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Chikere CB, Omoni VT and Chikere BO (2008). Distribution of potential nosocomial pathogens in a hospital environment. *Afr. J. Biotechnol.* 7: 3535-3539.

Moran GJ, Amii RN, Abrahamian FM, Talan DA (2005). Methicillinresistant *Staphylococcus aureus* in community-acquired skin infections. *Emerg. Infect. Dis.* 11: 928-930.

Pitout JDD, Church DL, Gregson DB, Chow BL, McCracken M, Mulvey M, Laupland KB (2007). Molecular epidemiology of CTXM-producing *Escherichia coli* in the Calgary Health Region: emergence of CTX-M-15-producing isolates. *Antimicrob. Agents Chemother.* 51: 1281-1286.

Pelczar JR, Harley JP, Klein DA (1993). *Microbiology: Concepts and Applications*. McGraw-Hill Inc., New York, pp. 591-603.

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Full Length Research Paper

Creating a high-throughput screening database to propose ligands capable of modulating the HIV-1 protease receptor

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Accepted 15 May, 2013

This is a report of a *de novo* design study that aimed to identify novel structures capable of inhibiting the human immune deficiency virus (HIV-1) protease ligand binding pocket (HIV-1 PR_LBP). Baseline information regarding ligand binding modality and affinity was obtained through analysis of the pdb crystallographic depositions describing the HIV-1 PR enzyme complexed with small molecule inhibitors currently available on the Protein Data Bank (PDB). Molecular visualisation and modelling was carried out using SYBYL[®] 1.1, and *in silico* predicted ligand binding affinity (LBA) was quantified using XSCORE_V1.3. The *de novo* design phase of the study was based on the utilisation of the bound coordinates of Lopinavir. This particular HIV-1 protease (HIV-1 PR) inhibitor was selected as a template owing to its superior *in vivo* activity and unique binding modality. Based on literature derived data, the cyclic urea moiety of Lopinavir was retained as a seed fragment, overlaid onto its counterpart moiety and planted into the HIV-1 PR_LBP with growth being allowed according to defined parameters utilising the genetic algorithm embedded in the GROW module of LIGBUILDER[®]V1.2. The result was the identification of 200 *de novo* designed structures with a predicted *in silico* ligand binding affinity (LBA) (pK_d) ranging between 9.63 and 10.00. A smaller cohort ($n = 35$) was also Lipinski rule of 5 compliant. The implication of this study consequently is that this series of novel structures may be compiled into a library that may be of utility in high throughput screening (HTS) processes and future iterative optimisation.

Key words: High-throughput screening (HTS), protein data bank (PDB) depositions, ligand binding pocket (LBP), ligand binding affinity (LBA), human immune deficiency virus (HIV)-1 protease (HIV-1 PR), acquired immune deficiency syndrome (AIDS).

INTRODUCTION

Contemporary rational drug design is often attempted through a *de novo* approach. Ligand binding pocket (LBP) mapping and the identification of molecular moieties identified through X-ray crystallography as critical for molecular stabilisation are retained in the context of the creation of seed on which growing sites may be assigned

such that novel affinity attachment may be sustained. Available software typically allows this process to be highly user driven such that the *de novo* designed structures lie well within Lipinski's rules for predicted bioavailability and low toxicity, and are also synthetically feasible (Lipinski et al., 2001). The value of the *de novo*

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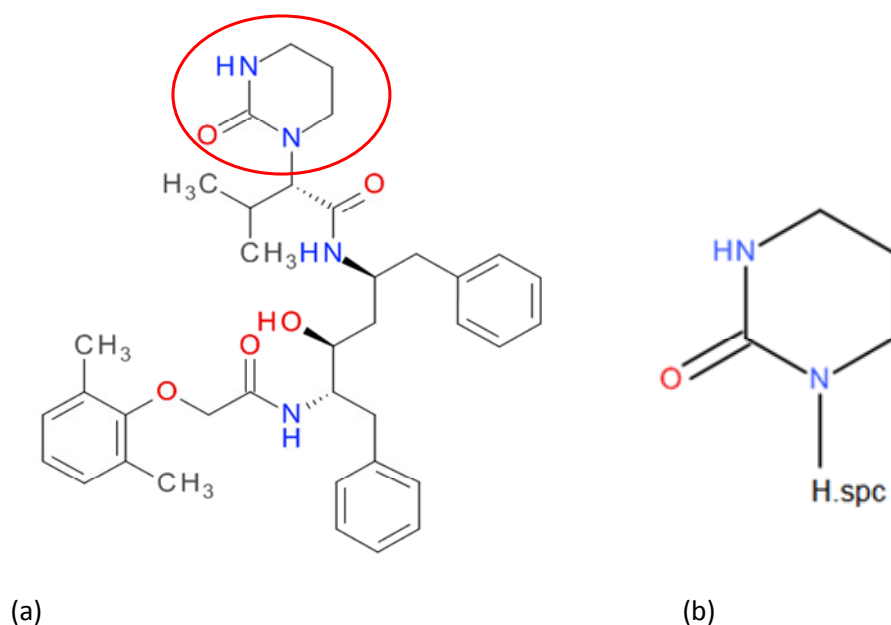


Figure 1. (a) The 2-D structure of the Lopinavir molecule with the cyclic urea moiety encircled in red whose chemical change is shown in Figure 1b. (b) The cyclic urea moiety whose adjacent Sp3 carbon atom was changed to H.sp3.

approach is speed and low cost, together with the ability to yield novel structures with proven affinity for their target and which consequently represent valid candidates for further optimization (Audie et al., 2013; Mandal et al., 2009). They are also valuable candidates for inclusion into molecular databases for high-throughput screening (HTS).

MATERIALS AND METHODS

The X-ray crystallographic depositions describing the bound co-ordinates of the HIV-1 PR enzyme bound to small molecule inhibitors available on the Protein Data Bank (PDB) between 1999 to 2004 were identified. These 12 depositions specifically 1EBW (Andersson et al., 2003), 1EBY (Andersson et al., 2003), 1EBZ (Andersson et al., 2003), 1EC0 (Lindberg et al., 2004), 1EC1 (Andersson et al., 2003), 1EC2 (Andersson et al., 2003), 1EC3 (Andersson et al., 2003), 1D4I (Andersson et al., 2003), 1D4H (Andersson et al., 2003), 1W5V (Lindberg et al., 2004), 1W5X (Lindberg et al., 2004) and 1W5Y (Lindberg et al., 2004) were read into the molecular visualisation and editing programme SYBYL[®] 1.1 (SYBYL 7.3 Tripos International, 1699). Each individual deposition was edited in SYBYL[®] 1.1 such that at the end of this process a file saved in *mol2* format containing the bound co-ordinates of each small molecule and another saved in PDB format containing the *apo* receptor devoid of all water molecules lying at the distance $\leq 5\text{\AA}$ of the LBP were generated. These files were exported to XSCORE_V1.3 (Wang et al., 1998). The score algorithm was then utilised in order to calculate the *in silico* predicted affinity (pK_d) between each HIV-1 PR conformation and its respective cognate small molecule which outcomes are shown in Figure 8. This

process effectively produced baseline affinity data which was set as benchmark for comparison in the *de novo* design phase of the study.

The *de novo* design phase of the study was based on the bound co-ordinates of the HIV-1 PR inhibiting small molecule Lopinavir complexed with the HIV-1 PR enzyme as described in the PDB deposition 1MUI. This particular deposition was selected based on the fact that Lopinavir is recognised to be a high affinity ligand with a unique binding modality for the HIV-1 PR_LBP (Stoll et al., 2002). The bound crystallographic co-ordinates of Lopinavir were consequently read into SYBYL[®] 1.1 such that seed fragments could be created for use in the *de novo* drug design phase of the study. During the seed creation phase, the cyclic urea moiety was retained. Retention of this cyclic urea was based on the fact that crystallographic evidence was suggestive of the fact that this moiety was capable of forging a novel hydrogen bonding arrangement within the HIV-1 PR_LBP, specifically with Asp²⁹ that had not been observed with other HIV-1 PR inhibitors. Furthermore, hydrogen bonding at Asp²⁹ has been correlated with significant potency gains for this class of drug.

Based on this evidence, all the chemical moieties extraneous to the cyclic urea of Lopinavir were edited in SYBYL[®] 1.1. Subsequently, an atom type change from Sp3 carbon atom to H.sp3 hydrogen was effected as shown in Figure 1b. This was important in order to direct molecular growth during the *de novo* design process.

De novo design was carried out using LIGBUILDER[®]V1.2 (Wang et al., 2000). During the first stage of the process, the bound co-ordinates of Lopinavir were used as probes in order to delineate the 3-dimensional (3D) volume and the chemical nature of the perimeter of HIV-1 PR enzyme as described in PDB ID 1MUI and in Figures 9-11. This was carried out using the POCKET algorithm of LIGBUILDER[®]V1.2.

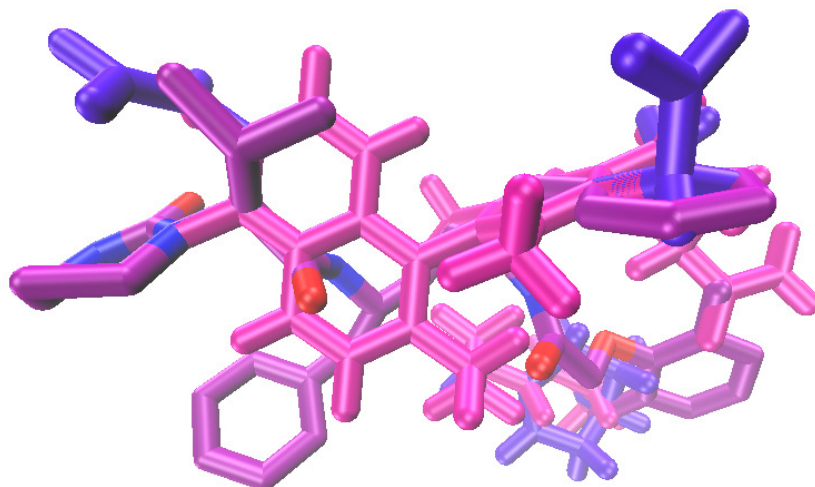


Figure 2. Superimposition of the highest affinity *de novo* molecules for family 1 (shown in violet and magenta) onto Lopinavir (shown according to molecular type).

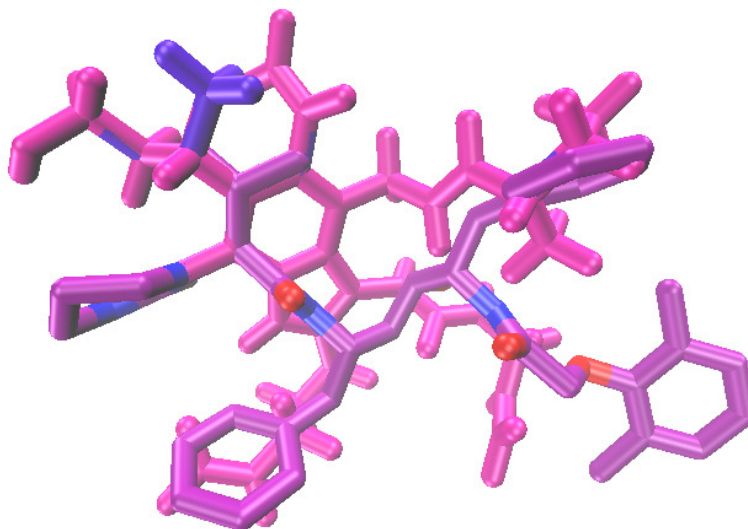


Figure 3. Superimposition of the highest affinity *de novo* molecules for family 2 (shown in violet and magenta) onto Lopinavir (shown according to molecular type).

The seed fragment created in SYBYL[®] 1.1 with 3D co-ordinates identical to its counterpart moiety in Lopinavir and having a pre-designated growing site was then directed into the HIV-1 PR_LBP with molecular growth being allowed to occur according to the parameters of the generic algorithm embedded in the GROW module of LIGBUILDER[®]V1.2. This process resulted in the elaboration of a number of analog series ($n = 6$) containing varying amounts of molecular structures whose predicted *in silico* affinity (pK_d), molecular weight (Daltons/Da) and logP were quantified as shown in Figure 12-14 respectively. The binding poses of the highest affinity members of each family are superimposed onto the bound co-ordinate of Lopinavir as shown in Figures 2 to 7.

RESULTS AND DISCUSSION

All of the small molecule HIV-1 PR inhibitors which were utilised during the baseline data establishment stage of the study were assessed for Lipinski rule of 5 (predictors of *in vivo* bioavailability) rule compliance. It was interesting to note that all of these molecules which are either currently being utilised clinically namely Lopinavir or which are currently under experimental evaluation did not comply with Lipinski's rules.

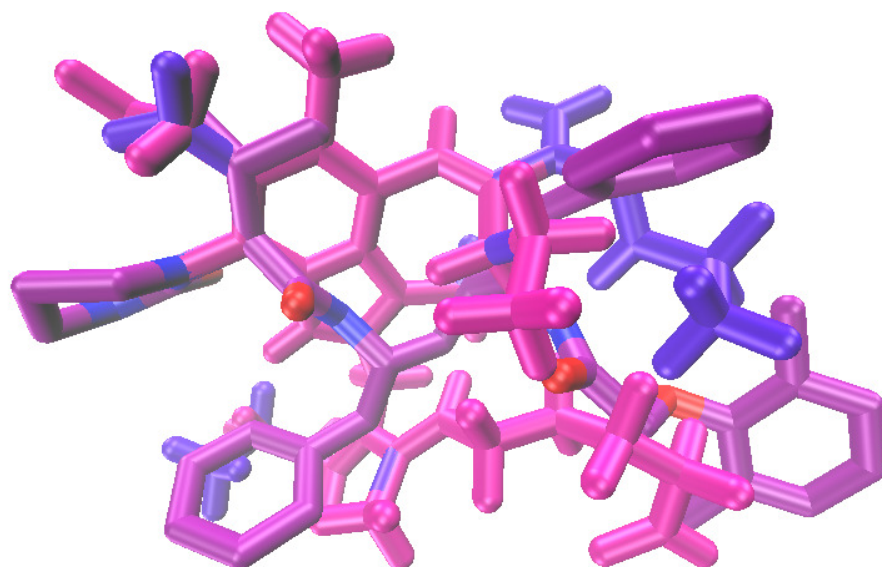


Figure 4. Superimposition of the highest affinity *de novo* molecules for family 3 (shown in violet and magenta) onto Lopinavir (shown according to molecular type).

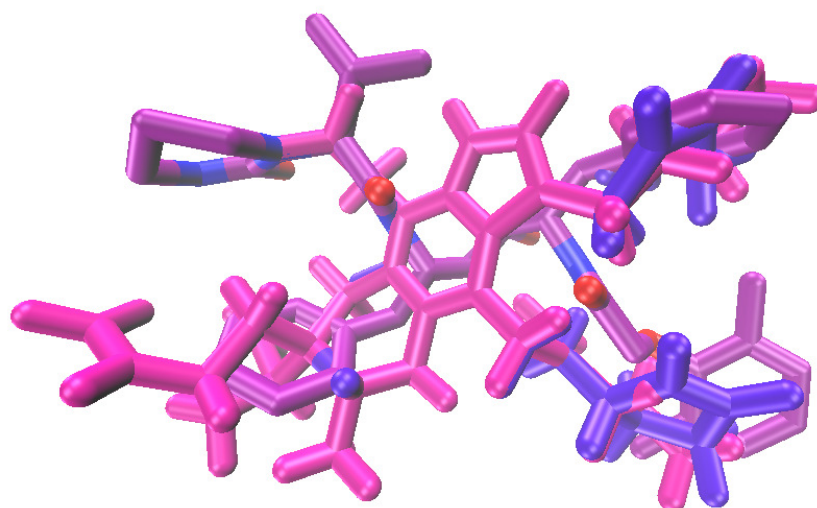


Figure 5. Superimposition of the highest affinity *de novo* molecules for Family 4 (shown in violet and magenta) onto Lopinavir (shown according to molecular type).

In all cases, non-compliance was attributed to a molecular weight that exceeded the cut-off value of 500 recommended by Lipinski et al. (2001) for acceptable *in vivo* bioavailability. Their molecular weight ranged from a minimum of 610 for 1D4H to a maximum molecular weight of 778 for 1EC1. All other molecules except 1D4H and 1D4I further violated Lipinski's rules with respect to the number of hydrogen bond donating and accepting

moieties, and 1EC1 also had a logP value of 6. All respective outcomes are shown in Table 1.

This data further reinforces the notion that there is scope for the design of improved novel members of this drug class. Given that Lipinski et al. (2001) recommend compliance with their rules in order to ensure acceptable bioavailability, and given also that evidence points to the fact the greater the number and extent to which these

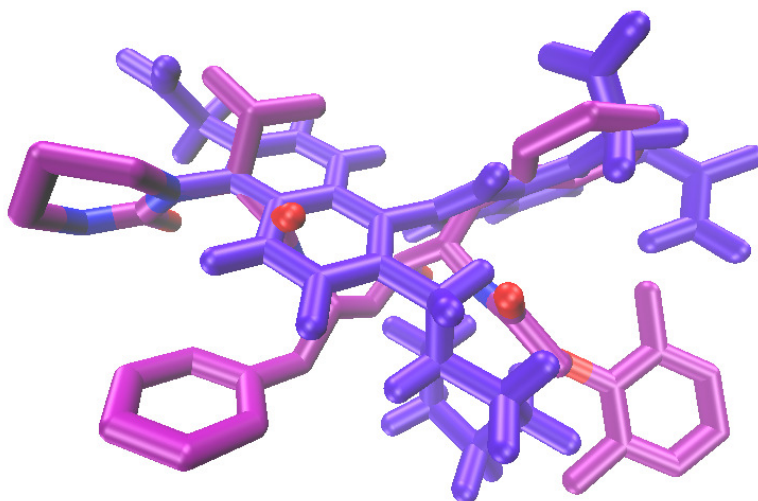


Figure 6. Superimposition of the only *de novo* molecule for family 5 (shown in violet) onto Lopinavir (shown according to molecular type).

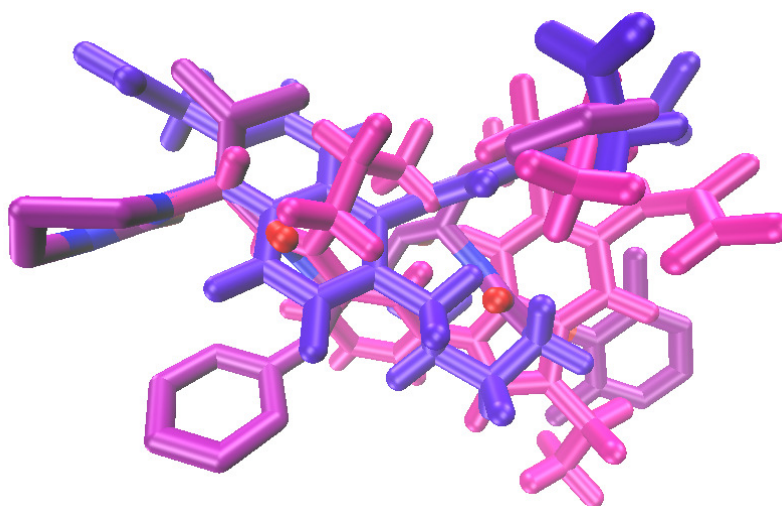


Figure 7. Superimposition of the highest affinity *de novo* molecules for family 4 (shown in violet and magenta) onto Lopinavir (shown according to molecular type).

rules are violated the lower is the predicted bioavailability, then the implication is that fine tuning of these HIV-1 PR inhibitors which are already being used successfully could result in novel structures with enhanced *in vivo* performance which could, in turn, imply decreased frequency of administration, better patient compliance and better overall disease management (David et al., 2013).. Furthermore, in a scenario in which drug resistance is an issue, increased patient compliance may also reduce the emergence of resistant strains.

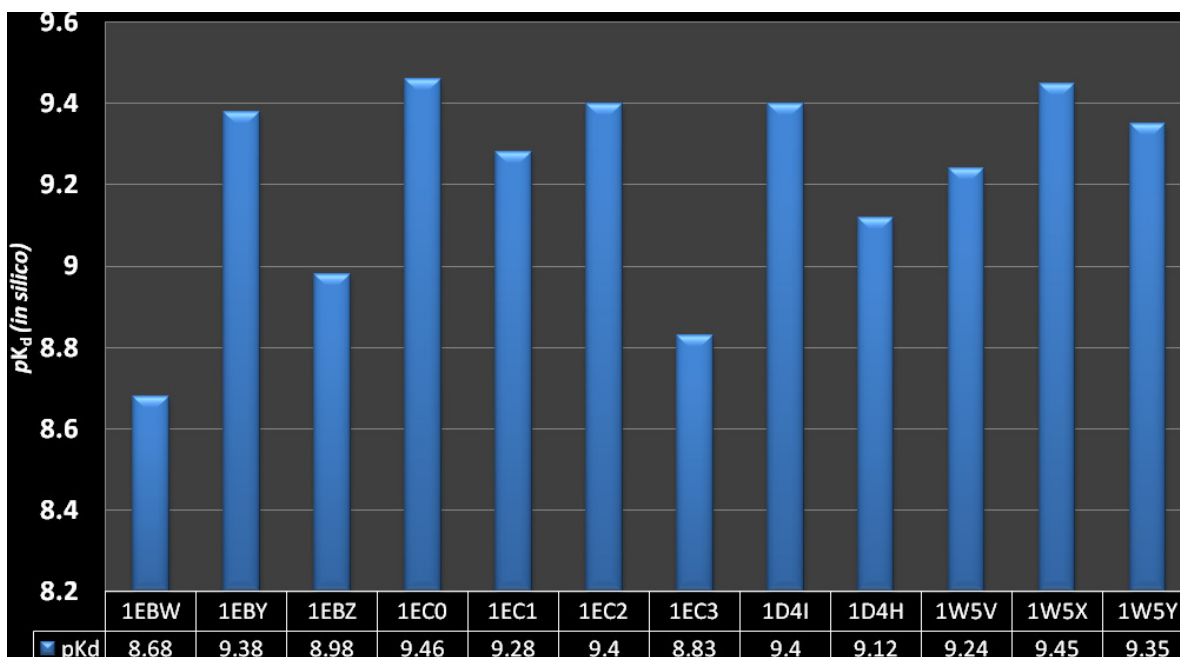
The *de novo* approach adopted in this study consequently attempted to identify novel high affinity HIV-1 PR inhibitors that were also Lipinski rule compliant. Lopinavir (PDB ID 1MUI) was selected as a template from which fragment seed structures were created owing to its quantified *in silico* ($pK_d = 8.44$) and *in vitro* ($K_i = 1.3$ pM) high affinity for the HIV-1 PR. Furthermore, its unique binding modality, coupled with the fact that its cyclic urea moiety was observed crystallographically to be capable of forging a hydrogen bond arrangement with

Table 1. The Lipinski Rule of 5 parameters for the selected PDB depositions and for Lopinavir.

PDB ID (Ligand ID)	Property	Pass/Fail the Lipinski rule of 5
IMU1 (AB1_100)	Molecular Weight = 628	Fail
	LogP = 4.8	Pass
	Number of Hydrogen donors = 4	Pass
	Number of Hydrogen acceptors = 9	Pass
1D4H (BEH)	Molecular Weight = 610	Fail
	LogP = 4.5	Pass
	Number of Hydrogen bond donors = 5	Pass
	Number of Hydrogen bond acceptors = 9	Pass
1D4I (BEG)	Molecular Weight = 636	Fail
	LogP = 3.7	Pass
	Number of Hydrogen bond donors = 5	Pass
	Number of Hydrogen bond acceptors = 9	Pass
1EBW (BEI)	Molecular Weight = 642	Fail
	LogP = 3.9	Pass
	Number of Hydrogen donors = 6	Fail
	Number of Hydrogen acceptors = 12	Fail
1EBY (BEB)	Molecular Weight = 652	Fail
	LogP = 3.4	Pass
	Number of Hydrogen bond donors = 6	Fail
	Number of Hydrogen bond acceptors = 10	Pass
1EBZ (BEC)	Molecular Weight = 633	Fail
	LogP = 3.2	Pass
	Number of Hydrogen bond donors = 6	Fail
	Number of Hydrogen bond acceptors = 11	Fail
1EC0 (BED)	Molecular Weight = 688	Fail
	LogP = 3.7	Pass
	Number of Hydrogen bond donors = 6	Fail
	Number of Hydrogen bond acceptors = 10	Pass
1EC1 (BEE)	Molecular Weight = 778	Fail
	LogP = 6.0	Fail
	Number of Hydrogen bond donors = 6	Fail
	Number of Hydrogen bond acceptors = 12	Fail
1EC2 (BEJ)	Molecular Weight = 768	Fail
	LogP = 4.3	Pass
	Number of Hydrogen bond donors = 6	Fail
	Number of Hydrogen bond acceptors = 14	Fail
1EC3 (MS3)	Molecular Weight = 768	Fail
	LogP = 3.8	Pass
	Number of Hydrogen bond donors = 6	Fail
	Number of Hydrogen bond acceptors = 14	Fail

Table 1. Contd.

1W5V (BE3_1100)	Molecular Weight = 688	Fail
	LogP = 3.7	Pass
	Number of Hydrogen bond donors = 6	Fail
	Number of Hydrogen bond acceptors = 10	Pass
1W5X (BE5_501)	Molecular Weight = 724	Fail
	LogP = 4	Pass
	Number of Hydrogen bond donors = 6	Fail
	Number of Hydrogen bond acceptors = 10	Pass
1W5Y (BE6_1100)	Molecular Weight = 724	Fail
	LogP = 4	Pass
	Number of Hydrogen bond donors = 6	Fail
	Number of Hydrogen bond acceptors = 10	Pass

Figure 8. A graph showing the pK_a (*in silico*) for the twelve selected PDB depositions.

Asp²⁹ which has not, to date, been observed with other approved HIV-1 PR inhibitors, and established this drug as particularly interesting from a drug design point of view (Stoll et al., 2002).

Also, as evidenced in Table 1, Lopinavir was found to be Lipinski rule non-compliant exclusively from a molecular weight perspective, the implication being that it was a molecule that did not require radical intervention in order to ensure Lipinski rule compliance. The *de novo*

approach adopted in this study consequently attempted to preserve the HIV-1 PR inhibitory action of Lopinavir and to design lower molecular weight molecules with a binding modality similar to that of Lopinavir. Maintenance of a binding modality to the HIV-1 PR enzyme similar to that of Lopinavir was approached through the creation of a seed structure that incorporated the moieties considered essential to the unique interaction of Lopinavir to the HIV-1 PR_LBP. Specifically, this included the

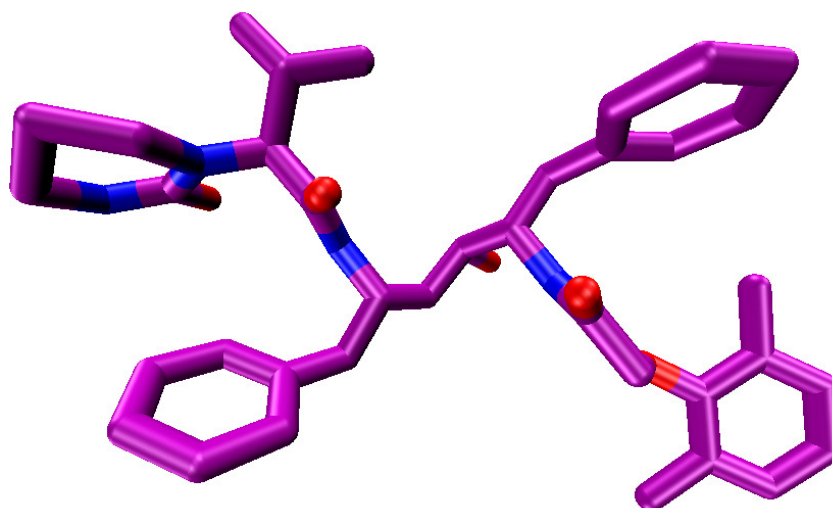


Figure 9. The Lopinavir molecule with the cyclic urea encircled rendered in VMD (Humphrey et al., 1996).

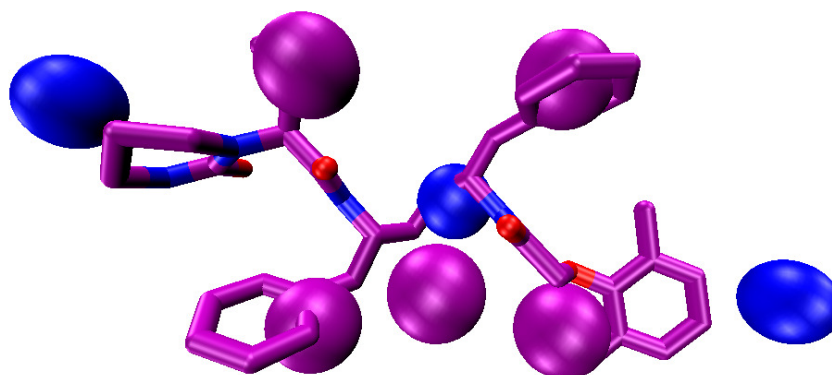


Figure 10. The Lopinavir molecule onto its pharmacophore shown in beads rendered in VMD.

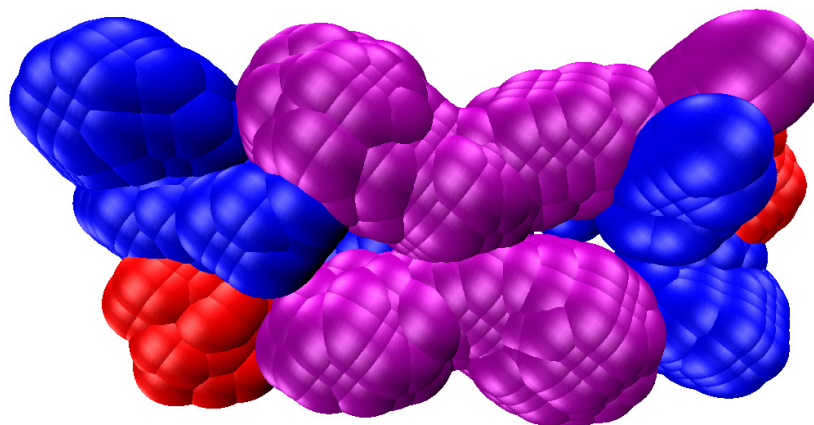


Figure 11. Key interactions sites of Lopinavir (hydrogen donor sites in blue, hydrogen acceptor sites in red and hydrophobic sites in purple) rendered in VMD.

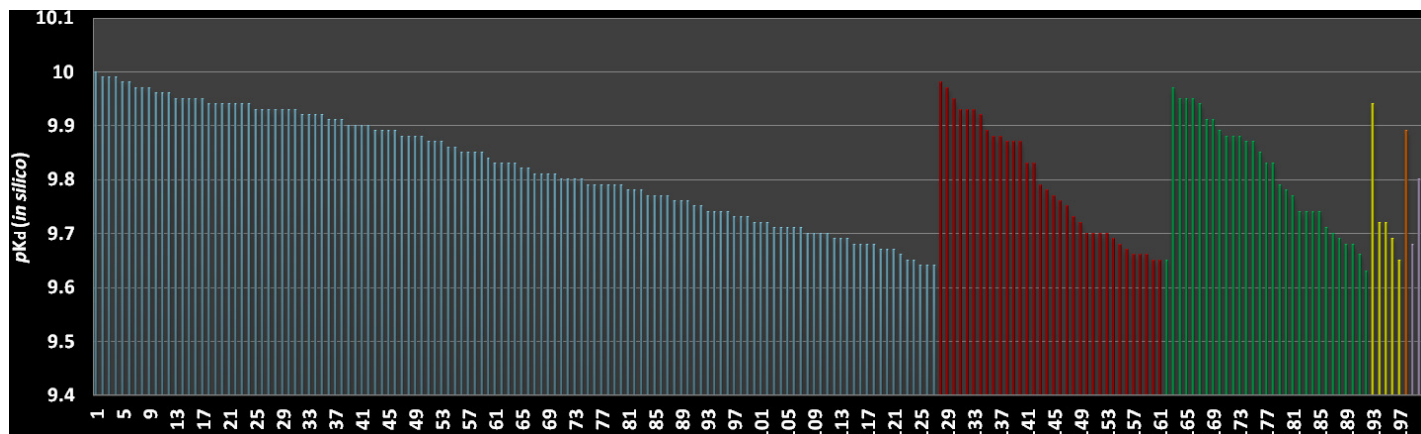


Figure 12. A graph showing the pK_a (*in silico*) for the 200 *de novo* designed ligands; the 6 different colours imply the 6 analog series.

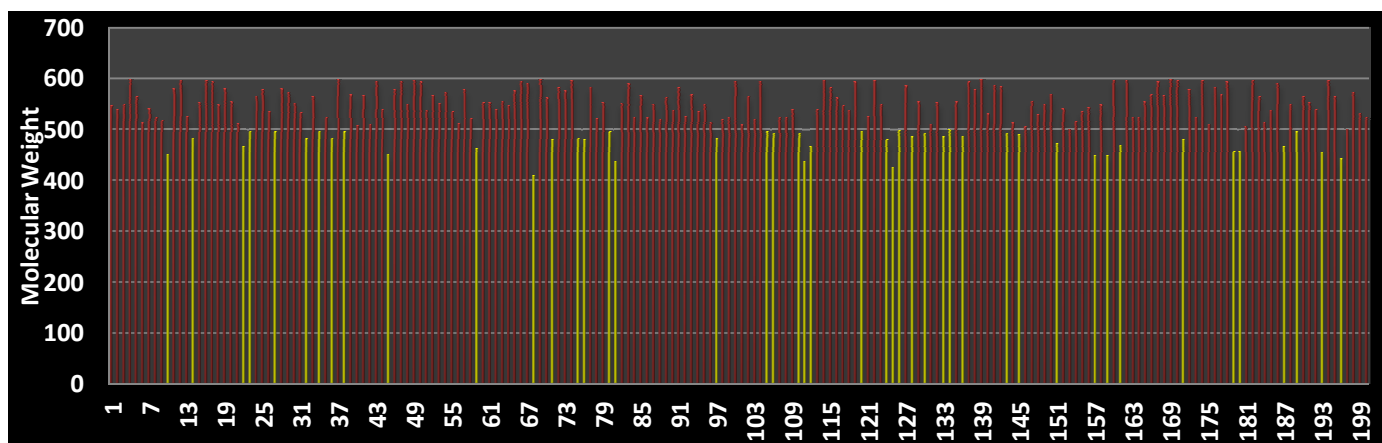


Figure 13. A graph showing the molecular weight for the 200 *de novo* ligands. The yellow colour indicates a molecular weight of less than 500 and thus compliance of such molecules with Lipinski rule of 5 with respect to molecular weight only.

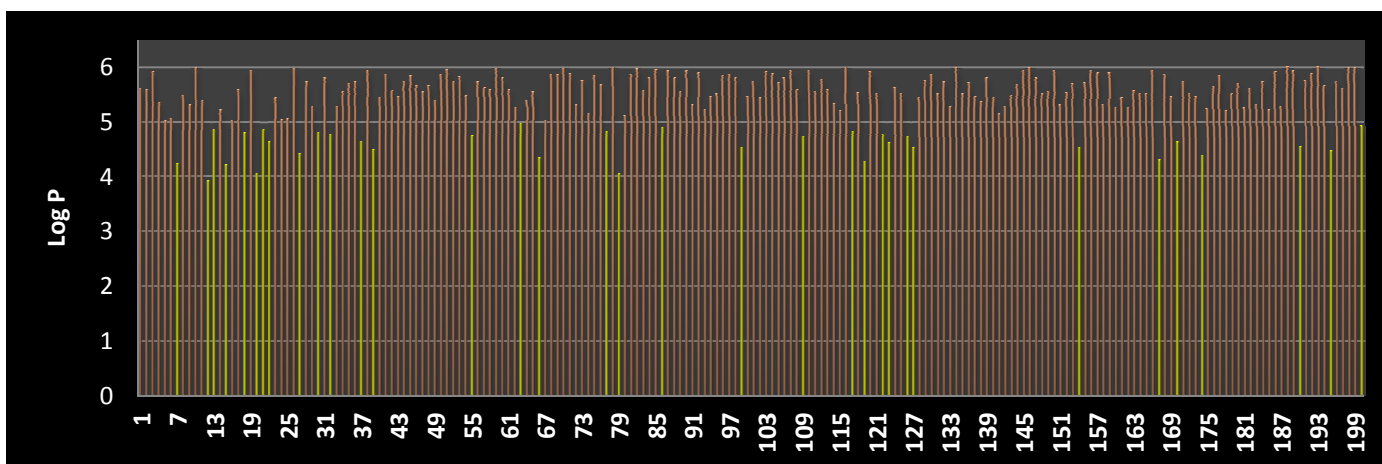


Figure 14. A graph showing the value of LogP for the 200 *de novo* ligands. The yellow colour indicates a value of less than 5 and thus compliance of such molecules with the Lipinski Rule of 5 with respect to LogP only.

Table 2. Molecular formula, binding affinity pK_d (*in silico*) and binding energy (Kcal mol⁻¹). These values are indicated in red for Lopinavir as a reference.

Ligand ID	Molecular formula	pK_d	Binding energy
Lopinavir	C37H48N4O5	8.84	20.643
10	C28H26N4O2	9.97	160.72
14	C28H26N4O4	9.95	88.228
22	C28H26N4O3	9.94	59.372
23	C29H28N4O4	9.94	48.969
27	C28H25N5O4	9.93	164.259
32	C28H27N5O3	9.93	60.724
34	C29H28N4O4	9.92	88.826
36	C28H26N4O4	9.92	79.936
38	C30H30N4O3	9.91	100.353
45	C28H26N4O2	9.89	148.948
59	C29H24N3O3	9.85	39.432
68	C26H23N3O3	9.81	142.23
71	C30H31N4O2	9.81	168.857
80	C32H29N5O3	9.79	51.441
81	C36H39N5O3	9.79	160.137
97	C29H39N5O3	9.74	66.713
105	C29H27N3O4	9.71	65.09
106	C29H29N5O3	9.71	187.298
110	C30H26N3O4	9.7	58.065
112	C28H23N3O4	9.7	44.389
120	C29H28N4O4	9.67	70.668
124	C29H28N4O3	9.65	111.497
125	C26H23N3O3	9.65	40.342
126	C28H27N5O4	9.64	64.22
128	C29H34N5O2	9.98	117.954
130	C28H40N6O2	9.95	150.674
133	C29H34N5O2	9.93	152.434
136	C29H36N5O2	9.88	145.68
143	C28H38N5O3	9.79	256.98
145	C28H36N5O3	9.77	320.506
157	C28H36N5O3	9.66	142.921
159	C26H34N5O2	9.66	171.695
179	C26H34N5O2	9.79	340.53
180	C28H32N4O3	9.78	264.248
187	C29H30N4O2	9.7	298.461

retention of cyclic urea with a change of the attached Sp3 carbon atom to an H.sp3 hydrogen as shown in Figures 1a, b and 9.

The genetic algorithm embedded in XSCORE_V1.3 generated 200 novel structures, 35 of which were Lipinski rule of 5 compliant (Table 2). This result must be discussed critically with a view to further iterative optimisation in the drug design process. The 35 Lipinski rule of 5 compliant molecules are, at this stage of the

design process still lead molecules, implying that further optimisation must be carried out prior to *in vitro* evaluation. Ideally at this stage of the study, the *de novo* designed leads would have been rule of 3 compliant (Ress et al., 2004). The implications consequently are that a tight rope is still being walked in the quest to design clinically useful rule of 5 compliant high affinity HIV-1 PR inhibitors. However, these 35 molecules whose LBAs for the HIV-1 PR enzyme range from pK_d *in silico* of 9.63 to 10.00, warrant further investigation and evaluation. It must also be highlighted that this rational drug design exercise employed a static model that did not take into account the mutations that the HIV is known to undergo. However, the identification of novel structures potentially capable of inhibiting the HIV-1 PR enzyme is also valid in this context in which the availability of different molecular structures which stabilise and antagonise the HIV-1 PR_LBP could have a retarding effect on the development of mutations.

CONCLUSION

Finally, it must be stressed that in the context of the design of a chemical library of known affinity for the HIV-1 PR enzyme, the remaining 165 molecules should also be included. There are 2 very important reasons which justify such a decision - the first is that, as already pointed out, all the HIV-1 PR inhibitors in successful current use are Lipinski rule violators. The second is the very real threat of the emergence of resistant strains of HIV which necessitates the existence of a broad based drug armamentarium at the disposal of clinicians. Furthermore, these molecules could be further optimised, through for example, bioisosteric replacement, such that their molecular weight could be reduced to conform to Lipinski et al. (2001) requirements.

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Full Length Research Paper

Assessment of potential risky sexual behaviors among Dilla University students: A survey study for enhancing self- protection from human immunodeficiency virus (HIV) infection

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The aim of this research was to examine risky sexual behaviors and pre-disposing factors among Dilla University undergraduate students and to design feasible strategies to mitigate acquired immunodeficiency syndrome (AIDS) and other sexually transmitted diseases. Mainly, a qualitative method of data collection was utilized to get a number of 187 participants (181 regular students and 6 academically dismissed female students) and 44 purposively selected informants from the administrative workers. The data were analyzed manually using the thematic framework method. The results of the study revealed risky behaviors of the students as follows: having sex without condom on campus, rape attempt, loss of virginity, unintended pregnancy, abortion, lawlessness of the students, substance and alcohol use etc. Moreover, various predisposing factors for risky sexual behaviors of the students were identified. To mitigate the problems, immediate holistic and integrated efforts are needed. Moreover, this finding also recommends new approaches such as providing pre-hand orientation for the fresh university students, reviewing the existing curriculum and academic promotion policies, integration or separate inclusion of sex education, including HIV issues into university and formal school curricula and provision of special attention to female students who are being dismissed from the universities.

Key words: Vulnerability, unintended pregnancy, self-protection, risky sexual behaviors, pre-disposing factors.

INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) caused by the human immunodeficiency virus (HIV) was first reported in the United States in 1981 and has now spread like a wild fire to all parts of the world; it has become a major worldwide pandemic. The wide prevalence of HIV/AIDS, is therefore, the biggest public health challenge and social problem in the world today (Cai et al., 2008). Sub-Saharan Africa remains the most severely

affected, with nearly 1 in every 20 adults (4.9%) living with HIV; they represent 69% of the people living with HIV worldwide ((UNAIDS, 2012). The epidemic is not only a health problem, but is also regarded as a major impediment to development and substantial threat to regional security (Sarker et al., 2005).

According to UNAIDS (2007), the estimated number of persons living with HIV worldwide in 2007 was 33.2

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million (30.6 to 36.1 million), over 2.5 million (1.8 to 4.1 million) people were newly infected and 2.1 million (1.9-2.4 million) people died of AIDS in the same year. This is mostly because of inadequate access to HIV prevention and treatment.

From the estimated number of death caused by AIDS in 2007, 76% occurred in Sub-Saharan Africa. AIDS remains the leading cause of mortality worldwide and primary cause of death in Sub-Saharan Africa. This shows that tremendous long term challenges lie ahead for the provision of prevention and treatment.

Studies have also shown that more than 40% of those newly infected with the disease among adults comprise young people from 15 to 24 years of age (UNAIDS, 2006), and more than 95% of these infection occur in developing countries. Sub-Saharan Africa is the home to almost 64% of the estimated 38.6 million individuals living with HIV infection (Singh et al., 2007). In this region, women represent 60% of the infected and 77% of the newly infected persons are from 15 to 24 years old (UNAIDS, 2006), indicating the needs for immediate integrated intervention to stop the spread of HIV infection among this population.

Ethiopia is one of the countries that are seriously affected by the epidemic, where nearly 1.4 million people are living with it and almost 129,000 people develop new infections every year. It is estimated that HIV is responsible for about a third of all adults' deaths in the age group of 15 to 49 years and leaves nearly three quarter of a million orphans between 0 to 17 years; there are over 30,000 new born babies with the virus (Getnet and Melese, 2008; USAIDS, 2007) cases in Ethiopia. Studies have shown that intervention on predisposing factors (any condition related to biology, behavioural, cultural, economic, demographic or personal factors etc.) that can increase the risk of involving in risky sexual behavior are the key factors to fight against HIV infection.

Moreover, studies have shown that common predisposing factors include epidemiological risk factors substance use (that is, drug use, alcohol abuse), behavioral and socio cultural factors such as poverty and gender inequality known as the drivers of HIV/AIDS epidemic (Getnet and Melese, 2008; UNICEF, 2008) that expose individuals to risky sexual behavior and HIV infection. Besides, biological vulnerability, lack of recognition of right partners among the youths etc., are additional risky predisposing factors (CDC, 2004, 2008) that need intervention for the creation of awareness and behavioral change among the community, in general, and students, in particular to curb the spread of HIV infection.

Why should a higher institution like Dilla University be involved in the fight against HIV/AIDS? One can enumerate tremendous risky behaviors that may contribute to contracting HIV infection among college students. According to CDC (1995), factors such as peer pressure, lack of maturity, alcohol and drug use and alcohol induced sexual behavior can make collage students to

exercise unprotected sex, exposing them to the risk of having HIV infection. Other studies also show that African Higher Education Institutions Responding to HIV/AIDS pandemic also discloses that factors that contribute to the risk of contracting HIV at the university level are high risky sexual behavioral patterns including sexual experimentation, unprotected casual sex, multiple partners, gender violence, *sugar daddy* relationships and prostitution on campus (Chetty, 2003; Katjavivi and Barnabas, 2003). Therefore, students of higher institutions are assumed to be exposed to many risky sexual behaviors.

Moreover, many Ethiopian adolescents that continue to engage in risky sexual behaviors are associated with low academic achievement and lack of parental communication; while individual and family-level protective factors appear to moderate the impact of risk (Land, 2004). In addition, studies also revealed that the academic achievement of the students has been significantly affected by the high school specialization than the university study (Matar and Muath, 1997; Odeh, 2007). This result confirms the need for quality high school education.

Since HIV is mainly transmitted by sex and due to no cure or effective vaccine (Cai et al., 2008), we should provide health education to the whole community in general and young people in particular. However, to bring about behavioral change, communities need all-round efforts and greater attention to give awareness on the nature of the virus, ways of transmission and means of prevention and control. These can be done through conducting orientations, sensitizations, peer education, life skill trainings, research undertakings, counseling, etc., to stop the spread of HIV and AIDS.

Rationale of the study

Ethiopia is undergoing higher education expansion and reform programs in dimensions like establishing new universities, introducing new courses, and increasing the enrollment rate of students. With clear understanding, the numbers of universities in Ethiopia are increasing with increasing number of student population, among which Dilla University is one.

The number of students is increased simultaneously, accompanied by tremendous bio-psycho social problems. Risky sexual behavior, unwanted pregnancy and abortion, gender violence, stress, academic failure, predisposing factors such as psychoactive drug addiction, and alcoholism may increase vulnerability of students to HIV infection. These factors are emerging and might be due to the age of the students (that is, puberty age), background of the students (either academic or social problems), absence of reproduction health education including HIV and AIDS and other sexually transmitted diseases; all of these factors need

holistic interventions.

Having the above facts in mind, the objective of this study is to assess potential risky sexual behaviors among Dilla University students so as to enhance self protection from HIV and other sexually transmitted diseases.

MATERIALS AND METHODS

Description of the institution

Dilla University is located at Dilla town, Gedeo Zone of the Southern Region of Ethiopia; it is 365 km South of the capital, Addis Ababa. The current Dilla University emerged from the Dilla College of Teacher Education and Health Sciences.

Since its foundation, the college has been known for producing competent teachers and health practitioners and is also recognized to be the center of excellence among the higher institutions in Ethiopia. After enjoying this reputation for eleven years, as part of the expansion of the higher education in Ethiopia, the college has been upgraded to the level of an independent university in 2006.

Currently, Dilla University is one of the fully accredited government universities, hosting a total of 15828 populations consisting of over 14,000 undergraduate students in regular, extension and summer programs under 12 schools and 1 institute; it has 1214 administrative staff and over 614 members of teaching staff.

Study design

The study was conducted on the campuses of Dilla University (that is, the new and old campuses) and off campus as well. We targeted university students for this study, because they are the group with high risk of contracting HIV infection. Data on predisposing factors and potential risky sexual behavior of the students were collected using qualitative data collection method that includes direct and silent visual observation of risky sexual behavior of the students; in-depth interview including autobiography of the dismissed female students; focus group discussion (FGD) with responsible students complemented by quantitative data collection including self administered questionnaire for the proctors, drivers and guards. This study was conducted from May to July 2009, from 6 pm to 3.30 am (12 to 9:30 local time); visual observation was done at night and the rest data collection methods were done during the day. Moreover, all the research activities were critically investigated and interpreted by the researchers.

Study participants and methods of sampling

A total of 231 consenting participants and informants were recruited for the study. These included 187 study participants (that is, 140 males and 47 female students) and 44 informants (38 males and 6 females).

The sampling techniques were based on the availability, accessibility and voluntary sampling techniques (purposive sampling) which might be due to several reasons. Primarily, the topic under investigation is highly sensitive and so many people do not want to disclose their sexual behaviors and other related manners. Secondly, it was so challenging and it took bold step to find participants who were vulnerable to pre-disposing elements and risky sexual activities. Thirdly, the problem is common to certain group of students. Fourthly, the researchers did not want to interfere directly into the privacy of the students due to ethical reasons and so they decided to maintain confidentiality of students who indulged in risky sexual behaviors.

Therefore, the involvement of the study participants was on

voluntary basis and the survey was anonymous. The selection criteria of the informants included good communicative skills, long experiences and service years in the university, ability to establish healthy relationship with the students and potential/ability to recall the past and the existing university life of the students.

Methods of data collection

The participants were classified into different occupational and social orientations. This means 187 students (that is, 181 regular students, 6 dismissed female students) and 44 informants including 19 guards, 9 drivers and 16 proctors were involved in the visual observation, in-depth interview, FGD and self administered questionnaire respectively.

In the case of visual observation, 172 participants were involved. Moreover, in the in-depth interview scheme, 6 dismissed female students were engrossed to catch information on the major jeopardizing risky sexual performances/behaviors of learners and further associated dynamics; while in the FGD, 9 participants were considered (that is, 3 females and 6 males students who are taking additional responsibilities in the university as anti-AIDS club, student council and girls club) to understand risky sexual behaviors of the students. A self administered questionnaire was provided for 44 administrative staffs (that is, guards, drivers and proctors) to collect information on the risky sexual behavior of the students. The two researchers were the primary instrument for data collection.

Visual observation: The visual observation consisted of a set of points developed to catch information on the risky sexual behaviors of the students. There are three main sections in this study: section one contains preliminary data collection (that is, with age, sex, department, year level, number of observed students, dismissed or not, type of observation), second part emphasizes narration of the incidents under observation scheme, and the last part contains major findings and conclusions.

In-depth interview including autobiographical method: During the in-depth interview, a snowball sampling technique was used and the triggering points were included, such as life history/personal experiences of the interviewees and how they passed through the university life. It included background of the respondents (age, sex, family background, high school educational status and student's passing marks, university life, department in the university, risky sexual behavior and specific life history including year of academic problem while in the university).

FGD: The guideline was aimed at collecting information on background of the respondents, risky sexual behavior of students (sex without condom, unintended pregnancy, abortion) and predisposing factors such as academic deficiency misbehavior of the students, etc.

Questionnaire: Structured and self administered questionnaire consisting of background information and behavioral aspects of the students was designed to collect information on the risky sexual behavior of the students, which were kissing, open sex, rape attempt, etc. This instrument was used in order to complement the other data collection tools.

Methods of data analysis

Research design is mainly qualitative data collection method complemented by quantitative data collection approach that provides information about predisposing factors and risky sexual behaviors of the students. Data triangulation as the major mechanism was employed in this study, so as to produce quality

research results. Qualitative data analysis was made by using descriptive approach while quantitative data were analysed using percentages and tables to meet the research objectives.

Ethical consideration

Researchers did not want to interfere directly in the privacy of the students due to ethical reasons. They decided to maintain confidentiality of the students who attempted to indulge in risky sexual behaviors; and therefore, the survey was anonymous. Furthermore, individuals who were involved in the interview were given verbal consent as a prerequisite before data collection. The target of the research was also in line with the objectives of research and dissemination office of Dilla University, which are to support the vision of the university in producing efficient, competent and HIV free graduates.

RESULTS AND DISCUSSION

Background characteristics of the respondents

A total of 187 participant and 44 informants (that is, total 231 individuals) were involved in the study (140 males and 47 female students) and 44 informants (38 males and 6 females) whose age ranged from 24 to 50. However, gender equity of the students was not maintained during sampling due to sampling limitation. Since visual observation took from evening till 3:30 AM, determination of exact age group of the study participants was not that possible; therefore, we estimated the age group of the participants to be 18 to 28 years who are supposed to be sexually mature adolescents and are capable of indulging in sexual intercourse.

Risky sexual behaviors

Data obtained from visually observed case studies and other tools confirmed the existence of risky sexual behaviors which are unsafe sexual practices among the students on and off campus. The followings verify the above (sexual behaviors) conditions.

Main results of visual observation

It was found that 38 pairs of male and female students in the two campuses were found kissing, hugging and cuddling each other in the 6 intermittent observation processes in the pocket and dark places within the university campus.

First case: A clear unsafe sexual behavior was observed as it is stated: It was on 10/11/01 E.C (that is, post exam dates) at 2.00 local time (8:00 pm) in the new campus around the shrubs (tagged as green hotel). The male and female students were from the Department of Civics and Ethical Education. The observers were rounding the dark strategic areas in the new campus to confirm the specu-

lation commonly expressed by different individuals. Some Dilla University students were getting into unsafe sexual behavior in the campus. Hence, the observers were moving along the pedestrian road; they moved from the backyard of the staff lounge to the main road, kept silent, critically investigating the surrounding with eagle eyes.

It was a mango tree having well paved green grass under it. One of the observers visualized an image lying down on the ground, and soon after instinctively, the hand light was pointed upon the image. Shockingly, two students were indulging in sex and one of the observers screamed to his colleague, saying, "Here is the drama!" Two students were acting like a thread and a needle, and immediately the second observer instinctively run to them because he thought that they may run away without getting counseling service. What a new incidence and lawlessness he observed in the university campus! The students wrinkled like millipedes to hide their identity. In fact, the observers left them to finish their sexual performance, but came back again to give counseling service. However, they were not using condom since they were afraid to collect it from the university clinic as they said. Moreover, existence of open sex in the campus was also witnessed by many of the participants and informants.

Second case: On the same day, risky sexual behaviour and rape attempt were observed. The situation is stated as follows: A group of boys were found trying to force a girl to have sexual intercourse with her, and the girl was screaming and rejecting the boys' request. The case study reads as follows.

It happened on 10/11/01 E.C (that is, post exam date) at 2:20 local time (8:00 to 8:20 pm) in the new campus called "Green Hotel". The students were from the Department of Law, the central town of Addis Ababa. The observers bumped into the students who were found making sex; harassing voices came into the auditory canal of the observers. Right after concluding the mission of counseling the students in the first case, the observers moved to the direction where hassling sounds were coming from. The observers approached a couple sitting in the dark Green Hotel; the boy unfastened his belt, and looked like he had been intoxicated due to sexual feeling or otherwise. The girl seemed to suspect the boy's actions; she had chosen forty five degree sitting, crossing her legs altogether tightly connecting with her hands. She put on trousers, and had a scarf round her neck. While the observers started asking why they were in the dark place, the boy screamed, saying: '*Echohalehu...u.u.u..elalehu! Miste nech, yetim bota yzhat ehedalehu, yefelekutin madreg eichilalehu...!*' ('I will shout 'u.u.u'. She is my wife, I can take her anywhere, I can do whatever I like') and the likes.

However, the girl was totally mute to respond to the boy as well as to the observers. Few minutes were gone to stabilize the boy. With strong communication made in between the two students, we advised them to go from

the 'Green Hotel' and go areas where there is light. Moreover, university guards were informed to make critical investigation and follow up on these students.

Third case: This observation was conducted on Saturday 06/10/01 E.C at 3:40 local time (9:40 pm). It was one of the blocks in front of the staff's building. Two students (the girl from History Department and the boy from Accounting) were talking to each other as if they were waiting for light. Marvelously, the girl over crossed on the boy, and they started kissing each other. It was dark; there was no light except at the library. The observers were around to check if there was HIV/AIDS related pre-disposing factor or not. Two students were sitting adjacent to each other in a dark place, in one of the lecture rooms in the new campus. The students were asked why they were there, and the response was due to light problem, and that they were waiting for light that comes at 4:00 local time (10:00 pm).

Another similar observation disclosed a pair of student around the registrar's office in the main campus. They said they are light phobic and wanted dark place to enjoy; however, the male student expressed his annoyance verbally by saying, "it is their right to enjoy". We were deeply ashamed of his behavior, claiming that it is their right to exercise sexual behavior in the university campus. On the same night, hugging and kissing were observed among more than 6 pairs of students at the back of the internet building as well as a non-consumable store and around the "begtera" in the main campus.

Cases reflected during in-depth interview

All of the interviewees witnessed the existence of risky sexual behaviors including open sex in the university campus as well as off campus. Some of the incidences are as follows.

Forth case: One of the participants in the interview session also expressed her feelings in relation to risky sexual behaviors as:

I remember four instances that confirm the presence of risky sexual behavior in the campus. Firstly, I observed a fetus/baby aborted in the campus while it was about being eaten by a dog at the back of a multi-purpose hall (This case was also supported by other participants and even investigation trial was done to know the criminal actor). Secondly, I saw a boy in our dormitory enjoying sex with one of our friends; they stayed there for certain time while we went to 'space'. Thirdly, I had a friend again in our dormitory, who told me that she and her mate were captured by the university guard when they were having sex around begtera. She told the guard, 'just get away, please!'; taking the Id (identification card) from her back pocket".

Lastly, I know a girl from English Department who got unwanted pregnancy after joining Dilla University and gave birth around Walame area".

Fifth case: Moreover, another participant of the in-depth interview was trying to share her experiences of perilous sexual behaviors out of Dilla University campus.

I am one of the victims who faced hazardous sexual behaviors. He was a graduating student in the Amharic Department. I am from Biology Department. It was a holiday, Ethiopian Easter, and we had gone to Dilla town to enjoy life. In the middle of the night, he kidnapped me secretly and made love to me without condom. It was that day I lost my virginity and got pregnant (unwanted pregnancy). What about the probability of contracting STD including HIV?

Right after the pregnancy, we were looking for abortion from the traditional witch craft doctors around "Kofe area". We paid 50 birr to abort the fetus by drinking a kind of powder mixed with water (traditional drug), although it was unsafe and not successful. I totally became sick physically and psychosocially. I utilized further alternative during my vacation. I paid 300 birr to a doctor in the private clinic. It was made unknown to my parents, but the guy was around me. The paradox was, right after the fifth month, I understood that the fetus was still in my womb. It was determined to get away the fetus again, but medical experts and people around me advised me not to do it again since it could lead to death". What would be the fate of the new born baby?

Sixth case: During the interview, one of the dismissed girls who was working in the hotel expressed her annoyance with some of the female university students, taking one episode among many into consideration,

I know two university female students who enjoyed sex with one young investor (tagged as sugar baby) over the night in a hotel. It was a strange and risky behavior that can expose them to sexually transmitted infection including HIV.

Seventh case: Another interviewee responded,

Sex is performed during the day and night, taking a construction worker as an example. The sex performing students and the construction worker (observer) had a conversation. After observing sexual activity openly during the day in the campus, a construction worker asked the sex performers, 'what are you doing please?' The sex performers replied by taking action using mobile photo camera for memory and the episode was proved by the photo being shown to us.

Cases from FGD

It revealed the following facts with regard to the presence

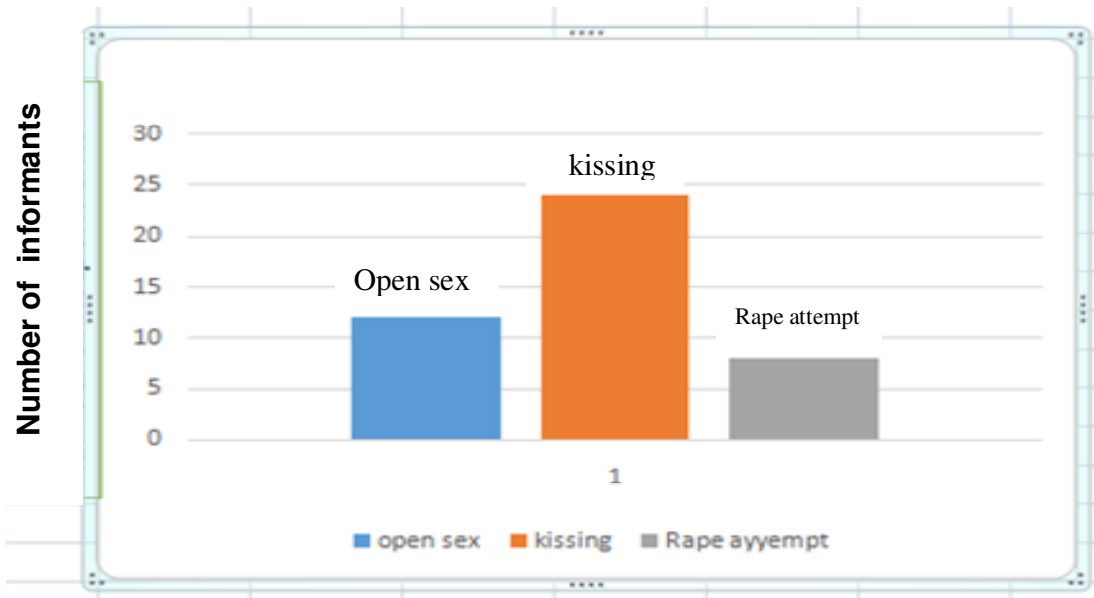


Figure 1. Types of risky sexual behaviors. From the graph it followed that, all of the informants 44(100%) replied on the presence of risky sexual behaviors of the students in the campus i.e. of the total informants, 12(27%), proved the presence of open sex, 24 (54.5%) kissing, and 8(18.2%), rape attempt, among Dilla University students, indicating the need for immediate intervention against risky sexual behaviors to fulfill the objectives of the university.

of unsafe sexual behaviors among the university students.

Case 1: When I was a first year student (that is, last year), I saw two students who put on scarf were indulging in sex around the previous History Department (the current Agriculture Department). However, later they were caught by the university police and their ID taken off; but disciplinary measure was not taken and the result was not known.

Case 2: Although I never observed open sex on this campus, kissing is like a daily meal around "BEGTERA" which may automatically lead to risky sexual intercourse.

Case 3: Right after my arrival on this campus, I saw two students around "BEGTERA" lining themselves with the wall of certain building, involving in precarious sex. I was new in the compound and shocked by the existing sexual behaviors of the students. A campus police soon arrived and asked them not to do such forbidden act in the university, and stopped them. However, a response forwarded by the students was, "we have no ears to listen to you: if you want our ID, it is at the back of our pockets; please, take it and get away soon." What were the disciplinary measures taken against this illegal act?

Case 4: Boys also attempt to have sex with prostitutes when they have money.

Case 5: I know a case where a second year student was welcoming a fresh girl student that came from a similar community. The girl arrived at the university very early and had been given a dormitory. She was alone having

no dorm mate, but the boy was helping her with all orientations about the university. While they were together, the boy asked to pass the night with her; the girl agreed because she had no information on the rules and regulations of the university. It was the first time the girl had sexual intercourse and it was confirmed that she was pregnant; her status was known right after two months. The boy was accused of committing forced sex and not using condom by the university gender office, but the appeal was aborted.

Responses based on the self-administered questionnaire

Furthermore, responses based on the self-administered questionnaire for different administrative workers (proctors, guards, and drivers) also uncovered risky sexual behaviors (kissing, open sex, and rape) among Dilla University students. The results are shown in Figure 1. The figure shows the reflection of informants on the presence of risky sexual behaviors of the students on the campus.

Major predisposing factors/driving forces

Results of visual observation and in-depth interview

Case one: It was an observation conducted on the first

year students after the second semester final exam conclusion (10/11/01 E.C). The two observers were visiting one of the local liquor houses at Dilla town from 2:30 to 9:00 local time (8:30 pm to 3:00 am); the observation result is described as follows:

There were around 92 fresh students (91 males and 1 female student) who were enjoying after their examination with traditional liquors such as "Tej, wine ("vino") and "caticala" in the traditionally decorated booth building, sheltered by bamboo. The students were sitting in groups separately, corner to corner, with some of them inside the rooms; while others were in outdoor service, drinking and smoking. A binge-drinking was the ingredient that seems to make life more meaningful to the youth groups. Dancing and singing were the positive ways of releasing emotional conflicts, including screaming, shouting, playing with condom like balloon and insulting each other (for example, "ENATIHIN LIBDA, ABATIH YIFENDA" (meaning: 'Let me fuck your mother, let your father be exploded'); talking about sex and sex related issues were the shocking and untraditional ways of getting away from emotional activities. Vomiting, losing balance and changing places and fighting each other were commonly observed. Furthermore, a remarkable scenario was that a commercial sex worker was observing the conditions in the liquor house, and some students were inclined even to communicate with the woman, being pushed by impulse due to intoxication of alcohol drinks.

Case two: The rules and regulations of the university are also considered as predisposing factors that influence students in general and girls in particular to be exposed to dangerous individual habits including risky sexual behaviors. The following instances confirm the above speculation. The verification that comes from the case study is stated as follows:

It was dated 06/10/01 E.C at 7:00:7:30 local time (1:00-1:30 am), mid-night and in the new campus; there were six students from Law Department, while the other one was from Sociology (a total of three males and four females). The two observers were tired due to the observation made for at least eight hours, starting from 5:00 p.m to 1:30 a.m, and were going home from the inside of the new campus, driving to the gate. Seven students (that is, 4 girls and 3 boys) were on heated drama with the guards to get in or not to get in. It was the rationalization that came from the guards: it is not the time to come into the university compound, rather stay somewhere else. Sheer luck permitted the observers to know the reason why they were late. Their response was that they were studying at their house and had come to the campus to sleep.

The observers were curious and skeptical to know whether they were from their home or some other places;

as a result, they were asked to tell them where their house was. One of them was not comfortable. Physically, the students looked smart (that is, well dressed, stylish, fluent etc) and from urban areas and well to do families. Despite the fact that the classroom was entirely untidy with garbage, "khat", cigarettes, and the sniff of ganja (substance abuse), we observed that there were no bed, chairs, tables; rather a single layer of blanket to chew 'khat' and study on.

Third case: Failing to choose proper time, place and condition (Tables 1 and 2) are other predisposing risky elements that may expose students to harassment and abduction. Therefore, choosing the right place and time so as to entertain or to carry out daily activities is one of the basic life skills; however, this skill is in some cases being violated by some of Dilla University students. This speculation is verified by the following facts:

This happened on 05/10/01 E.C Friday, from 1:30 evening onwards at (7:30 pm local time). The observers were moving to Dilla town so as to conduct an observation on the pre-disposing factors to HIV infection. Three elegant girls were going down taking line taxi from the gate of the main campus. One of the girls took transport while two of her friends returned back to the campus. The leader of the team started discourse with the girl on several issues including the time she managed to go to Hawassa and why she was going to there? And she pretended that she had a medical checkup early in the morning of the next day. The justification given by the girl was a little bit shocking, and to find transport that takes her to Hawassa at 1:30 local time (7:30 pm) is too late and dangerous even for males. Moreover, she traveled 90 km alone, with such reckless prevalence of car accidents and forced sexual intercourse. Anyway, she got off the car at "POST RENDEZVOUS"; looking for the mini-buses, she had to stay for at least 30 min; however, she was unable to find the mini-buses and had taken a line taxi, and disappeared from our sight.

This case observation reflects how some girls are really bold enough to dare into non-secured environments which may expose them to risky conditions like gender based violence and unwanted sexual exposure. This result of visual observation was also supported by the responses obtained from other tools as indicated. Focus group discussion revealed that six girls were coming from Dilla town enjoying weekends at 5:00, local time (11:00 pm). They were captured by the male gang groups from the town; hence, their mobiles were snatched and they were raped one by one. This shows that misusing time is a predisposing factor.

Forth case: Low academic achievement and lack of parental communication are also predisposing factors which contribute to risky sexual behaviors. This fact was reflected by girls who were dismissed from the Dilla University; they shared their autobiographic experiences

Table 1. Major dark and pocket areas in the new and old campuses.

No.	Old campus	New campus
1	“Beg tera”	Green hotel (that is, forests and shrubs)
2	At the back of internet room	Small eroded hallways in the green hotel
3	The back side of lecture hall (that is, the front and right side of computer department and counseling office)	The corridor of each class room building/block
4	The right side of non-consumable resource store house	Around the former clinic, but the present students deans office
5	Around the registrar, dark pocket area	At the back of under each large lecture halls
6	Around the left side of the main library	Leaning to the service buses in the compound
7	Around the former dining hall	Within unfinished new buildings

Table 2. Summary of the fancy time to indulge into unsafe sexual behaviors.

No.	Time (local)	Observed cases	Number of major sexual risks or pre-disposing behaviors
1	11:00-1:30 evening	4	Going to town and showing up by colleagues; however, kissing, warm upping, and sexual negotiations in the campus
2	1:30-4:00 night	8	Dating, eating and drinking alcohol in the hotels and local liquor houses; but kissing, hugging, open sex and forcing for sex/rape attempt in the campus
3	4:10-9:00 midnight	9	Dancing , fighting/quarreling each other/ with others in the night club and /or on the main streets ;conversely, kissing, warm upping and forcing for sex in the campus etc

during the in- depth interview. Their preparatory grades and challenges coupled with what they faced in the University are as follows:

I had poor grades when I joined the university and even the grades I earned were copied from my fellow friends. I was not able to resist academic competition and now, I am working in the bar/hotel because I cannot go back to my family, since they are poor and expecting money from me. This idea was shared by other three girls who faced academic dismissal. They said, “their preparatory passing marks to university were 140/500, 226/500 and 265/500 and these marks were also copied or guessed”. This indicates the needs to reassess the existing promotion policy of the ministry of education.

Professional and ethical problems also root up from the university among few lecturers and

graduate assistances. The following incident proves this fact:

Another girl boldly explained “ *I took all the exams, but a teacher made me not to complete my education and this was due to my refusal to “his unprofessional request “. Therefore, I was dismissed mainly because my teacher tried to harass me”.*

Case five: The girl who was a participant in an in-depth interview witnessed that girls do share their mobile addresses with the rich merchants “sugar daddy or baby“ using the hotel waiters as intermediate actors for transacting sexual communication. Other predisposing factors which we observed also include: non- dormitory life of the students (living off campus), peer pressure, lack of maturity and biological vulnerability; and these factors may expose them to risky sexual

behavior.

Major hotspots and periods/time or occasions that expose students to risky sexual behaviors

Data obtained from different mechanisms including our visual observation revealed the time and places when and where risky sexual behaviors occur. Moreover, our visual observations also verified that dark and pocket areas in the campuses are highly preferred by students for entertaining sexual behaviors. Tables 1 and 2 depict the location of hotspots and appropriate time for enjoyment. If not used appropriately, time is also another predisposing factor which influences students to exhibit risky sexually behaviors. To verify this statement, the following facts (Table 2) are considered. Moreover, favorable conditions/days or occasions when

students indulge in risky sexual behaviors mainly include:

1. Weekends: With regard to the extent weekend celebrations make learners to indulge in unwarranted sexual and related behaviors, the following incidents validate the actuality. For example, the case of the girl who intended to go to Hawassa as pretence for medical checkup was on a Friday (that is, 05/10/01 E.C).

"It is better for me to get out on these days (that is, Friday, Saturday and Sunday) since I am busy on the rest of the days with all academic duties". (Response from the student).

The interview conducted with the first year student from Anthropology Department in the new campus revealed that:

"You just need to visit "Molash Tej Bet", a traditional liquor house, on Saturday to examine how far students get ducked into "Tej"; I am also one of the drama actor".

2. National and cultural holidays: Holidays are more favorable for the students to indulge in risky sexual behavior, which may lead to HIV infection and related problems. The following cases obtained from the interview verify these conditions:

A student was raped by her boyfriend, lost her virginity in the process, got pregnant, tried to abort the baby but gave birth. She was finally dismissed from the school. These happened on Ethiopian Easter.

3. Post-exam dates: Learners seem to engage in sex and related issues during post-exam days; the following information obtained from observation proves this statement.

About 92 first year students were seen at "Molash Tej Bet" on the final date of their second semester. Furthermore, there was open sex in the "Green Hotel"; another boy was trying to rape a girl; all took place on the same date (Friday, 10/11/01 E.C).

4. Pre-exam days (that is, right after their arrival on campus in every semester) are considered as one of the factors that cause students to engage in risky behaviors, and the reflection obtained from the interview confirmed the prevailing fact.

A big gap was observed between the time of academic new year, semester break, and when the actual teaching-learning processes start; this gives the students chance to indulge in risky sexual behavior and other risky habits like substance use such as drinking, smoking, chewing using hashish etc.

4. Vulnerable academic year students: Informants includ-

ing proctors, drivers and guards say that the tendency of students' involvement in undesirable risky behaviours may vary among different level of students. The following facts depict which level of students is most vulnerable to HIV and AIDS related misbehaviors and associated misconducts?

All the informants 44(100%) replied that students from all academic the levels were vulnerable to undesirable sexual behaviors. However, of the total informants, 19(43.2 %) say all academic levels were more vulnerable, whilst 8 (18.2%) say first year students; 7(15.9%), second year students; 10 (22.7%), third year students. Moreover, the total data triangulation indicated that first year students were more vulnerable to risky sexual behaviors than those in other levels.

Discussions

Risky Sexual Behaviors

Different instruments/tools exploited during the data collection showed risky sexual behaviors and predisposing factors among the undergraduate students of Dilla University. Risky sexual behavior included sexual initiation (hugging, kissing etc.), rape, sex without condom in the campus, loss of virginity, choosing multiple sexual partners (for example, sexual experimentation with sugar baby/ daddy in a hotel), unintended pregnancy, abortion and sex with prostitutes. This finding is reflected in similar studies carried out in Ethiopia, which showed, among the respondents, 267(26.9%) had had sexual intercourse. Mostly, 75.6% started sexual intercourse during their secondary schools; and among whoever had sex, 51.0% had sex in the last 12 months and 28.3% had multiple sexual partners. Consistent condom use with non-regular partner in the last 12 months was 69.1% (Gurmesa et al., 2012). There are variations in the findings due to methodological differences in the data collection.

Another similar study also was conducted on the pattern of the risky behavior among undergraduate students. It showed that among the respondents, about 355 (28%) students reported to have had sexual intercourse. Most of the students, 271, (77.2%) who reported to have commenced sexual intercourse had their first sex with a girl or boy and 60 (33.5) had sex with two or more partners. Six (2%) male students reported having had first sexual intercourse with commercial sex workers. Forty three (22.8%) reported to have had their first sexual intercourse after they joined the university while twenty two (6.4%) of the sexually active students reported to have practiced sex with the same sex partner from which 17 (5.7%) were males and 5 (11.4%), females. Five female students (12.2%) reported that they had been raped; one of them was raped after joining the university. Among the students reported to have ever had sexual intercourse, 220 (64.1%) had used a condom at

least once. Less than half (116, 32.7%) had used condoms during their first sexual encounters (Tariku et al., 2012).

In addition to these findings, studies have also shown that sex initiation and exercising start at early ages among students including collage students, worldwide (CDC, 2004). In Ethiopia, studies have also shown that in a school of youths (15 to 19 years), about 10% had premarital sex, and of those who were reported to have had sex, 40.6% had sex before 15 years (BSS II, 2005); while among college students in Dessie, 48.3% of males and 25.9% of females were reported to have had sex with two or more sexual partners (Yimer, 2007). Moreover, our findings included high risky sexual behaviors (unprotected sex sexual experimentation on the campus and out- off the campus, and multiple sexual partnerships) which could expose university students to health hazards such as sexually transmitted infections (STI) including HIV, unintended pregnancy and abortion. In support of our study, other studies conducted on African Higher Education Institutions Responding to HIV/AIDS pandemic also disclose that contributing factors to the HIV risk at the university level are high risky sexual behavioral patterns including sexual experimentation, unprotected casual sex, multiple sexual partners, gender violence, *sugar daddy* relationships and prostitution on campus life (Chetty, 2003; Katjavivi and Barnabas, 2003).

The impact of STI infection is also magnified by its potential to facilitate the spread of HIV infection (WHO 1999; UNAIDS, and WHO 1999)). In addition, a study conducted on the prevalence and associated factors of sexually transmitted infections among the undergraduate students of Wolaita Sodo University, in Southern Ethiopia shows high prevalence of sexually transmitted infections (STIs) (19.5%) among the university students who had risky sexual behaviors (Bereket et al. 2013). This result clearly indicates the vulnerability of the university students to HIV infection which demands holistic intervention including effective sex education for students in Ethiopia and elsewhere. Our finding has been reflected in studies conducted in other countries. The study conducted among university students in Madagascar in 2000 revealed that 80% of students have had sexual experiences (Rahamefy et al. 2008) and the study conducted on Nigerian university students, 76.8% have had sexual practices (Okafor and Obi, 2005). Moreover, the study conducted among Slovak University students shows that among 832 students, those with sexual experiences were 62%; inconsistent condom use has been the most prevalent risky behaviour (81% in females and 72% in males (Ondrej et al., 2009). The overall results show that students start sex from their early ages; however, risky reduction measures are not reliable.

Our finding also showed that first year students were more vulnerable to risky sexual behaviors than those in other levels. This finding is supported by other studies which explain that most vulnerable students with low

retention in all institutions of higher education are the first-year students, who are at greatest risk of dropping out of school in the first semester of study or not completing their program /degree on time (Horstmannshof and Zimitat, 2007., Noble et al. 2009). This indicates that the first year students are under different pressures and these pressures may expose them to risky sexual behaviors. Another study conducted on first year students also shows that first-year students are most vulnerable to dangers of alcohol, exposure to alcohol-related injuries or death, getting in trouble with the police or the university, getting into a fight, doing poorly on a test, missing class, or being taken advantage of sexually (Eagle, 2006); these may expose them to risky sexual behaviors. Therefore, the first year students urgently need more attention of the universities and their parents to attain their objectives.

The overall results on risky sexual behaviors demand special attention to support students in high schools, colleges and universities, including private colleges. This will bring change on risky sexual behavior to mitigate the spread of HIV infection. This action also needs bold and feasible intervention such as integration or inclusion of reproductive health and sex education into formal education as part of biological sciences at primary and secondary levels and common course at the university and college levels, to bring about behavioral change among the students.

In support of the above rationale, more than 70 developing countries now mandate life skills based education with HIV prevention component in national school curricula (UNICEF, 2007); and therefore we need to include sex education in our school curricula.

Predisposing factors to risky sexual behaviors

Our study also showed various predisposing factors including substance use, misbehavior of the students, loose regulation of the institution, misuse of time and dates or occasions, low academic achievements and lack of parental control, professional and ethical problem of few instructors and graduate assistants, address exchange with investors (*sugar daddy and baby*) by some female students to have transactional sex, out- off campus living, peer pressure, dark and pocket areas on campus, night clubs(red light houses), traditional liquor houses, and biological vulnerability of the students. This finding has have been partly reflected in similar study carried out in Ethiopia. This study result shows lack of parental control, being in the youth age group (immaturity), living out-off campus, substance use, peer pressures, campus and outside environment and low income level are the predisposing factors for risky sexual behaviors among Jimma University students in Ethiopia (Gurmesa et al., 2012). Our finding is also in conformity with other study results. According to Getnet and Melese

(2008), these predisposing factors are the driving forces that may enhance the vulnerability of community in general and students in particular to HIV infection. Therefore, we need to prioritize working to reduce the behavior of vulnerability of students to HIV infection.

Effects of peer pressure, lack of maturity, dark places and substance use

In line with our results, other studies carried out among college students in Ethiopia also show substance use. For example, in 2007, the study carried out to assess knowledge, attitude and practice on reproductive health problems among Jima University and Jima Teachers Collage indicates that among the respondents, 46.4 percent used to drink alcohol, 25.1 percent used Khat (chewing chat), 14.9 percent used tobacco, and 10.9% used shisha (Tilahun et al., 2007). This shows the involvement of students in using substance like alcohol, and they are more likely to engage in a high risky behavior. Moreover, attendees who were tested during HIV counseling and testing (HCT) in Addis Ababa (Ethiopia) used alcohol and are more likely to be HIV positive than those who are non drinkers.

In line with our study, other studies conducted in other countries also show predisposing factors that are associated with risky sexual behaviors; they are mainly substance use including alcohol, peer pressure, lack of maturity and dark places. According to CDC (1995), factors such as peer pressure, lack of maturity, alcohol and drug use and alcohol induced sexual behavior can make collage students to involve in unprotected sex, exposing them to a risk of HIV infection. Our studies also showed that students were using hotspots (risky conditions) such as dark places, night clubs,(red light houses), traditional liquor houses, where they enjoy kissing each other, drinking alcohol and perform unprotected sex (non use of condom),which may adversely expose them to risky sexual behaviors. This result is also in line with the results stated by the Leigh and Stall (1993), where they show that both causal and chronic substance users are more likely to engage in a high risky sexual behavior such as unprotected sex when they are under the influence of drug or alcohol abuse. Moreover, recent study also showed that respondents who attended night club and abused alcohol in the last three months were about two times more likely to have had sexual intercourse as compared to non- attendants in this study (Gurmesa et al.2012).

In addition to this report, studies conducted in South Africa also reported that low lighting (i.e., dark places), seductive (that is, attractive or tempting) music, unisex toilets, and lack of condom use instigated sexual intercourse, when combined with heavy alcohol consumption. These in turn contribute to the incidence of unsafe sex (Seloilwe, 2001; ICAP, 2009). There are other several studies that have been conducted among university

students with the results showing that drug use, alcohol abuse, sexually transmitted infections, behavioral and socio cultural factors are predisposing factors called the drivers of the HIV/AIDS epidemic (Getnet and Melese, 2008)

These risky behavioral activities of the students do not only hinder the vision of the university, they are also potential threats to life of the students in particular and country in general; and hence we need to intervene immediately to bring about behavioral changes of the students.

Out- off campus living style and lack of choosing the right place and time

Our study also showed "out- off campus living behavior/lifestyle "of the university students and we visually observed that they were vulnerable to risky sexual behavior, that may expose them to HIV infection. In line with our study, another study on HIV sero-behavioural study in six universities in Tanzania also shows overall, male students and female students who are living outside university campus (either renting private apartment or residing at university hostel outside university campus) have relatively higher risks including prevalence of HIV infection than students who are either living with guardian/parent or living at the university campus (Abu et al.2010).This result shows universities need to act like guardians/parents of the students to get rid off or to reduce vulnerability of the students to HIV infection due to living out-off the campus. Moreover, choosing the right place and time to entertain daily activities are considered to be the basic life skills to lead a positive life. However, our visual observation clearly indicated that this skill in some cases was being violated by some of the university students, where non- dormitory group of students (both males and females) who live away from their parents enjoy their life, indulge in substance use including *shisha* and live together free life. A girl unbelievably dared to go to Hawassa alone at 1:30 local time ((evening) (7:30 pm) and non dormitory students ventured to enter a new university campus at 7:30 local time (1:30 am). These show violation of place and time factors and open sex in the university campus were some of the way students violated regulations, misused time and place. This result also indicates that university students who are away from parental control and living out- off campus are more vulnerable to HIV infection. Therefore students who live out- off the campus need the attention of the university authorities and be attached to their parents for them to be protected and achieve their academics goals.

University regulations and misbehavior of the students

Our study also showed misbehavior of the students:

misuse of time /dates or occasions, substance use, sexual experimentation, risky sexual behavior (kissing, engaging in open sex in the university campus), ignoring the rules and regulations of the university etc. Few instructors and graduate assistants had professional and ethical problem probably due to loose regulation of the university. Universities have a vision to produce competent and HIV free graduates in the long run and this goal totally depends on how the universities manage the behavior of the students in the campus. Therefore, if the rules and regulations of the university are not well managed they can be considered as a predisposing factor that influences behaviors of the students. For instance, we have observed the following instances that confirm the above assertion.

Having sex in the university campus, misuse of time/dates, intoxication, dismissed male student staying in girls' dormitory for two months etc are practiced in the university campus. This indicates that the rules and regulations of the university are loose and this needs reassessment of how the university manages the students.

Moreover, measures against these illegal practices were not taken appropriately. This strengthens the lawlessness of the students, leading to risky sexual behaviors; and also encourages exposure to HIV infection. Furthermore, a focus group discussion and in-depth interview showed that academic calendar is also considered as a pressing factor (stressful). This means the gap between entrance and academic resumption of the semester, mid exam and final exams in many cases overlaps with each other. This likely speeds learners' academic failure which in turn makes them idle; and as a result, they indulge in precarious sexual behaviors.

Furthermore, results of the focus group discussion and the in-depth interview have clearly indicated that the university campus lacks fence, male and female dormitories are close to each other, absence of toilet rooms and water supply in the new campus, unknown individuals get into the university and likely harass girls, while they study in the space during the middle of the night; all these may initiate lawlessness of the students in the campus. Moreover results of the in-depth interview showed unethical problem of few instructors and graduate assistants who approach female students for sex in exchange for improved grades, which is unethical as well as unprofessional behavior. The findings above are in accord with previous results reported by *Goyette et al.*(2000) who stated that "the increase in student misbehavior is associated with habit of ignoring rules, due to higher attrition rates, academic failure, substance abuse as well as poverty and unemployment in adulthood". Another study also shows some students act ethically because they are worried about being "caught" by faculty members; others choose more ethical behavior because they realize that dishonesty/ misbehavior harms them, their instructors and other students (Bennett, 2005). This result is also supported by other study result

which expresses that even though policies/rules are in place in some institutions, some students clearly do not feel that they are protected and guided by rules (Monita et al.2013).

Other studies also show poor professional conduct prevails across Sub-Saharan Africa and South Asia. For instance, education officials in Malawi face exorbitant numbers of disciplinary cases related to teachers; they are sexual misconduct with pupils, fraud, absenteeism, substance abuse (drug and alcohol) and stealing of teaching and learning materials (plagiarism) (Bennell and Kwame, 2007). Other similar study on the misconduct of the teachers reveals that in some cases male lecturers may feel they have the right to have sex with the female students, and a student reporting sexual harassment would likely experience negative consequences (Morley, 2011). However, when lecturers harass students for sexual favors, a risk of greater vulnerability for unprotected sex and sexual coercion exist more than in situations in which females approach lecturers for sex in exchange for improved grades (Monita et al.2013). Such misconduct is ultimately expected to account for students' misfortune, low academic achievement and returns to education are observed in developing countries (Oyelere 2010).

These results indicated risk of low academic achievement, misbehavior of students and few lecturers and graduate assistants can spoil the objectives of the universities. Therefore above all, instructor/lecturers and graduate assistants should be guided by professional ethics to achieve the objectives of the students as well as the universities. Students need to target their vision and know they are protected and guided by the rules of the universities. Moreover, rules and regulations of the universities should be tight based on convention to achieve the goals and objectives of the universities as well as the students.

Effects of poor academic background of the students

Furthermore, Focus Group Discussion and interview showed students have had poor grade achievements, before entering the university. Be it in the high schools or in the university, the reasons behind low academic performance are more likely due to lack of study skills and concentration during reading, lack of confidence during examination, absence of experiences to succeed in academics; poor reading habit, peer pressure, lack of time management skills, low self-esteem or totally lack of self-esteem etc; and these factors may be considered as predisposing factors. Therefore, these predisposing factors may cause students to lose their self reliance and become dependent on others, which could expose them to dependency, rape, dangerous sexual harassment and other related risky behaviors.

Academically weak students in many cases are also subject to sexual assault by few instructors, senior

students, investors, (i.e., investors or commonly tagged as “sugar daddies or babies”). This has also become a factor that prompts learners to resort to unwanted sexual and related activities, and for that matter they do not negotiate sexual concerns, and even show rejection to concerned bodies

Our results also showed that low academic achievement may lead to risky sexual behaviors including life of prostitution. Results from in-depth interview of dismissed female students showed that those who were dismissed from the universities were engaged in unsatisfactory business including hotel life (prostitution). This result is in line with other study result which reveals that many Ethiopian adolescents continue to engage in risky sexual behaviors associated with low academic achievement and lack of parental communication; while, individual and family-level protective factors appear to moderate the impact of risk (Land,2004). Moreover, studies also revealed that academic achievement of the students has been significantly affected by the high school specialization rather than the university study (Mater and Muath, 1997, Odeh, 2007) and this confirms the need to improve high school education. Moreover, Sujit et al. (2006) show that test competence is an important factor for distinguishing students with low vs. high academic performance. Therefore, enrolment of students at each grade level, including the universities should be based on test competence so that the student enrolled can cope with the demands of the courses at different schools and university levels.

Predisposing factors identified in the university campus and off the campus could increase the vulnerability of the students to risky sexual behaviours that may lead to HIV infection and other sexually transmitted diseases. Female students who were dismissed from the universities due to academic problem are running unsatisfactory life including commercial sex work. Therefore, since university students are the basis of the future and represent the hope for an HIV/AIDS free generation, universities should design feasible strategies to take urgent risk reduction measures such as behavioural change communication (BCC) interventions. Moreover, dismissed female students are high risky groups and they need to: (a) Be engaged in income generating activities (IGA) (for only the girls who will voluntarily want to perform this activity); (b) re-attach themselves with their family members (after counselling from their parents and assessing their willing) and; (c) capacity building: Re-admitting them in college or university, provided that if the dismissed female students have academic potential to do so to save their livelihood.

CONCLUSIONS AND RECOMMENDATIONS

We observed serious risky sexual behaviors among the students which may expose them to sexually transmitted infections including HIV. To mitigate the problems, holis-

tic and integrated efforts including that of policy makers, university officials, students, their parents and the surrounding community are needed to underline the sensitivity and seriousness of the situation. . Moreover, this finding also recommends new approaches such as providing pre-hand orientation for the fresh university students, reviewing the existing curriculum and promotion policies, integrating or separate inclusion of sex education including HIV issues into the university and formal school curricula, and provision of special attention to female students who are being dismissed from the universities.

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Full Length Research Paper

Geriatric human immune deficiency virus (HIV) Infection in Nigeria: A case-series report

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This study involves a case-series of 3 elderly male patients with human immune deficiency virus (HIV) infection managed between 2009 and 2010 at the antiretroviral clinic (ART) University of Ilorin Teaching Hospital, Nigeria. They were all within the age range of 73 to 100 years and had multiple sexual partners. They were also co-managed for hypertension, diabetes mellitus and benign prostatic hyperplasia. Baseline CD4 count was < 350 cell/mm³ for all of them and their chemistry and haematology results were within normal ranges. Sputum acid fast bacilli (AFB) was also negative. They all had first-line anti retroviral (ARV) therapy and cotrimoxazole prophylaxis. Initially, adherence was perfect in all of them ($\geq 95\%$) especially as their relatives who double as the treatment-partners ensured their regular intake of ARV and clinic attendance but later adherence became poor ($< 80\%$) which was reflected in the fallen CD4 counts. Reasons for this include dementia and polypharmacy. One developed severe anaemia due to zidovudine (ZDV)-induced bone marrow suppression and was appropriately managed. Two of the three cases died < 2 years post-HIV diagnosis. Conclusively, geriatric HIV infection management entails multidisciplinary approach and a sound working knowledge of antiretroviral therapy with all the peculiar characteristics in the elderly.

Key words: Human immune deficiency virus (HIV), geriatric, adherence, highly active antiretroviral therapy (HAART), people living with HIV (PLHIV).

INTRODUCTION

Geriatrics, known as the care of the elderly (≥ 65 years), is fraught with multiple pathologies. These illnesses or disabilities can be categorized into 'age-determined', which are as a result of the inevitable changes associated with the aging process, or 'age-related' which result from an accumulation of risk factors such as poor nutrition, cigarette smoking, excessive alcohol intake, lack of exercise and unprotected exposure to multiple sexual partners (Walensky et al., 2006). The latter group can therefore be slowed down or prevented by a healthy lifestyle and adoption of health promotion measures while the former group of morbidities are to a large extent

inevitable. Human immune deficiency virus (HIV) infection in the elderly fall into the latter category.

Since the discovery of HIV 30 years ago, there has been a substantial increase in the average age of HIV infected patients worldwide. Much of this increase is because of improved survival of patients on antiretroviral therapy (ART), changes in behavior that have resulted in HIV-1 seroconversion at a more advanced age and a lack of clinical suspicion of HIV-1 infection, which leads to diagnostic delays in older individuals (UK Collaborative HIV Cohort (CHIC) Study Steering Committee, 2007; Centers for Disease Control and Prevention, 1998).

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Because of the low prevalence of recognized infection in older patients and rapid disease progression during the earlier phases of the epidemic, HIV-infected patients are considered to be “elderly” when they were older than 50 years of age (Centers for Disease Control and Prevention, 1998).

Probably due to delayed diagnosis, HIV-infected elderly patients generally have more advanced disease than do younger patients at the time of diagnosis (Centers for Disease Control and Prevention, 1998). Also, mortality rates within 1 year of acquired immune deficiency syndrome (AIDS) diagnosis are substantially greater in older versus younger patients (Centers for Disease Control and Prevention, HIV/AIDS surveillance report, 2006). There are no manifestations of HIV-1 disease that are unique to the elderly. However, some prominent symptom complexes and AIDS-defining illnesses frequently associated with the elderly HIV infection include peripheral neuropathy, weight loss, HIV associated esophageal candidiasis, wasting, and HIV-associated dementia (HAD) (Centers for Disease Control and Prevention, 1998)

Another key distinguishing clinical feature of HIV-1 infection in the elderly is the higher prevalence of comorbidities. To a large extent, personal habits (for example, tobacco, substance, or alcohol use) and the normal consequences of aging contribute to the occurrence of comorbid conditions. Also, various antiretroviral agents are associated with multiple acute and long-term medical complications, and HIV infection itself also contributes to the onset and severity of comorbid conditions (Lodwick et al., 2008; Phillips et al., 2008; Weber et al., 2006). All these factors could make management of HIV infection in the elderly very challenging especially in the low resource settings where necessary medical tools and equipments may not be readily available and these elderly patients are often too poor to afford quality healthcare service in the absence of social benefits.

Globally, in 2002 there were 605 million old people of which 400 million were living in low-income countries, and It is projected that by 2025, the number of elderly people would have risen to more than 1.2 billion with about 840 million of them in low-income countries (Park, 2007). The increasing number of old people is due to improvement in medical and social services with increase in the standard of living worldwide. In the United States in 2006, persons 50 years of age or older accounted for 14.9% of all new diagnoses of HIV-1 infection and 19.9% of all new diagnoses of AIDS. They make up 25.3% of all individuals living with HIV-1 infection and 36.9% of all deaths of HIV-infected persons (Lodwick et al., 2008) and by 2015, one half of all HIV-infected patients in the United States will be older than 50 years of age (US Department of Health and Human Services, 2009). Figures for low resource settings are unavailable.

The majority of patients enrolled in most HIV clinical trials have generally been too young to provide good

insight into the management of older HIV-infected patients. In some studies, participants were younger than 40 years of age. Hopefully, increased attention to elderly (that is, older than 50 years of age) HIV-infected patients will increase their inclusion in clinical trials and provide the data we need to give them better medical care. This case-series obtained from the ART clinic of University of Ilorin teaching hospital, Nigeria therefore aimed to bridge the knowledge gap in geriatric HIV infection, highlight the challenges in managing elderly HIV infected patients and the peculiarities of geriatric HIV presentation in a developing country like Nigeria and the need for multi-disciplinary approach to care.

CASE-SERIES PRESENTATION

Case 1

Mr. Y. M was a 100 year old, butcher, married to 4 wives and had 15 children, lived in Ilorin, Kwara State, Nigeria. He was diagnosed as HIV seropositive on July 22nd, 2009 while undergoing pre-surgical investigations for herniorrhaphy. At presentation, there was history of chronic weight loss and recurrent genital and perineal rashes. He later developed cough, which was productive of whitish sputum, night sweat and fever. He was screened for pulmonary tuberculosis with sputum acid fast bacilli (AFB) and chest x-ray, both of which came out with negative results. There was no history of previous surgery and blood transfusion but there were remarkable scarification marks on the body and face. These marks and the multiple sexual partners constitute risk factors of HIV infection in this case. Baseline CD4 count was 253 cells/mm³ with normal haematology and chemistry results. Blood sugar was normal too. He had adherence counselling and was commenced on highly active antiretroviral therapy (HAART) (NVP 200 mg + 3TC 150 mg + D4T 30 mg, 12 hourly) with cotrimoxazole 960 mg daily after a thorough adherence counselling. Concurrent management of the hypertension, diabetes mellitus and the prostatic hyperplasia (BPH) conditions of the patient by the the other medical, endocrinology and the urological teams continued. Adherence to ARV was initially perfect (> 95%) but later became poor and the CD4 count declined to 118 cells/mm³ over a period of 3 months on ARV therapy. Other causes of declining CD4 count like presence of opportunistic infections and human and mechanical errors in the laboratory were ruled out. He claimed to have disclosed to one of his wives and a son who was his treatment partner and accompanied him to the clinic. HIV status of the other 3 wives was unknown. He defaulted his last clinic appointment; was last seen in the ART clinic in July 2010, and was tracked to his home where it was learnt that he died on October, 2010; 16 months after HIV diagnosis. Cause of death was unknown.

Case 2

Mr. M. S was a 73 year old retiree, married to a second wife after the demise of the first wife in a road traffic accident. He lived in Ilorin, Nigeria. He was diagnosed to be HIV seropositive on 7 August, 2009. At presentation, he complained of generalized body rashes with chronic weight loss, no fever or diarrhea. On examination, nothing was significant except a herpetic rash on the left lower thoracic region with a septic focus on the chest (Herpes Zoster), and for this he was given antibiotics and analgesics. He was a known diabetic and hypertensive patient diagnosed more than a year ago. These conditions were well controlled with oral hypoglycemic and antihypertensive drugs by the endocrinology and the internal medicine units. He was also seen by the chest physician for his bronchial asthma. He later developed productive cough with no fever or night sweat, sputum AFB and microscopy (MCS) done were negative (CXR was not done). He also presented with symptoms of prostatitis and benign prostate enlargement (BPH) confirmed with ultrasound scan of the prostate (PSA was not done), and was referred to the urologist.

Baseline CD4 count was 281 cell/mm³ with normal haematology and chemistry results. He was started on HAART (NVP 200 mg + 3TC 150 mg + D4T 30 mg, 12 hourly) with cotrimoxazole 960 mg daily. D4T (stavudine) was later substituted with zidovudine 300 mg bd (ZDV) to avoid side effects (peripheral neuropathy). Ongoing adherence counseling service was accessed by the patient. There was improvement in the patient's condition as the CD4 count increased from 281 cell/mm³ to 368 and 375 cell/mm³ at 6th and 12th month follow up visits, respectively. The adherence which was perfect during this period nose-dived later as the patient started denying his HIV serostatus (senile dementia). However, he did not default in his clinic appointment as his wife, who was his treatment partner, brought him regularly to the hospital. The wife was HIV negative. Patient was last seen in January, 2011 but died at home in February, 2011; 17 months after HIV diagnosis. Cause of death is unknown.

CASE 3

Mr Y. A is a 77 year old widower with three children, a civil servant retiree living in Ilorin, Kwara State, Nigeria. He was diagnosed HIV positive in 2010 while attending diabetes mellitus clinic. No prior history of surgery or blood transfusion, no scarification mark. Wife's cause of death was unknown and sexual experience with other women unknown. Baseline CD4 count was 264 cell/mm³ with normal haematology and chemistry results. He was then commenced on NVP 200 mg + 3TC 150 mg + ZDV 300 mg, 12 hourly but had to be changed to NVP 200 mg + 3TC 150 mg + D4T 30 mg, 12 hourly as the haemoglobin level fell from 14 g/dl (PCV: 42%) at baseline to 3 g/dl (PCV: 9%) over a period of 4 months.

Patient had to be transfused with 4 pints of packed cell and placed on haematinics, leading to marked improvement in the haemoglobin level. Other causes of severe anaemia like nutritional deficiency, GIT bleeding etc. were ruled out apart from zidovudine-induced bone marrow suppression. D4T was also replaced with abacavir (ABC) later to avoid side effects of the drug (peripheral neuropathy, lactic acidosis, lipid dystrophy etc). He claimed to have disclosed his status to two of his children, and one of the daughters is his treatment partner who accompanied him to the clinic. At the last clinic visit which was September 7th, 2011, CD4 count was 396 cell/mm³, weight was 68 kg, had no complaint and was generally looking well.

DISCUSSION

An increasing number of new HIV diagnoses continues to be reported among persons aged 50 years or older. The CDC estimates that there were close to 7,000 new cases in this age group in 2009 in the US alone (US Centers for Disease Control and Prevention, 2009). Many practitioners are beginning to see more of HIV infection in the geriatrics group. Though sexual activity may decline with increasing age, it is still fairly common for many older individuals. Older persons have distinct risks for HIV infection, and therefore needs counseling regarding HIV prevention. Many older adults may find themselves newly single-widowed or divorced, often with little knowledge of the need to protect their sexual health or the skills required to do so. There may be specific age-related barriers to condom use in both men and women. Postmenopausal women, for example, may be less concerned about pregnancy prevention, whereas men may have erectile dysfunction and avoid condom use for this reason. Moreover, lower estrogen levels can lead to vaginal dryness, which is likely to increase the risk of HIV transmission in women. The baseline CD4 count was less than 350 in all the three cases and two of them died less than 2 years after HIV diagnosis despite being placed on HAART. This means they all presented at advanced HIV infection and had a rapid progression of the disease even though the exact time of HIV exposure and seroconversion are not known.

In 2005, 53% of older HIV-infected persons in the United States versus 37% of younger persons developed AIDS within 12 months of their diagnosis of HIV-1 infection (Linley et al., 2007). Similarly, the rates of death within 1 year of AIDS diagnosis are substantially greater in older versus younger patients (Lodwick et al., 2008). The more rapid progression of HIV-1 disease; age-related immune senescence which may be independent of CD4+ T-cell count, the increased prevalence of co-morbidities which may be exacerbated by HIV-1 infection; and decreased rates of immune reconstitution provide a plausible rationale for beginning therapy at higher CD4+ T-cell counts (that is, > 350 cells/mm³) in older patients than

is generally recommended for younger individuals.

Age-related declines in immune function, including decreased thymic function, as well as deficits of naive and memory CD4+ T-cell function, number, and regeneration contribute to and exacerbate the rate of CD4+ T-cell count decline and disease progression in older HIV-infected patients (Appay and Sauce, 2008; Aw et al., 2007; Haynes et al., 2000; Kovaiou and Grubeck-Loebenstein, 2006). Though not done in these cases due to lack of availability, viral load would have helped in monitoring for virological failure in these patients.

The negative sputum AFB test results seen in these patients despite being TB suspects could mean that they either do not have pulmonary tuberculosis or have negative-smear Koch's disease, which was not surprising too as studies have shown that patients with HIV-related pulmonary TB more often have negative sputum smears (43% versus 24%) (Gupta et al., 2005). There were also adherence problems with two of the 3 cases, even though the use of relatives as treatment partners in the three cases was associated with regular clinic attendance and perfect adherence (> 95%) at the initial stage. Comorbidities necessitating intake of multiple drugs and onset of dementia common in the geriatric population may pose a serious challenge to adherence as seen in one of the cases.

The sudden drastic drop in the haemoglobin level of the 3rd patient due to zidovudine-induced bone marrow suppression should be a source of concern when managing elderly patients irrespective of the baseline haemoglobin. Other ARV adverse reactions common in the elderly include, increased risk of myocardial infarction, cardiovascular disease and/or cerebrovascular event found among patients receiving PI-containing ART, increased rates of cardiovascular toxicity among patients on abacavir and didanosine, especially in patients with previous underlying risk factors for vascular disease (Strategies for Management of Anti-Retroviral Therapy/INSIGHT; DAD Study Groups, 2008; Sabin et al., 2008). Also the rate of development of diabetes has been reported to be more than 3 times higher among HIV-infected men receiving ART (Brown et al., 2005) especially with current use of NRTIs, particularly stavudine, zidovudine, and didanosine agents that cause mitochondrial depletion. Incidence of metabolic syndrome (that is, dyslipidemia, abdominal adiposity, elevated blood pressure, and insulin resistance common in HIV-infected patients increases with age and PI exposure (US Department of Health and Human Services, 2009). The risk of kidney disease associated with HIV infection which is exacerbated by age is worsened with the use of tenofovir.

Careful selection of ARV regimen is important in geriatric patients because of pharmacokinetic interactions between the antiretroviral drugs and other drugs used for other comorbidities for example drugs in classes such as HMGCoA reductase inhibitors (statins), selected antiarrhythmic agents (for example, amiodarone),

medications that inhibit gastric acidity, anticonvulsants, warfarin, and selective serotonin uptake inhibitors may be candidates for drug-drug interactions with antiretroviral medications.

HIV infection can cause respiratory disease as a consequence of pneumonia, it is also associated with increased rates of chronic obstructive pulmonary disease and pulmonary hypertension hence it is not surprising that one of the cases developed asthma in the course of management. Regular screening and health maintenance are particularly important in older persons with HIV. In addition to baseline ART evaluations, monitoring of cardiovascular risk, monitoring of fasting lipid and glucose levels, markers of inflammation, renal function, and markers of bone disease, cancer should be undertaken as part of routine medical follow-up to monitor the preexisting age-related comorbidities and laboratory abnormalities, which may be exacerbated by the additive effect of HIV infection itself coupled with adverse effects of ART.

The effects of aging on drug absorption, distribution, and metabolism; the complexities of polypharmacy and drug-drug interactions in patients with concomitant comorbidities; and the increased frequency of pre-existing and emergent laboratory abnormalities with the use of ART warrant special attention in this patient population and often necessitate joint management with other specialties. Also, the geriatric specialists who work with these patients require training in the special issues surrounding HIV infection, and those who work with HIV-infected patients need to be trained in the special issues surrounding aging and these two groups of physicians must communicate.

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ABBREVIATIONS

ART, Antiretroviral therapy; **ARV**, antiretroviral drugs; **CD4-CD4-bearing**, T-lymphocytes; **Sputum AFB**, sputum acid-fast bacilli test; **NVP**, nevirapine; **3TC**, lamivudine; **ZDV**, zidovudine; **D4T**, stavudine; **CXR**, chest x-ray; **MCS**, microscopy, culture and sensitivity; **PSA**, prostate antigen; **PCV**, packed cell volume; **GIT**, gastrointestinal; **ABC**, abacavir.

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Full Length Research Paper

Gaps in preventing mother to child transmission (PMTCT) and human immune deficiency virus (HIV) exposure among infants in a Nigerian City: Implications for health systems strengthening

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In many countries, paediatric human immune deficiency virus (HIV) has been virtually eliminated. Nigeria however still records an unacceptably high number of HIV positive births. This study aims to identify HIV exposure rates among infants and to quantify gaps in preventing mother to child transmission (PMTCT) services in a major Nigerian city. A cross-sectional design was used to assess the prevalence of HIV sero-positivity in infants and use of PMTCT services among mothers in routine immunization clinics across the city. A total of 2,125 mother-infant pairs from 53 Primary Health Care Facilities were studied. More mothers who had received Ante natal care (ANC) services from orthodox health facilities were screened for HIV; 77.5% compared to 42.5% of those who used non-orthodox care providers ($p < 0.001$). In all, 0.6% of mothers were people living with HIV/AIDS (PLWHA). Overall, 0.9% of infants tested positive for HIV, only one infant was confirmed by DNA polymerase chain reaction (PCR) to be HIV infected. Only one of the 18 mothers of the HIV exposed infants had been previously diagnosed as having HIV infection. Among the newly diagnosed HIV positive mothers, 58.8% had received antenatal care from an orthodox health facility and 35.3% had been screened for HIV in pregnancy. Most mothers had practiced mixed feeding of their babies. The low HIV exposure rates among infants indicate progress in limiting mother-to-child transmission of HIV infections in Nigeria. However, the achievement of National PMTCT targets will need joint action of all stakeholders to reach those women without access to orthodox health facilities.

Key words: Human immune deficiency virus (HIV), polymerase chain reaction, preventing mother to child transmission.

INTRODUCTION

Sub-Saharan Africa is home to 2.3 million out of the 2.5 million children living with HIV worldwide with Nigeria contributing 14% of the total African burden of paediatric Human immune deficiency virus (HIV) (World health organization, 2010). In many developed countries, paediatric HIV has been virtually eliminated. Many high burden, low-resource countries have also made significant progress in preventing new paediatric infections. Although some progress has been reported in scaling up

of access to prevention of mother to child transmission of HIV (PMTCT) services in Nigeria, with an annual HIV positive births of 56,681, much work remains to be done (NACA Fact Sheet, 2011). In response to the UNAIDS 'getting to zero' strategy, Nigeria had renewed commitments to expand the coverage of PMTCT services with the aim of eliminating the transmission of HIV from mother to child during pregnancy, labour and breast feeding (NACA Fact Sheet, 2011). Even in countries with

Table 1. Mothers' and Infants' demographic characteristics.

Characteristic	N=2125 (%)
Age of infant (weeks)	
<6	420 (19.8)
6-11	730(34.4)
12-23	442(20.8)
24 and above	533(25.1)
Sex	
Male	1051 (49.5)
Female	1074 (50.5)
Mothers demographics	
Marital status	
Married	2110 (99.3)
Not married*	15(0.7)
Educational level	
No formal education	37 (1.7)
Primary	522 (24.6)
Secondary	1118 (52.6)
Post secondary	447 (21.0)
Social class	
I	7 (0.3)
II	585 (27.5)
III	1266 (59.6)
IV	267 (12.6)

*Not married includes separated, widowed, single

strong PMTCT programmes, some level of complacency has been recorded. As such, one of the strategic visions of the World Health Organization is to track programme performance and impact on MTCT rates (World health organization, 2010).

In Nigeria, availability of early infant diagnosis (EID) at PMTCT sites and children hospitals have been identified as a challenge to the effectiveness of PMTCT in the country (NACA Fact Sheet, 2011). To inform recommendations on the scale of EID services, it becomes necessary to provide information on HIV exposure rates among infants in Nigeria. At present, only a small number of studies exist on community estimates of HIV exposure rate and new infections in infants in Nigeria. This study aims to bridge this knowledge gap by identifying HIV exposure rates among infants and to quantify gaps in PMTCT services in a major Nigerian city.

METHODOLOGY

This study was conducted in Ibadan, the largest and capital city of Oyo State, South western Nigeria. The latest sentinel survey put HIV prevalence for Oyo state at 3% (Federal Ministry of Health,

2010a). Of the 1,169 health facilities of which 667 are primary health centres (PHCs), 10 offer comprehensive PMTCT services while 5 of these are private-owned health facilities. All of these PMTCT centres are located in secondary and tertiary centres. However, many primary health centres are able to screen for HIV.

A cross-sectional design was used to assess the prevalence of sero-positive HIV infants and use of PMTCT services among mothers in routine immunization clinics across the city. Half of the PHCs (minimum 4) in each local government area were randomly selected, by balloting, to be included in the study. Children \leq 1 year (infants) presenting for immunization, were consecutively enrolled into the study between December, 2010 and June, 2011. Mothers were interviewed on PMTCT services accessed in pregnancy such as HIV counselling and testing, anti-retroviral therapy if indicated, infant feeding and counselling. Mothers were offered voluntary HIV counselling and HIV testing for their babies. Pre- and post- HIV test counselling were performed by trained personnel using the "opt out" method as recommended in the World Health Organization (WHO) and National PMTCT guidelines. Post-test counselling was provided individually in private rooms for confidentiality.

Infant HIV status was assessed using Determine^R and Unigold^R rapid antibody testing method in series. Results were disclosed on the same day during post-test counselling. Mothers whose infants tested positive were subsequently screened using Determine^R and Unigold^R. Infants with positive rapid screening test results were then referred for follow-up in the existing PMTCT programme at the University College Hospital, Ibadan where DNA polymerase chain reaction (PCR) was carried out to confirm HIV status. Infants with positive rapid screening tests who were aged less than six weeks at the time of the study had their DNA PCR confirmatory test at 6 weeks of age. Mothers testing positive with the rapid tests were linked up with the adult HIV care programme in the University College Hospital. A structured questionnaire was used to collect socio-demographic, pregnancy, delivery, postpartum and HIV testing data.

Definition of outcome

1. HIV exposed infant were those infants positive to HIV rapid antibody tests;
2. HIV infection in infant was defined as being positive to DNA PCR
3. HIV infection in mother as positive test result for HIV rapid antibody tests.

Sample size was calculated based on the HIV prevalence rate in Oyo state which is 3.0% from the most recent sentinel survey (Federal Ministry of Health, 2010b). Using a standard deviation of 1.96 which corresponds to 95% confidence interval and a level of precision of 2%, the desired sample size for the study was 2125. Data were analysed with statistical package for social sciences (SPSS) version 15.0 (SPSS Inc., Chicago, Illinois, USA). Proportions were compared with the Chi square and Fisher's exact tests. Significance level was set at 0.05 level. Permission and ethical approval was obtained from the Oyo state Ethical Review Board. Screening for HIV was preceded by counselling and consent of the mother. Mothers were assured that refusal of consent would not result in their child being denied appropriate management in the PHC.

RESULTS

A total of 2,125 mother-infant pairs from 53 PHCs were studied. The median age of the infants was 12 weeks (range: 0.1 to 55 weeks). Table 1 shows that infants aged 6 to 11 weeks were the largest proportion of the infants

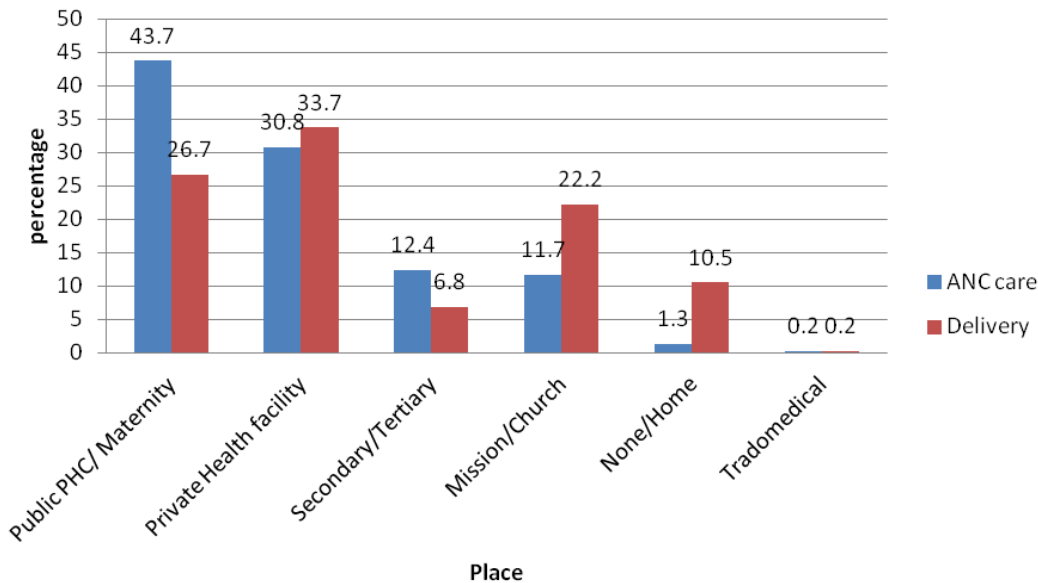


Figure 1. Antenatal care and place of delivery.

(34.4%). The sex ratio was 0.9: 1. Almost all the mothers were married with many (73.6%) having at least secondary level education. More than half (59.6%) were from social class III. The use of Ante-Natal Centre (ANC) services and the place of delivery of index infant are shown in Figure 1. While many (43.7%) mothers received antenatal care at the public PHCs, fewer mothers (26.7%) actually delivered their babies at the PHCs. About a tenth (10.5%) of mothers delivered their babies at home.

Comparison of the PMTCT services received during antenatal care reveal a significantly higher proportion of those receiving ANC services from orthodox health facilities screened for HIV which is 77.5% compared to 42.5% of those who used non-orthodox care providers ($p < 0.001$). HIV detection rate and ARV prophylaxis for seropositive mothers did not differ significantly. There was also no significant difference in the use of ARV prophylaxis for children of seropositive mothers when the place of delivery was compared. In all, 0.6% of mothers were PLWHA (Table 2).

HIV exposure and infection among Infants

Overall, 19 of the Infants tested positive for HIV rapid antibody tests, only 1 infant was confirmed by DNA PCR to be HIV infected (Table 3). All (18) mothers of HIV exposed infants also tested positive to HIV rapid antibody tests. One mother had died from symptoms suggestive of HIV infection but was unconfirmed. The infant of the mother who had died was the only confirmed HIV infected infant. He was aged 10 weeks and had symptoms of HIV disease. Only one of the 18 HIV infected mothers had been previously diagnosed as having HIV infection

and the infant had received ARV prophylaxis at birth. Among newly diagnosed HIV positive mothers, 10(58.8%) had received antenatal care from an orthodox health facility, 8(47.1%) had delivered at an orthodox facility. Overall, 14(82.4%) had a skilled attendant during delivery. HIV testing in pregnancy was reported by 6(35.3%) of the mothers, none of the mothers had received ART and only one mother reported ARV prophylaxis being given to her baby at birth. 13 of the mothers had practiced mixed feeding of their babies (Table 4).

DISCUSSION

The HIV exposure rate among infants attending routine immunization clinics in the city of Ibadan was low. 19 infants were found to be exposed to HIV while 1 was confirmed to be infected. Although few local studies have assessed HIV exposure in infants from a well-child clinic such as a routine immunization clinic, still these rates are much lower than previous reports (UNICEF, 2010). This confirms the downward trend in HIV infections in the country, as National estimates have also shown (NACA Fact Sheet, 2011).

In a similar vein, this is additional evidence of improved PMTCT coverage. Over three quarters of women using orthodox health service had received HIV testing during the index pregnancy compared to less than 20% reported for Oyo state in previous studies (Bashorun et al., 2010). More of the women without access to PMTCT services are those already marginalized populations unable or unwilling to access orthodox health care providers. This is not an uncommon finding (Bashorun et al., 2010).

However, the fact that many of those with HIV exposed babies were those using non-orthodox care providers

Table 2. Comparison of PMTCT services received from antenatal care provider.

PMTCT service	ANC provider utilized in pregnancy		Chi-square	p-value
	Orthodox health facility	Non-orthodox health facility		
HIV testing during index pregnancy				
Yes	1428(77.5)	119(42.5)	150.459	<0.001*
No	415(22.5)	161(57.5)		
Reported HIV detection rate for mothers				
Sero-positive	10(0.5)	3(1.1)	1.093	0.296
Sero-negative	1833(99.5)	279(98.9)		
ARV prophylaxis for seropositive mothers (N=13)				
Yes	2(20)	1(33.3)	Fisher's exact test	1.000
No	8(80)	2(66.7)		
Place of delivery				
	Orthodox health facility	Non-orthodox health facility		
ARV prophylaxis for baby (N=13)				
None	1 (11.1)	1 (25.0)	Fisher's exact test	1.000
NVP and AZT	8 (88.9)	3 (75.0)		

NVP – Nevirapine, AZT – Zidovudine, *significant.

Table 3. HIV Test results of infants attending immunization clinics in Ibadan.

Test result	Infant	
	Determine+unigold (N=2125)	DNA PCR (N=19)
Seropositive	19 (0.9)	1 (5.2)**
Seronegative	2106 (99.1)	15 (79.0)
Not done	0 (0.0)	3 (15.8)

implies that this population remains an important one to target for PMTCT interventions. More than half of those who had accessed ANC from non-orthodox providers were not screened for HIV compared to about one fifth of those who had used orthodox providers. Extending PMTCT coverage to other community based providers might help to improve coverage since the inaccessibility to health services seems to be the major risk factor for unidentified, HIV-exposed and HIV-infected children (Braun et al., 2011).

By and large, it appears that the optimism about eliminating all cases of mother-to-child transmission of HIV infections in Nigeria is not misplaced, provided the same progress in limiting MTCT is recorded and maintained in other states of the country. However, the achievement of national and global PMTCT targets will only be dependent on the joint action of health services, communities and the wider society to reach those women beyond the reach of the orthodox health facilities (Richter, 2012).

HIV screening of all infants at immunization clinics has

been suggested as an acceptable and feasible method to monitor the impact of PMTCT programmes on peripartum infection and to provide surveillance data on paediatric HIV (Rollins et al., 2009). The opportunity to detect those women who might have fallen through the cracks of the health system through screening of their infants may afford another justification than the opportunity to diagnose HIV infection in infants and children missed within the health system. However, the low yield demonstrated by this study questions the cost effectiveness of this approach in a low prevalence site as in Ibadan. The recommendation for routine screening of all infants as reported in a South African study where routine HIV testing of infants revealed prevalence of more than 20% among tested infants may need to be appropriately contextualised (Rollins et al., 2009). A more targeted approach such as limiting screening of infants to only those with mothers with unknown HIV status as recommended by an American study (Shah et al., 2011) may be more appropriate in this setting.

Table 4. Exposure to PMTCT among newly diagnosed HIV positive mothers.

Variable	N=17(%)
Place of ANC	
Orthodox HF	10(58.8)
Non-orthodox facility	7(41.2)
Place of delivery	
Orthodox HF	8(47.1)
Non-orthodox facility	9(52.9)
Skilled attendant at delivery	
Yes	14 (82.4)
No	3 (17.6)
Screening in pregnancy	
Yes	6(35.3)
No	11(64.7)
ARV prophylaxis in mother	
0(0)	
ARV prophylaxis for infant	
None	16(94.1)
NVP and AZT	1(5.9)
Feeding pattern	
Exclusive breastfeeding (with no water, herbal medicine, etc)	4(23.5)
Mixed feeding	13(76.5)
Formula	(0)

LIMITATIONS

This study is beset by some limitations. The level of acceptance or uptake of infant HIV testing among the mothers was not measured because of the opt-out method used to enrol infants for HIV screening. In addition, PMTCT coverage was based on self-reports which could not be verified and could have been over or underestimated.

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Full Length Research Paper

Predictors of intended infant feeding options among HIV positive pregnant women in Addis Ababa: The perspective of theory of planned behavior

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Although exclusive breast feeding during the first six months of life or replacement feeding are crucial in prevention of mother to child transmission of human immune deficiency virus (HIV), mothers intention on feeding options remain unstudied in Ethiopia. Therefore, this study was intended to assess HIV positive pregnant women's intention towards infant feeding options. The data were collected from 196 HIV positive pregnant women who were recruited consecutively from nineteen public health institutions in Addis Ababa. The study revealed that 159 (81.12%) and 25 (12.76%) of the respondents intended to exclusive breast feed and use replacement feeding, respectively. Mixed feeding intention was very low (6.12%). Not attending formal education, increased knowledge about preventing mother to child transmission (PMTCT), favorable attitude towards exclusive breast feeding, increased control belief (perceived ability to control the difficulties) to use exclusive feeding were significantly associated with intention to use exclusive feeding ($p < 0.05$). Mixed feeding intention was mainly associated with low control belief to use either exclusive or replacement feeding ($p < 0.05$). Recommended feeding option might have the chance to be practiced by most of the respondents. However, health professionals are still required to provide tailored messages which addresses attitude and beliefs related to recommended feeding and how to control a condition that makes behavioral performance difficult.

Key words: Intention, infant feeding options, exclusive breast feeding, preventing mother to child transmission (PMTCT), theory of planned behavior.

INTRODUCTION

Ethiopia is one of the countries with the largest populations of human immunodeficiency virus (HIV) infected people in the world (Federal Ministry of Health- Federal HAPCO, 2007). In 2009, adult HIV prevalence was estimated to be between 1.4 and 2.8% (Ethiopian Health and

Nutrition Research Institute, 2010). Although adult prevalence (ages 15 to 49) is declining, HIV prevalence among pregnant women remains high; estimated at 1.1% in 2009. In 2011, approximately 42,900 pregnant women living with HIV delivered (Unite for Children against AIDS,

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2012). As a result, pediatric HIV infection remains the major concern in Ethiopia. For instance, in 2009 and 2011, 14,140 and 13,000 positive births were recorded, respectively (HAPCO-Ethiopia, 2010). On top of that, access to prevention of mother to child transmission (PMTCT) and anti retroviral therapy (ART) services are very limited in Ethiopia. In 2010, PMTCT services were available in only 43% of all Ante Natal Care (ANC) facilities (World Health Organization (WHO), 2011). HIV testing coverage (26% in 2010) among pregnant women is still very low (WHO, 2011).

In 2011, only 24% of people living with HIV (PLWHIV) received ART regimens for preventing mother-to-child transmission (MTCT) of HIV (UNAIDS, 2012). As a result, the mother-to-child transmission rate was very high; estimated at 30% in 2011 (UNAIDS, 2012). Beyond the health impact, HIV is a social and economic problem in Ethiopia; 16% of the orphaned children are due to acquired immune deficiency syndrome (AIDS) in Ethiopia (HAPCO-Ethiopia, 2010). Breastfeeding plays an important role in the transmission of HIV from mother to the child. Evidence has shown that 5 to 20% of the infections occur through breastfeeding. Globally, in 2010, approximately 40% of HIV-positive pregnant women have CD4 counts ≤ 350 cells/ μl^3 and these women account for greater than 75% of MTCT risk, and greater than 80% of this infection occur during postpartum period (WHO/UNICEF/UNAIDS, 2010).

In Sub-Saharan African countries, breast milk causes between 30 and 40% of the cases of pediatric HIV infection (WHO/UNICEF/UNAIDS/UNFPA, 2008). The revised WHO infant feeding guideline for positive women recommends exclusive breast feeding (EBF) with an ART intervention for the first six months, and continued breast-feeding with complementary feeding until the child is at least a year old. Alternatively, where it is acceptable, feasible, affordable, sustainable and safe, WHO recommends complete avoidance of all breastfeeding and encourages replacement feeding (RF) option (WHO/UNICEF/UNAIDS/UNFPA, 2010). Unfortunately, encouraging mothers to practice exclusive breastfeeding is far from easy. In many societies, especially in sub-Saharan Africa, it is normal for a baby to be given water, teas, porridge or other foods as well as breast milk, even during the first few weeks of life (WHO, 2006; FHAPCO and FMoH, 2007). In addition, many women are concerned that their breast milk is not sufficient for their infant; because they are malnourished (FHAPCO and FMoH, 2007).

Ethiopia has adopted the WHO 2010 PMTCT guidelines (UNICEF, 2010). However, some report shows that the latest guidelines have not been disseminated in many countries, leaving women dangerously confused about the best nutritional path to protect their children from contracting the virus (UNICEF, 2013). In order to prevent

the baby becoming infected with HIV, a greater empathize has laid on breastfeeding options (UNICEF, 2009). As mothers are the implementers of the guideline, the beliefs and attitude they would hold on feeding options plays crucial role in the effort being under taken to reduce MTCT. However, the beliefs, attitudes and behavioral intentions of expectant mothers, regarding the new guideline, have not been subjected to scientific inquiry in Ethiopia. Therefore, this study was aimed to fill this evidence gaps.

Conceptual basis of the study

This study used theory of planned behavior (TPB) as conceptual basis. TPB was developed by Ajzen and is one of the most popular behavioral theories (Bruce et al., 1984; Karen et al., 2008). According to the TPB, the most important determinant of human behavior is behavioral intention; measure of motivation or readiness to act. Studies indicate that intention can be used as a proximal measure of behavior (Bruce et al., 1984; Karen et al., 2008). Behavioral intention is directly determined by a person's attitude toward performing the behavior, subjective norm and perceived behavioral control (PBC). Attitude is determined by the individual beliefs about outcomes or attributes of performing the behavior (behavioral beliefs), weighted by evaluations of those outcomes or attributes. Thus, a person who holds strong beliefs that positively valued outcomes will result from performing the behavior will have a positive attitude toward the behavior (Bruce et al., 1984; Karen et al., 2008; Christopher and Mark, 2001). Similarly, a person's subjective norm is determined by his or her normative belief (whether important referent individuals approve or disapprove of performing the behavior), weighted by his or her motivation to comply with those referents.

A person who believes that certain referents think she should perform a behavior and is motivated to meet expectations of those referents will hold a positive subjective norm (Bruce et al., 1984; Karen et al., 2008; Christopher and Mark, 2001). Likewise, PBC is determined by control beliefs (the presence or absence of facilitators and barriers to behavioral performance) weighted by their perceived power (the impact of each control factor to facilitate or inhibit the behavior) (Karen et al., 2008; Christopher and Mark, 2001). PBC is relevant where the behavior is not under complete volitional control. In summary, the TPB asserted that attitude toward the behavior, subjective norm, and perception of behavioral control lead to the formation of a behavioral intention and the more favorable the attitude and subjective norm, the greater the perceived control, and the stronger should be the person's intention to perform the behavior in question (Karen et al., 2008; Christopher

and Mark, 2001). The TPB is open to the inclusion of additional external variables. As a result, we included some variables which are external to the TPB.

The TPB has adapted as a conceptual framework for several reasons. First, it is the most widely researched behavioral theory to study behavioral intentions. Secondly, TPB allows for an understanding of the cultural perspectives influencing the behavior as it provides a methodology for the elicitation of the salient beliefs of the population under study. Thirdly, behaviors under investigation is not fully under volitional control because mother's decision to adopt one infant feeding options is a result of intra and inter personal processes (Matji and Wittenberg, 2008). Thus, the theory is very useful to design tailored interventions to promote recommended infant feeding options in the case of HIV positive women (Bruce et al., 1984; Karen et al., 2008; Christopher and Mark, 2001).

METHODS AND MATERIALS

Study setting and population

A facility based cross sectional study was conducted among HIV positive pregnant women attending PMTCT services in Addis Ababa (the capital city of Ethiopia) in public health facilities over a period of one month (March 15 to April 15, 2011). In 2009, 2279 HIV positive pregnant mothers were registered for and following PMTCT services in Addis Ababa city and PMTCT services was being given in 31 health facilities. The sample size was calculated using single population proportion formula $[(n = (Z_{1-\alpha/2})^2 p(1 - p)/d^2)]$ using a prevalence rate of 26% (prenatal intention to breastfeed or mixed feed) based on an estimate from South Africa study (Human Science Research Council/South Africa, 2008), 5% marginal error (d) and confidence interval of 95%. This yields a total sample size of 296 respondents. As the number of population (HIV positive pregnant women) was less than 10,000 in the study area, the sample size was corrected and considering 10% non-response rate, the final sample size was 194 individuals. New clients were not included in the study.

Sampling procedures

Nineteen public health institutions (two hospitals and seventeen health centers) providing PMTCT services were selected by simple random sampling method. Then, the sample size was proportionally allocated to each health institution based on the average number of client which visited each health institution during the last two months prior to the start of data collection. Finally, HIV positive pregnant women who visited the selected health institutions for ANC/PMTCT follow up were consecutively included in the study during days of data collection until the allocated size was obtained. New clients were not included in the study.

Measurements

Data collection instruments were developed according to the standard guideline of the theory of planned behavior (Bruce et al., 1984; Karen et al., 2008). First, elicitation study was conducted to

identify salient belief underlying attitude, subjective norm and perceived behavioral control. Then, the data obtained from the interview were analyzed and used to develop quantitative Likert scale questionnaires for each dimension of the TPB and translated to Amharic and pre-tested on similar population.

Intention to use different feeding options [EBF, RF and mixed feeding (MF)].

In this study we measured intention as outcome variable. To assess intention, respondents were asked nine items (three items for each aspect of feeding options). Each item was scored on a five point Likert scale ranging from 'strongly disagree' to 'strongly agree'. Then, for each feeding options the items were summed up separately, and based on respondents' total score to each option, intention classification was made. If a woman received highest score for EBF, then she was classified as intender of EBF. The same method was used for mixed and replacement feeding.

Attitude towards each breast feeding option

Attitude toward each feeding option was assessed in two ways: directly and indirectly (belief based attitude). For direct measures, respondents were asked 15 items (five items for each) on five point ordinal scale to rate their attitude towards each infant feeding option. Then, total score to each feeding option was computed and used for regression analysis. Indirect measures of attitude were constructed from items asking belief regarding using each feeding option (behavioral belief) and the evaluation (outcome evaluation) of the belief. Eighteen items (3 items for each feeding options) were used to assess the behavioral belief and outcome evaluation. Items of behavioral beliefs and outcome evaluation were used to compose the indirect attitude scale where each behavioral beliefs item scores were multiplied to its corresponding outcome evaluation item scores and then summed up to compose the belief based attitude scale. The higher the score indicates the higher favorable attitude.

Subjective norms

Subjective norms (respondent's own estimate of the social pressure to adopt one of the recommended infant feeding options) were assessed using direct and indirect methods. In the direct method, respondents were asked to rate whether "most people important to them think that they should use EBF or mixed feeding or replacement feeding for their baby after birth". Twelve items (4 items on each option) were addressed to them on a 5-point Likert scale with end point "strongly agree" and "strongly disagree". Then, a total score was computed for each option separately and used for further analysis. The indirect measures, referred to as weighted normative beliefs, was obtained by having respondents rate whether different referents think they should approve and use one of the three infant feeding options and their motivation to comply with those referents. Eighteen items (9 for normative belief and 9 for motivation to comply) were used to assess the indirect measure of subjective norms. Composite measure was computed by multiplying normative belief score with its corresponding motivation to comply. The higher the score indicates the higher the favorable attitude.

Perceived behavioral control (PBC)

PBC was assessed in two ways: directly by asking respondents to

rate the extent they would be able to follow one of the feeding options. Seventeen items were used on five point Likert scale, and the result scores was computed as the sum of these items. The indirect measures of perceived control (weighted control beliefs) were constructed from 9 control belief and 9 perceived power items. The weighted control scores were computed by multiplying control belief score with its corresponding perceived power items. The higher the score shows the higher the belief on one's own ability to control factors which may impede intended feeding option. In addition to the constructs of TPB, other information such as socio-demographic characteristics, previous breast feeding experiences, knowledge related to HIV transmission, and disclosure of HIV sero status were collected from the respondents. Respondents' knowledge regarding PMTCT of HIV were assessed using five items on 'yes' and 'no' format. A correct answer was coded as '1' and incorrect answer was coded as '0'. Then, a total score was computed by summing up all the five items together. A higher score indicates the higher level of knowledge.

Data collection

The data were collected by PMTCT counselor in each institution. They were trained by principal investigators on the purpose of the study, how to interview and recruit participants. Close supervision was under taken throughout the data collection process.

Statistical analysis

The data were analyzed using STATA 11.0 according to the TPB analysis guideline (Karen et al., 2008). First, bivariate analysis was carried out to identify candidate variables for the multivariable regression analysis. Second, to identify the predictors of feeding options, only variables that were significantly associated in the bivariate analysis were entered into a multinomial regression model in blocks. In the first regression model, the effects of socio-demographic variables were assessed while in the second and the third models, the effects of direct and indirect measures of TPB constructs were assessed, respectively. Finally, explanatory variables which had statistically significant association with the dependent variable ($P < 0.05$) were entered to the final regression model. Interactions between different variables were checked and collinearity diagnostics was done by checking the variance inflation factor. All tests were two sided and $P < 0.05$ was considered statistically significant. We report the result as odds ratios (ORs) and 95% confidence intervals.

Ethical consideration

This study was approved by the Ethical Clearance Committee of the Jimma University. Written informed consent was sought from each respondent. The data was collected by service providers to keep the confidentiality of the participants.

RESULTS

Socio-demographic characteristics of the respondents

All respondents approached (196 person) participated in

the study yielding response rate of 100%. Table 1 presents socio-demographic characteristics of the respondents. Accordingly, half of the respondents were in the age range of 26 to 30 years. In terms of educational status, about 29 (15%) of the respondents did not attend formal education.

Knowledge about PMTCT, breast feeding experience and future intention

Table 2 shows respondents' knowledge, past experience and future intention of breast feeding. As displayed in the table, almost all, 187 (95.47%) of the respondents knew that HIV can be transmitted during breast feeding, and 168 (85.71%) had heard about infant feeding options during their ANC/PMTCT visit. Most, 169 (86.22%), of the respondents had disclosed their HIV status to others. With regard to the intended feeding options, 159 (81.12%) intended to exclusive breast feed (EBF), 25 (12.76%) intended to replacement-feed (RF) and the remaining intended to use mixed feeding (Table 2).

Socio-demographic predictors of intended infant feeding option

Table 3 contains the result of regression analysis of the effects of socio-demographic variables on infant feeding intention. A woman with primary (AOR = 0.64, 95% CI = 0.01 to 0.78) and secondary level (AOR = 0.71, 95% CI = 0.14 to 3.73) of education were less likely to intend to use mixed feeding as opposed to women without formal education. However, the latter was not significantly associated. Similarly, educational attainment of women had an inverse relation with intention to replacement feeding but the result was not significant. On the other hand, women with higher knowledge score had a reduced likelihood of both intention to replacement and mixed feeding as compared to women with lower knowledge score. A unit increase in the score of knowledge about MTCT significantly reduced the likelihood of intention to mixed feeding by 58% (AOR = 0.42, 95% CI = 0.22 to 0.82) and replacement feeding by 49% (AOR = 0.51, 95% CI = 0.29 to 0.91).

Predicting infant feeding intention from direct TPB constructs

The effect of direct measures of TPB variables on infant feeding intention is presented in Table 4. Accordingly, attitude toward exclusive breast feeding, subjective norms to EBF and perceived behavioral control to exclusively breast feed directly associated with exclusive

Table 1. Socio- demographic characteristics of the respondents, Addis Ababa, May, 2011.

Socio-demographic characteristics (n=196)	Frequency	Percentage
Age of respondents		
17-25	58	29.59
26-30	98	50.00
31-35	24	12.24
36-40	16	8.16
Educational status		
No formal education	29	14.80
Primary education	87	44.39
Secondary education and above	80	40.82
Religion		
Orthodox	157	80.10
Muslim	25	12.76
Others	14	7.14
Occupation		
Housewife	122	62.24
Others*	74	37.76
Marital status		
Married	149	76.02
Single	24	12.24
Widowed/divorced	23	11.73
Ethnicity		
Amhara	102	52.04
Oromo	49	25.00
Others**	45	22.95

*Government employee, private employee, **Gurage, Tigire.

breast feeding, however, the result for subjective norm to EBF is not statistically significant. For instance, a unit increase in score of attitude towards exclusive breast feeding would reduce the likelihood of intention to replacement feeding by 26% (AOR = 0.74, 95% CI = 0.58 to 0.95). Likewise, a unit increase in score of attitude toward exclusive breast feeding would reduce the odds of intention to mixed feeding by a factor of 0.74. Similarly, the higher favorable attitude, subjective norm and perceived behavioral control to use RF are the larger likelihood of intention to practice replacement feeding is. However, only the result for perceived behavioral control to replacement feeding had a statistically verified positive effect on intention to replacement feeding. This regression model explained 47.3% of the variance in the outcome variable ($R^2 = 0.473$).

Predicting infant feeding intention from indirect TPB constructs

Effect of indirect measures of the TPB variables on infant feeding intention was assessed and the result of regression analysis is displayed in Table 5. Behavioral belief toward replacement feeding had positive effect on intention to replacement feeding; a unit increase on score to this scale increased the likelihood of intention to replacement feeding (AOR = 1.11, 95% CI = 1.03 to 1.21). The higher control belief score on exclusive breast feed, the smaller the likelihood of intention to replacement feeding (AOR = 0.89, 95% CI = 0.84 to 0.95) as compared to intention to exclusive breast feeding. Although the results are not significant, behavioral and normative beliefs towards EBF also operate to the detriment of the odds of

Table 2. Respondents' knowledge, experience and intention, Addis Ababa, May 2011.

Variables	Frequency	Percentage
Knowledge		
Know that HIV can be transmitted during pregnancy	182	92.86
Know that HIV can be transmitted during delivery	182	92.8
Know that HIV can be transmitted during breast feeding	187	95.41
Know that there is a medication to reduce MTCT	182	92.86
Heard about infant feeding options during ANC/PMTCT visit.	168	85.71
Past breast feeding experience		
Exclusively breast feeding	93	47.45
Mixed and replacement feeding	36	18.36
Did not have children	67	34.18
HIV disclosure status		
Yes	169	86.22
No	27	13.78
Intended breast feeding options		
Exclusive breast feeding	159	81.12
Replacement feeding	25	12.76
Mixed feeding	12	6.12

detriment of the odds of intention to replacement feeding as opposed to EBF. On the other hand, control belief to mixed feeding had a direct relation with intention to mixed feeding (AOR = 1.12, 95% CI = 0.04 to 1.21).

Overall predictors of intended infant feeding options

The effect of significant direct and indirect measures of TPB variables on infant feeding intention was also evaluated and the result was presented in Table 6. Accordingly, control belief (weighted) to exclusive breast feed had negative effect on intention to replacement feeding (AOR = 0.91, 95% CI = 0.86 to 0.97). However, behavioral belief (weighted) towards replacement feeding had positive effect on intention to replacement feeding (AOR = 1.10, 95% CI = 1.03 to 1.16). Likewise, control belief (weighted) towards mixed feeding significantly predicted intention to mixed feeding (AOR = 1.08, 95% CI = 1.03 to 1.14). This regression model explained 53.7% of the variance ($R^2 = 0.537$).

DISCUSSION

HIV positive mothers' decision to EBF, MF or RF is influenced by their attitude and the perceived control over the behavior. This study assessed intended breastfeeding

options and the influence of attitude, social norms and perceived behavioral control regarding intention to use different infant feeding options using the TPB as a theoretical framework. The finding indicated that four in five women (81%) intended to use EBF; 13% intended to use RF; 12 (6%) intended to use MF. This is inconsistent with a study conducted in South Africa which showed that 74% intended to formula feed their babies, while 26% planned to breastfeed or mixed feed (Luyo and He, 2008). This difference may be due to the new guideline on infant feeding counseling which recommends EBF in the first six months in Ethiopia and might show the effectiveness of counseling on infant feeding options. In addition, the fact that formula is not being provided during counseling program, women may be less intended to use formula feeding.

The majority (93%) of the women knew that HIV can be transmitted during pregnancy and delivery and 95% knew that HIV can be transmitted during breast feeding. This is similar with a study conducted in China (Luyo and He, 2008) but higher than findings from the Ethiopian Demographic Health Survey (EDHS) (Central Statistical Agency of Ethiopia, 2006). This might be because this group of women has more access to information on ways of mother to child transmission and about medication.

In this study, respondents' with higher knowledge on MTCT of HIV chose EBF. This might be due to the fact they were well informed about ways of mother to child

Table 3. Socio-demographic predictors of infant feed options Addis Ababa, May, 2011.

Variable	Infant feeding option			
	Replacement feeding		Mixed feeding	
	Crude OR	Adjusted OR (95% CI)	Crude OR	Adjusted OR (95% CI)
Age				
17-19	1.00		1.00	
20-25	1.23	0.86 (0.86-8.72)	0.46	0.19 (0.01-2.77)
26-30	0.92	0.71 (0.07-6.66)	0.29	0.14 (0.01-1.86)
31-35	0.65	0.61 (0.04-8.51)	0.61	0.48 (0.30-7.72)
36-40	0.46	0.25 (0.01-5.76)	0.92	0.30 (0.015-6.10)
Educational status				
No formal education	1.00		1.00	
Primary education	0.38	0.33 (0.097-1.18)	0.08*	0.64 (0.01-0.78)*
Secondary education	0.53	0.41 (0.12-1.43)	0.86	0.71 (0.14-3.73)
Marital status				
Single	1.00		1.00	
Married	0.70	0.73 (0.20-2.65)	1.57	1.33 (0.13-13.20)
Dissolved	0.75	0.70 (0.12-4.02)	1.00	0.54 (0.02-15.54)
ANC/PMTCT visit	1.25	1.22 (0.74-1.99)	0.94	0.87 (0.38-1.99)
Monthly income	1.00	1.00 (0.99-1.00)	1.00	1.00 (0.99-1.00)
Knowledge about ways of MTCT	0.58*	0.51 (0.29-0.91)*	0.45*	0.42 (0.22-0.82)*

Reference category for outcome variable=intention to exclusive breastfeeding, (*indicates significant association at $p < 0.05$).

Table 4. Predicting infant feeding intention from direct TPB constructs, May 2011.

Direct measure of TPB	Infant feeding option			
	Replacement feeding		Mixed feeding	
	Crude OR	Adjusted OR (95% CI)	Crude OR	Adjusted OR (95% CI)
Attitude to EBF	0.62*	0.74 (0.58-0.95)*	0.69*	0.74 (0.56-0.97)*
Attitude to RF	1.44*	1.23 (0.92-1.63)	1.32*	1.27 (0.92-1.76)
Attitude to mixed	0.83*	1.20 (0.89 -1.62)	0.71*	0.93 (0.69-1.26)
Subjective norm to EBF	0.66*	0.91 (0.73-1.15)	0.79*	0.96 (0.74-1.24)
Subjective norm to RF	1.33*	1.19 (0.93-1.51)	1.23*	1.06 (0.83-1.35)
Subjective norm to MF	1.20*	0.86 (0.65-1.14)	1.36*	1.01 (0.73-1.38)
Perceived control to EBF	0.74*	0.63 (0.45-0.86)*	0.91	0.95 (0.66-1.37)
Perceived control to RF	1.31*	1.40 (1.05-1.87)*	1.47*	1.06 (0.79-1.43)
Perceived control mixed	1.18*	1.39 (0.96-2.01)	1.30*	1.18 (0.83-1.67)

Reference category for outcome variable=intention to exclusive breastfeeding, (*indicates significant association at $p < 0.05$).

transmission and recommended feeding options. Thus, lack of understanding about transmission was therefore an unlikely cause of planning mixed feeding in this study population. It is possible that this would be a more

important factor. In this study, women who intended to use EBF (94.3%) answered the question 'can the virus that cause AIDS be transmitted from MTC during breast feeding?' correctly in more cases than those intending to

Table 5. Predicting infant feeding intention from indirect TPB constructs, May 2011.

Indirect measure of TPB	Infant feeding option (predicted)			
	Replacement feeding		Mixed feeding	
	Crude OR	Adjusted OR (95% CI)	Crude OR	Adjusted OR (95% CI)
Behavioral belief to EBF	0.88*	0.97 (0.90-1.05)	0.91*	0.92 (0.83-1.01)
Behavioral belief to RF	1.10*	1.11 (1.03 -1.21)*	1.05*	1.03 (0.95-1.12)
Behavioral belief to MF	1.06*	1.02 (0.93 -1.11)	1.08*	1.06 (0.97-1.15)
Normative belief to EBF	0.89*	0.93 (0.83-1.04)	0.94*	0.97 (0.89-1.07)
Normative belief to RF	1.02	1.04 (0.92-1.18)	1.03	1.03 (0.94-1.12)
Normative belief to MF	0.98	0.89 (0.78-1.02)	1.05*	0.91 (0.80-1.02)
Control belief to EBF	0.89*	0.89 (0.84-0.95)*	0.94*	1.00 (0.93-1.07)
Control belief to RF	1.07*	1.05 (0.98-1.12)	1.04*	0.96 (0.89-1.03)
Control belief to MF	1.04*	1.03 (0.97-1.10)	1.10*	1.12 (1.04-1.21)*

Reference category for outcome variable=intention to exclusive breastfeeding, (*indicates significant association at $p < 0.05$).

Table 6. Predicting infant feeding intention from direct and indirect TPB constructs, May 2011.

Direct and indirect measure of TPB	Infant feeding option			
	Replacement feeding		Mixed feeding	
	Crude OR	Adjusted OR (95% CI)	Crude OR	Adjusted OR (95% CI)
Attitude to EBF	0.62*	0.89 (0.68-1.17)	0.69 *	0.83 (0.62-1.09)
Perceived control to EBF	0.74*	0.85 (0.62-1.16)	0.91*	0.89 (0.66-1.21)
Perceived control to RF	1.31*	1.32 (1.03-1.69)*	1.47*	1.11 (0.85-1.44)
Behavioral belief to RF	1.10*	1.10 (1.03-1.16)*	1.05*	1.03 (0.97-1.09)
Control belief to EBF	0.89*	0.91 (0.86-0.97)*	0.94*	0.98 (0.92-1.04)
Control belief to mixed	1.04*	1.02 (0.96-1.07)	1.10*	1.08 (1.03-1.14)*

Reference category for outcome variable=intention to exclusive breastfeeding, (*indicates significant association at $p < 0.05$).

use RF (88%) and intending to use MF (83.3%). It must be noted that the remaining from each category answered the question incorrectly and there is only a slight difference in their knowledge on each specific ways of mother to child transmission. It may therefore be that knowledge on HIV transmission during breast feeding alone is insufficient in some cases to influence the choices that women make to use a particular feeding option.

In contrast to knowledge on ways of MTCT and educational status, level of disclosure, number of ANC/PMTCT, income, marital status and family size did not have an impact on feeding intention of the women in this study. This implies that if a woman knows how to prevent her baby from getting the virus and has a better understanding of MTCT, she will prefer to use EBF. The findings indicated that the constructs of the TPB were significantly associated with women's infant feeding intention and this finding is similar with cluster-randomized trial based on

the TPB which showed mothers' intention towards recommended feeding behaviors was positively associated with mothers' attitudes, subjective norms and self-efficacy (Matji and Wittenberg, 2008).

Attitude towards exclusive breast feeding, subjective norms to EBF and perceived behavioral control to exclusively breast feed were significantly associated with exclusive breast feeding, however subjective norm to EBF was not significantly associated. However, attitude toward RF and perceived behavioral control to RF are positively associated with intention to replacement feeding. This is consistent with the TPB assumption that when attitude and perceived control become positive toward the behavior the likelihood of performing the behavior is high (Bruce et al., 1984; Karen et al., 2008). The simultaneous predictive power of direct measures of TPB (attitudes, subjective norms and perceived behavioral control) on intended infant feeding option in terms of the adjusted R^2 was 0.473 (that is, explained only 47.3% of

variance).

On multinomial regression analyses, the indirect predictors of intention, higher behavioral belief (weighted) score on RF associated with increased intention to RF. However, control belief (weighted) towards exclusive breast feeding significantly reduced intention to RF. Control belief towards mixed feeding significantly increased intention to MF compared to EBF. This is in line with the assumption of TPB (Bruce et al., 1984; Karen et al., 2008; Christopher and Mark, 2001). The simultaneous predictive power of weighted behavioral belief, normative belief and control belief on intention in terms of the adjusted R^2 was 0.579.

Limitations of the study

The finding of the study may suffer from social desirability bias as the data were collected by service providers at health facility settings and the theme of the study is relatively sensitive. In addition, the fact that the interview took place at health facilities, respondents may have over emphasized the importance of knowledge obtained at health facility than their real intention.

CONCLUSIONS

Despite these limitations, it could be concluded that more than three-quarters of the women who participated in this study intended to use EBF which indicates that the recommended feeding option might have the chance to be practiced by most of the mothers in the study area. This study also indicated that counseling on feeding choices for HIV- positive pregnant women should be extremely sensitive to the numerous internal and external factors impinging on that decision. For example, internal factors like attitude, perceived behavioral control and social pressures. Thus, health care providers and counselor need to explore and address the salient behavioral beliefs underlying preference for infant feeding options. Further efforts are needed to foster women's ability and confidence (behavioral and power of control) to practice infant feeding options as per guideline of HIV infant feeding in HIV positive mothers.

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Full Length Research Paper

Pre-exposure prophylaxis in sero-discordant male partners of human immune deficiency virus (HIV) positive women desirous of natural conception – a clinical setting experience

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The reproductive health needs of sero-discordant couples are issues of concerns, especially in view of high cost of various assisted conception methods in the low-resource economies. Often times, many of these couples resort to un-informed and unsafe practices of unprotected heterosexual intercourse, leading to human immune deficiency virus (HIV) acquisition. The magnitude of the health burden of these populations in Nigeria and other developing economies are currently not fully determined. Pre-exposure prophylaxis (PrEP) in conjunction with other HIV prevention strategies provides the only veritable and possibly safe mean of achieving their reproductive desire. This is a cohort study of 42 HIV-1 sero-discordant male partners of known HIV-1 positive women who were desirous of conception. All the male participants recruited were aware of their female partners' status, had their HIV status determined by fourth generation enzyme linked immunosorbent assay kit and were HIV negative, but declined the offer of assisted conception. The HIV positive women were all on highly active antiretroviral therapy (HAART). Thirty sero-discordant partners were sequentially and equally randomised into the two treatment groups [TDF and daily tenofovi/emtricitabine (TDF-FTC)], while 12 participants who declined PrEP made up the control group. In resource constraint settings, where assisted conception methods are either unacceptable, declined or un-affordable to male sero-discordant couples in heterosexual relationships, pre-exposure prophylaxis, preferably oral daily tenofovir-emtricitabine combination may be considered in addition to other HIV prevention strategies and timed sexual exposure, towards achieving safe reproductive health needs.

Key words: Human immune deficiency virus (HIV), pre-exposure prophylaxis, sero-discordant heterosexual partners, reproductive desire.

INTRODUCTION

The World Health Organisation (WHO) reports indicated that about 68% of all people living with human immune deficiency virus (HIV) in the world resided in sub-Saharan Africa (WHO, 2011), of which 60% are women (WHO, 2008). Also, in sub-Saharan Africa, 47% of HIV-infected

women are reportedly in stable sero-discordant relationships (Eyawo et al., 2010). According to a national probability study, in the United States, 52% of HIV-infected women reported being in a sero-discordant relationship and approximately half of HIV sero-discordant

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heterosexual couples desire children (Chen et al., 2001).

Pre-exposure prophylaxis (PrEP) is the use of antiretrovirals in HIV-uninfected people to block the acquisition of HIV infection (Peng et al., 2012). World Health Organisation (WHO) in its July 2012 publication has reported five large studies that had come to varying conclusions on the effectiveness and safety of PrEP in either sero-discordant same sex or heterosexual couples. However, the summation of systematic review of evidence by WHO concluded that in countries where HIV transmission occurs among sero-discordant couples, where discordant couples can be identified and where additional HIV prevention choices for them are needed, daily oral PrEP (specifically tenofovir or the combination of tenofovir and emtricitabine) may be considered as a possible additional intervention for the uninfected partner. These needs in Africa and other low resource economies with greatest burden of HIV are recognised, but are currently not fully determined (Iliyasu et al., 2009; Oladapo et al., 2005; Hughes et al., 2012). For these populations of patients in developing economies, with greatly hampered economic strength, absence of health care support and high cost of assisted conception methods, the option left is natural conception through heterosexual relationship. This however is fraught with high risk of HIV acquisition.

Beyeza-Kashesya et al. (2010) reported from Uganda that 59% (135/228) of the participants desired to have children. The belief that their partner wanted children was a major determinant of the desire to have children, irrespective of the HIV sero-status. Among couples in which the woman was HIV-positive, young age and relatives' expectations for children were significantly associated with increased fertility desire. Oladapo et al. (2005) in South-Western Nigeria reported that despite the fact that 79.6% (117/147) of the respondents already had 1 or more children, 68.4% (65/95) of women aged 18 to 45 and 53.8% (28/52) of men aged 18 to 55 still desire children (Eyawo et al., 2010). Pre-exposure prophylaxis (PrEP) in conjunction with other HIV prevention strategies provides the only veritable and possibly safe mean of achieving their reproductive desire.

PrEP still remain an emerging intervention strategies in HIV prevention programs with attempts to provide guidelines and recommendations on its application amongst both heterosexual and same sex sero-discordant partners (WHO, 2012). At the moment, drugs reported with some benefits are oral tenofovir (TDF), combination of oral tenofovir (TDF)/emtricitabine (FTC) or tenofovir vaginal gel (WHO, 2012; Baeten et al., 2012; Okwundu et al., 2012). This study reports our experience with PrEP amongst some sero-discordant heterosexual couples in our practice.

MATERIALS AND METHODS

This is a cohort study of 42 HIV-1 sero-discordant male partners of

known HIV-1 positive women and desirous of conception. The study was conducted between March, 2008 and July, 2010, at Ladoko Akintola University of Technology Teaching Hospital Osogbo, Nigeria. All the male participants recruited were aware of their female partners' status, had their HIV status determined by fourth generation enzyme linked immunosorbent assay (GENSCREEN® Ultra HIV Ag/Ab, Bio-Rad Laboratories, Hercules, CA) kit and were HIV negative, but declined the offer of assisted conception, due to lack of fund. The HIV positive women were all on highly active antiretroviral therapy (HAART) of zidovudine 300 mg b.d, lamivudine 150 mg b.d and nevirapine 200 mg b.d combination, with median duration of HAART use of 5 months. The baseline CD4 counts were above 350 cells/ μ l.

Thirty sero-discordant male partners voluntarily accepted antiretroviral therapy for use as pre-exposure prophylaxis were recruited into the "treatment arms"; however 12 partners who declined both the assisted conception methods and the offer of pre-exposure prophylaxis were recruited and allocated into the "no treatment" arm. The thirty participants had their baseline serum creatinine and creatinine clearance determined (> 60 ml/min by Cochrout-Gault formula) at enrolment into the study and thereafter commenced on oral PrEP. Enrolments into the two treatment groups were by random allocation through balloting, using pre-labelled allotment papers, concealed in opaque envelopes, into daily tenofovir disoproxil fumarate 300 mg (TDF) or combination of daily oral tenofovir disoproxil fumarate 300 mg (TDF)/emtricitabine 200 mg (FTC). All participants provided written informed consent and received a comprehensive package of HIV-1 prevention services: HIV-1 testing with counselling before and after testing, individual and couples risk-reduction counselling, screening and treatment for sexually transmitted infections (STIs) including hepatitis B infection and free condoms with training and counselling. Also, none of the sero-discordant male partner was uncircumcised. HIV screening with the Ag/Ab kit were repeated in the sero-discordant male partners at interval of every 3 months, as well as serum creatinine levels. Unprotected sexual exposures were limited to the periods of female partners' ovulation which was determined from presumptive ovulation period based on calculation (timed sexual exposure); otherwise, condom use was advised at other times.

The hospital ethical committee reviewed and approved the protocol for the study. All participants were followed up monthly for a period of 12 months. Adherence was monitored with monthly pill counts and re-enforced with counselling. Outcome measures were incidences of HIV acquisition and conception rates in the groups. Data were analysed for simple frequencies, percentages, mean (standard deviation) and median (range) as appropriate, using statistical package for social sciences version 16 (SPSS Inc, Chicago, IL, USA).

RESULTS

In this study, the ages of the HIV 1 positive women were between 24 to 35 years, with the parity median of 1 (range = 0 to 2). The CD4 counts at the point of enrolment ranged between 363 to 570 cells/ μ l. Among the sero-discordant male partners, the mean ages in the groups were 38.2 ± 4.1 years (TDF), 36.6 ± 3.2 years (TDF-FTC) and 39.1 ± 4.4 years (control), respectively. Majority of the male partners in the treatment groups (9/15 each) were of the secondary school level of education, in comparison to 7/12 in the control group with primary school level of education. In the treatment groups, 12/15 (TDF) and 13/15 (TDF-FTC) were engaged

Table 1. Characteristics of serodiscordant male partners.

Characteristics	TDF group (n=15)	TDF-FTC group (n=15)	Control (n=12)
Age, mean (SD)	38.2 (4.1)	36.6 (3.2)	39.1 (4.4)
Educational status			
None	-	-	2
Primary	4	6	7
Secondary	9	9	3
Tertiary	2	-	-
Occupation			
Unemployed	-	-	-
Unskilled	2	2	5
Skilled	12	13	7
Professional	1	-	-
Religion			
Traditional	1	-	2
Christianity	7	9	5
Islam	7	6	5

in skilled occupation, while this group was 7/12 in the control group. Participants in the 3 groups were majorly Christians and Muslims (Table 1). Table 2 showed at enrolment the mean CD4 counts of the respective group was 424 cells/ μ l (TDF), 403 cells/ μ l (TDF-FTC) and 395 cells/ μ l (controls) ($F = 0.209$; $p = 0.812$). The highest proportion of sexually transmitted (mainly *Trichomonas vaginalis*) infection (50%) was recorded in the control group at enrolment and also during the study (33%).

The incidences of successful conception in each group by the 12th month of the study duration were 60.0, 40.0 and 16.7% in the TDF, TDF-FTC and the control groups, respectively. The highest rate of loss-to-follow-up of 8/12 (66.7%) was recorded in the control group. Overall, the incidence of HIV sero-conversion adjusted for loss-to-follow-up in the study was 9/33 (27.3%) The highest group incidence per 100 women year was recorded in the control group at 38.1 and least in the TDF-FTC group at 6.6. The relative reductions in the rates of HIV acquisition were 61 and 79% in the TDF only and TDF-FTC groups, respectively (Table 3). Side effects reported in the treatment groups were mainly nausea/vomiting in 5/15 (33.3%) of the TDF group and 7/15 (46.7%) of the patients in TDF-FTC group, fatigue in 3/15 (20%) and 7/15 (46.7%) of the TDF and TDF-FTC groups, respectively. On a preference scale, 11/15 (73.3%) and 6/15 (40%) in the TDF and TDF-FTC groups, respectively expressed satisfaction with their drug regimen.

DISCUSSION

The reproductive health needs of sero-discordant couples

have in recent times become issues of concerns, especially in view of high cost of various assisted conception methods in the low-resource economies. Often times, many of these couples resort to un-informed and unsafe practices of unprotected heterosexual intercourse, leading to HIV acquisition. The magnitude of the health burden of these populations in Nigeria and other developing economies are currently unknown. In this cohort (observational) study, we report on 42 sero-discordant male partners in heterosexual relationship with HIV-1 positive female partners who are desirous of conception, but declined all offers of assisted conception methods. Majority of the sero-discordant male partners in the 3 groups were Christians and were in skilled occupations. However, there was a preponderance (7/12) of primary/elementary education levels among the control group. This might have influenced the decision making abilities in this group, who despite health education and counselling, declined both the offers of assisted conception methods and PrEP. Peng et al. (2012) had reported that education level influenced willingness to accept PrEP with 32.8% of Chinese female sex workers with elementary levels of education unwilling to use PrEP.

The immunological statuses of the HIV-1 positive female partners were comparable across the groups and all were highly motivated and regular on HAART. However, the incidences of STIs at both enrolment and during the study were proportionately highest in the control group's female partners. Hayes et al. (2010) reviewing evidences from observational and biologic data had concluded that evidence strongly supports the

Table 2. CD4 count status at enrollment and incidence of sexually transmitted infections in the HIV positive women.

Factor	TDF (n=15)	TDF-FTC (n=15)	Control (n=12)
CD4 count at Enrollment (Cells/μl)			
Mean (SD)	424 (135)	403 (121)	395 (105)
STI (at enrolment), n (%)	1 (6.7)	3 (20.0)	6 (50.0)
STI (during study), n (%)	-	1 (6.7)	4 (33.3)

STI = Sexually transmitted infection.

Table 3. Incidence of conception, loss to follow-up in the study groups and HIV infection in male partners.

Factor	TDF n =15	TDF-FTC n = 15	Control n = 12
Conception			
Conception at 6 months	3	2	-
Conception at 7 - 12 months	6	4	2
No of conception by 12 month, n (%)	9 (60)	6 (40)	2 (16.7)
Loss to follow-up			
Loss to follow-up at 6/12	-	-	3
Loss to follow-up at 12/12	-	1	5
Total Number of Loss to Follow-up, n (%)	-	1 (6.7)	8 (66.7)
No of Participants who completed the study, n (%)	15 (100)	14 (93.3)	4 (33.3)
Incidence of HIV seroconversion in partners, n (rate/100 women year)	2 (13.3)	1 (6.6)	4 (38.1)

concept that STI treatment prevents HIV infection (Hayes et al., 2010), though doubts have been raised about the link between STI and HIV risk. This is possibly because intervention studies were not conclusive and designs/implementations of interventions were not clearly outlined (Ward and Ronn, 2010). In this study, identified STIs were promptly treated in both partners to minimize the risk of HIV acquisition.

The findings in our study suggested that once-daily oral TDF and TDF-FTC were associated with risk reductions of 61 and 79%, respectively against HIV-1 infection acquisition in sero-discordant male partners, when combined with other HIV-1 prevention services and timed sexual exposure. These findings are similar to those reported by Baeten et al. (2012) though the risk reduction in our study with oral TDF was 51%, which is lower than the 67% reported by Baeten et al. (2012). Also, Thigpen et al. (2012) had reported an overall 63% risk reduction in heterosexual men and women in Botswana. However, another study reported that with higher levels of adherence, as suggested by TDF levels in plasma, the effectiveness of oral TDF was 86% and that of the TDF/FTC combination was 90% (Donnell et al., 2012). The incidence of STI, when considered in the context of the HIV acquisition rates observed in this study, might suggest involvement of some participants in this study in

extra-marital affairs. However, giving the sensitivity of this issue, especially in the context of this study, it was difficult to verify this suspicion.

However, while effectiveness of PrEP seems clearer amongst sero-discordant male partners in this and other studies, reports are conflicting amongst women. The trial of daily oral TDF/FTC in African women at higher risk of HIV in Kenya, South Africa and the United Republic of Tanzania was terminated early when equal numbers of infections were seen in the PrEP and placebo arms at interim analysis. The likely cause of apparent futility of this study had been attributed to poor adherence with resultant low drug concentrations in study participants (Van Damme et al., 2012). However, Vernazza et al. (2011) conducted an observational study in Switzerland among serodiscordant couples seeking conception where the male partner was HIV-infected with a suppressed viral load on ART and the female was HIV-uninfected. Of the 46 couples who chose periconceptional PrEP, 75% of couples successfully conceived by 12 months with no cases of incident HIV.

The desire for natural conception in these couples and refusal or inability to fund assisted conception techniques necessitated this study. The overall conception rate over the 12 months study period was 40.5% (17/42). The incidence of group conception was highest (60%) in the

TDF group and least (16.7%) in the control group. However, with very high loss to follow-up (66.7%) in the control conception in this group might be under-reported. In this study, our great concerns were problems of adherence, loss to follow-up and possible drug resistance. To mitigate the first two concerns, monthly follow-up meetings were scheduled for each couple to address all emerging issues, and re-emphasize risk-reduction counselling, as well as evaluate and support PrEP adherence (pills count inclusive). Evaluation for drug resistance is presently not available in our institution.

HIV acquisition incidences were 13.3, 6.6 and 38.1 per 100 women year, respectively in the TDF, TDF-FTC and control groups. This translated to HIV acquisition risk reduction, compared with the control group of 61 and 79% for both the TDF and TDF-FTC groups in this study, respectively. Side effects recorded in the treatment groups were mainly nausea/vomiting in 33.3% of the TDF group and 46.7% of the patients in TDF-FTC group and fatigue in 20 and 46.7% of the TDF and TDF-FTC groups, respectively. On preference scale, 11/15 (73.3%) and 6/15 (40%) in the TDF and TDF-FTC groups, respectively, expressed satisfaction with their drug regimen while TDF has been reported to cause small but insignificant reduction in the glomerular filtration rates in a population of HIV-1 positive patients (Cooper et al., 2010). This observation could not be ascertained in our study, as none of the patients had evidence of elevated serum creatinine throughout the study. However, the small size and the limited duration of our study preclude a definite statement in this regard.

The recorded side effects and patients' likely preference/tolerability of drug burden might be some factors to consider in drug adherence issues and should be addressed at every session of counselling to elicit the maximum understanding and cooperation of the patients. In our study, the highest incidence was recorded in the first 6 weeks of commencing the PrEP and abated thereafter.

While this our study is observational in nature, the limitations inherent are the small population of participants, high incidence of loss-to-follow-up and infrastructural constraints resulting in inability to determine viral load in the HIV positive female partners, inability to assess for drugs serum levels in the male sero-discordant partners to monitor adherence and viral sensitivity test to determine possible drug resistance. These shortcomings notwithstanding, the obligations on the part of Researchers and Clinicians are to convince national agencies on HIV control programs for policy change in favour of universal accessibility to PrEP to those at risk of HIV acquisition in their quest to fulfil their reproductive desires and identify ways to promote reliable and assessable adherence.

CONCLUSION

In resource constraint settings, where assisted concep-

tion methods are either unacceptable, declined or unaffordable to male sero-discordant couples in heterosexual relationships, pre-exposure prophylaxis, preferably oral daily tenofovir-emtricitabine combination may be considered in addition to other HIV prevention strategies and timed sexual exposure towards achieving safe reproductive health needs.

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