral Hospital, 2005 to 2013.

Variable	Alive (n=379, %)	Death (n=261, %)
Base line prophylaxis		
Not given	35 (9.20)	38 (14.60)
Cotrmoxazole	338 (89.20)	212 (81.20)
INH	4 (1.10)	7 (2.70)
Fluconazole	2 (0.50)	4 (1.50)
Base line weight (kg)		
<60	333 (87.90)	237 (90.80)
≥60	46 (12.10)	24 (9.20)
Base line CD^{4+} (cells/µl)		
<50	55 (14.50)	66 (25.40)
50-99	74 (19.50)	64 (24.60)
100-200	205 (54.10)	108 (41.50)
201-350	44 (11.60)	22 (8.50)
>350	1 (0.30)	0 (0.00)
Baseline Hgb (g/dl)		
<10	34 (11.30)	69 (33.20)
≥10	268 (88.70)	139 (66.80)
Not recorded	77 (12.00)	53 (8.28)
Functional Status		
Working	299 (78.90)	125 (47.90)
Ambulatory	116 (44.40)	9 (2.40)
Bedridden	71 (18.70)	20 (7.70)
WHO staging		
Stage I and II	109 (17.03)	35 (5.47)
Stage III and IV	270 (42.20)	226 (35.31)
ART eligibility criteria		
WHO staging	40 (10.60)	17 (6.50)
Immunologic	108 (28.50)	48 (18.40)
Both	231 (60.90)	196 (75.10)
Side effect		
Yes	212 (55.90)	25 (9.60)
No	167 (44.10)	236 (90.40)
ART adherence		
Good	369 (97.40)	215 (82.40)
Fair	4 (1.10)	17 (6.50)
Poor	6 (1.60)	29 (11.10)

and the care given to patients has been improving. Prior free- ART treatment, no adequate voluntary counseling and testing (VCT) services and high prevalence of HIV related stigma all lead to advanced presentation of patients to clinical care.

This study showed that high mortality of patients during early phase of treatment in line with different studies (Jerene et al., 2006; Amuron et al., 2011; Assefa et al., 2011; Mulissa et al., 2010; Dean et. al, 2011; Dupont, 1990; Schoenfeld and Richter, 1982; Mageda et al., 2012) even though, none of the observational studies indicated the exact cause of high mortality at initial phases of treatment.

In the present study, patients with hemoglobin < 10 g/dl at baseline were at high risk of death. Study on cause-specific mortality indicators study from low and middle income countries (LMIC) (Sabin et al., 2009) in Tanzania rural hospital (Jerene et al., 2006), studies in Ethiopia (Amuron et al., 2011; Abose and Enkusilassie, 2012; Tsehaineh, 2010) indicated that patients with anemia were at high risk of death after ART initiation. The possible explanation for this phenomenon could be 234 of the patients took zidovudine (ZDV) which is responsible for persistent anemia as indicated in other study (Kebebew, 2011). Functional status during ART initiation was significant predictor of mortality. Patients in ambulatory functional status and bedridden were at increased hazard rate of death by 2.72 and 2.38 times than patients in working functional status, respectively. This finding is consistent with many studies done in Ethiopia; for example, study done in eastern Ethiopia showed a 4.09 time of mortality risk for patients in bedridden functional status than working ones (Solomon, 2011).

As stated in southern Ethiopia, the risk of death among working patients is lowered by 55% than bedridden patients during ART initiation (Amuron et al., 2011). The mortality risk of patients in ambulatory and bedridden functional status is 2.11 and 3.35 times compared to working patients in Military Hospital in Addis Ababa, Ethiopia (David Jr., 1999). Ambulatory and bedridden functional status is 2.87 and 6.90 times at risk of death than the working status (Mageda et al., 2012). The risk of mortality was increased in ambulatory and bedridden patients by 1.53 and 2.99 times than working patients (Jerene and Lindtjorn, 2005). Therefore, patients who are of ambulatory and bedridden functional status should get due attention in order to reduce their mortality rate.

In this study, patients with fair and poor ART adherence were at high risk of death (2.16 and 1.88) times than those with good adherence. In line with this, patients who have poor adherence were at risk of death by 3.92 than with those who have good adherence patients in Addis Ababa (Kebebew, 2011). Eventhough adherence assessment technique was not as such reliable in the current study (self reported), it was a significant predictor of death. This could be an alarm for further study of the reasons for adherence and also to increase the survivals of patients by establishing ways to good adherence. So, patients with poor ART adherence should be followed more frequently to decrease risk of death.

Late presentation of patients for clinical care was seen in this study in which majority of patients were at WHO clinical stages III and IV. This resulted in increased risk of

Table 4. Bivariate and multivariable Cox-regression analysis of clinical characteristics of the cohort studied (n=640 patients) in Debremarkos referral hospital, 2005-2013.

Variables	Frequency		CHR (95% CI)	AHR (95% CI)	P- value
Baseline prophylaxis	**Alive**	**Dead**			
Not given	35	38	1	-	-
Cotrmoxazole	338	212	1.23 (0.74-0.94)	1.75 (0.61-5.06)	0.29
INH	4	7	0.66 (0.55-2.76)	0.83 (0.52-1.39)	0.45
Fluconazole	2	4	1.24 (0.44-3.49)	2.94 (0.49-17.48)	0.23
Base line weight (kg)					
<60	333	237	1.37 (0.90-2.09)	1.02 (0.57-1.83)	0.92
≥60	46	24	1	1	
Hemoglobin (g/dl)					
<10	34	69	2.76 (2.06-3.69)	1.86 (1.31-2.64)	0.0001*
≥10	268	139	1	1	
Functional Status					
Working	299	125	1	1	-
Ambulatory	116	9	3.24 (2.51-4.18)	2.72 (1.90-3.90)	0.0001*
Bedridden	71	20	4.18 (2.59-6.74)	2.38 (1.32-4.27)	0.004*
Baseline CD^{4+} (cells/µl)					
<50	100	21	1	1	-
50-99	130	8	0.75 (0.53-1.05)	1.02 (0.63-1.64)	0.93
100-200	301	12	0.51 (0.37-0.69)	1.11 (0.71-1.73)	0.64
≥201	60	7	0.47 (0.29-0.77)	0.70 (0.34-1.45)	0.34
WHO staging					
Stage I and II	109	35	1	1	0.02*
Stage III and IV	270	226	2.23 (1.56-3.19)	2.16 (1.10-4.25)	
ART eligibility criteria					
WHO staging	40	17	1	1	-
Immunologic	108	48	1.04 (0.60-1.81)	1.50 (0.67-3.34)	0.31
Both	231	196	1.81 (1.10-2.98)	1.28 (0.69-2.39)	0.42
Side effect					
Yes	212	25	1	1	0.0001*
No	167	236	8.02 (5.31-12.14)	7.81 (4.58-13.31)	
ART adherence					
Good	369	215	1	1	-
Fair	4	17	3.49 (2.12-5.74)	2.16 (1.03-4.56)	0.04*
Poor	6	29	4.10 (2.76-6.08)	1.88 (1.08-3.29)	0.02*

*Significant at p<0.05, CI= confidence interval, ** marginally significant at p<0.05, AHR =Adjusted Hazard Ratio; CHR=Crude Hazard Ratio

death among patients by 2.16 times than patients at stages I and II. This is similar with studies in Tanzania which was 4.16 times risk of death in advanced WHO stage (Johannessen et al., 2008). But the difference in magnitude may be due to many subjects (201) in stage IV in Tanzanian study. Also, studies in Ethiopia supported this finding (Worku and San Sebastian, 2009; David Jr., 1999). Moreover patients in advanced clinical stages are prone for TB infection (Mageda et al., 2012; Tsehaineh, 2010; David Jr., 1999). This was evidenced that absence

Table 5. Bivariate and multivariate Cox regression analysis of base line opportunistic infection among ART follow up patients (n=640) in Debremarkos referral hospital, 2005-2013.

Opportunistic infections	Frequency		CHR (95%CI)	AHR (95% CI)	p-value
Esophageal candidacies	**Alive**	**Dead**			
Yes	3	31	1	1	0.58
No	30	184	0.68 (0.46-1.00)	0.89 (0.60-1.33)	
Oral recurrent candidacies					
Yes	9	73	1	1	0.06
No	24	142	0.48 (0.37-0.68)	1.35 (0.98-1.87)	
Unexplained chronic diarrhea (> 1 month)					
Yes	4	68	1.43 (1.07-1.92)	1.53 (1.09-2.15)	0.01*
No	29	147	1	1	
Unexplained wt loss >10%					
Yes	2	23	1	1	0.15
No	31	193	0.59 (0.44-0.79)	0.76 (0.52-1.11)	
Severe bacterial pneumonia					
Yes	55	45	1	1	0.13
No	28	170	0.55 (0.32-0.95)	0.54 (0.24-1.21)	
Recurrent URTI					
Yes	4	27	1	1	0.67
No	30	189	0.82 (0.63-1.06)	0.93 (0.67-1.28)	
Herpes zoster					
Yes	61	39	1.01 (0.72-14.22)	1.32 (0.86-2.03)	0.19
No	318	221	1	1	
TB screened during ART start					
On treatment	5	41	3.90 (2.77-5.48)	2.33 (0.82-6.60)	-
Positive	8	26	3.46 (2.30-5.19)	2.07 (0.73-5.82)	0.27
Negative	366	193	1	1	0.11
TB prophylaxis given					
Yes	97	11	1	1	0.0001*
No	282	249	5.85 (3.20-10.70)	3.98 (1.87-8.44)	
TB treatment recently					
Yes	18	67	3.18 (2.41-4.21)	1.12 (0.41-3.08)	0.81
No	361	193	1	1	

*Significant at $p < 0.05$, CI= confidence interval, AHR =Adjusted Hazard Ratio; CHR = crude hazard ratio.

of TB prophylaxis is risk for death by 3.98 times than those with TB prophylaxis. Therefore, patients in advanced clinical stage were highly at risk of death and may be because of high prevalence of opportunistic infections (OI) including TB that calls an attention for routine screening and provision of prophylaxis as per the guideline. Patients with side effect survive more than those patients with no recorded side effects. Probably this is due to high mortality rate in early periods of treatment in which side effects are not commonly seen. Unexplained chronic diarrhea increased risk of death by 1.53 times. Studies in LMIC on cause-specific mortality predictors among adult on ART patients show that chronic diarrhea contributes (10.00 to 25.00%) to death compared to other causes of

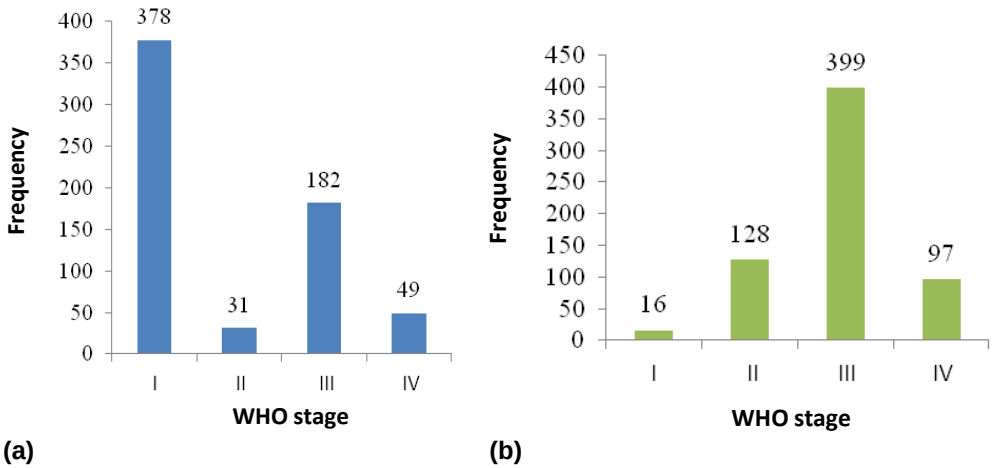

Figure 1. Baseline and recent WHO clinical stages of patients on ART in Debremarkos referral hospital, 2005-2013. (a) Recent WHO staging, (b) Baseline WHO staging.

death (Sabin et al., 2009). Therefore, patients with unexplained diarrhea should be treated accordingly and to be closely followed to decrease risk of death.

Conclusion

High mortality rate was observed during early phase of ART especially within the first 6 and 12 months. The independent predictors of mortality were lower baseline hemoglobin, being in ambulatory and bedridden functional statuses, advanced WHO clinical stage, poor ART adherence, non-recognition of side effects of drugs, non-provision of TB prophylaxis and unexplained persistent diarrhea.

RECOMMENDATIONS

For clinical practitioners

1. Patients being on ambulatory and bedridden functional status should be assessed for other possible concomitant disease conditions and treated with closer follow up so as to minimize the risk of death.
2. Hemoglobin should be measured at every visit and re-adjust medications that aggravate anemia since it is main predictor of death.
3. Patients with unexplained chronic diarrhea, oral candidacies, and herpes zoster should be followed with special attention and these symptoms should be treated promptly.
4. Since poor adherence to ART is significant predictor of mortality, every patient has to be counseled intensively than what is done previously.
5. Important clinical characteristics of patients like WHO staging, CD4 count, Hgb and other OIs should be documented correctly and regularly.

For adherence supporters, case managers and counselors

1. These groups of the health team should access health status information of patients particularly on advanced age, being in ambulatory and bedridden functional status.
2. Adherence preparation, supporting and assessment mechanisms must be employed.

For researchers

The cause for early mortality should be studied further.

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UPCOMING CONFERENCES

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