Journal of AIDS and HIV Research

Volume 9 Number 9 September 2017
ISSN 2141-2359

Academic Journals

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Journal of AIDS and HIV Research

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academicJournals

Vol. 9(9), pp. 179-186, September 2017
DOI: 10.5897/JAHR2017.0429
Article Number: 9A803F065774
ISSN 2141-2359

http://www.academicjournals.org/JAHR

Journal of AIDS and HIV Research

Full Length Research Paper

An assessment of awareness level and sources of information on HIV/AIDS among market women in Ibadan, Oyo State, Nigeria

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Received 12 April, 2017; Accepted 11 July, 2017

In Nigeria, the HIV sero- prevalence is steadily decreasing. It is presently put at 1.9 % among pregnant women. This implies that about 2 out of every 100 women of reproductive age have chance of getting infected with HIV. Market women are at risk and good target groups to enhance information dissemination to their children as well as neighbors. The objective of this study was to determine the level of awareness and source of information on HIV/AIDS among market women in Oyo State. A semi-structured interviewer administered questionnaire was used which assessed respondents' demographic characteristics, their level of knowledge and sources of HIV related information. Data was analyzed with Epi-info version 7 software. There were 300 market women who participated in this study. It was found that 22% of respondents were not aware of HIV/AIDS. Furthermore, more than 40% of the respondents wrongly mentioned sharing toilet as mode of transmission, followed by eating together (35%), sharing market stall (31%), handshake (30%), and sharing same bed (28%). 31% of respondents who had awareness of HIV, had accessed HIV screening. Most of those who had not accessed HIV screening did not do so because of fear of death (55%), stigmatization (33%) and not just wanting to test or screen for HIV (20%). It was gathered that the main source of information on HIV/AIDS among respondents was mass media. Results indicated that despite global effort on increasing awareness of HIV/AIDS, there are still needs for improvement among artisans, especially increasing knowledge on mode of transmission and need to get tested and know their HIV status. It is hence recommended that with the major source of information being mass media, efforts should be made to increase programming and jingles on HIV/AIDS in local languages; this will aid understanding and increases testing.

Key words: Market women, awareness, knowledge, HIV/AIDS.

INTRODUCTION

In an average Nigerian community, women constitute a larger percentage of the population and their domestic roles cannot be over-emphasized. Women also play a major role in the economy most especially at the market place. They dominate the marketing channels of goods and services, especially in the informal sector, thereby contributing to household income generation and cumulatively the growth and sustainability of national

economy. However, the productivity of women is threatened by health issue such as HIV/AIDS. The failure in women health care will not only have impact at household level, but also significant impacts in sustainability of economy up to the national level. A survey conducted in Nigeria by National HIV/AIDS and Reproductive Health Survey (NARHS, 2012) revealed that sexual intercourse begins much earlier in female respondents at median age of first sex to be around 16.9 years. The survey also revealed that the adult HIV prevalence has increased from 1.8% in 1991 to 4.5% in 1996 and 5.8% in 2001. Most of the respondents knew all forms of HIV transmission, and misconceptions about the transmission are high. However, the most common type of non-marital non-cohabiting relationship is the boyfriend-girlfriend relationship, and nine percent of the sampled females had sex with boyfriends in 12 months preceding the survey (NARHS, 2012). Nigeria has the second largest HIV epidemic in the world (FMOH, 2013). Although HIV prevalence among adults is remarkably small (3.1%) compared to other sub-Saharan African countries such as South Africa (19.2%) and Zambia (12.9%), the size of Nigeria's population means 3.5 million people were living with HIV in 2015 (UNAIDS, 2016). Spread of the disease is therefore critical among those in informal sector due to their lack of adequate information (Babalola and Babalola, 2013). Most especially, local markets are dominated with women that lack formal education and adequate information about HIV/AIDS, therefore involved in risky sexual behavior that further increase their chance of getting infected (Ilo and Adeyemi, 2010).

Information increases the level of certainty in any human decision process; little wonder, Zizlsperger (2012) posits that information is indispensable for human development. The present information and education campaign to forestall the spread of the disease should be pursued with vigor but some energy should be dissipated to the care of people already afflicted (Arinola and Adekunjo, 2012).

Mooko and Aina (2007) opine that every individual, whether literate or illiterate, needs information for a variety of issues essential for his or her survival. It is therefore, not surprising that information is needed for awareness, increase productivity and health. They further assert that users of information are complex, while some are homogenous such as professionals, students, policy makers, researchers, some could be heterogeneous like rural inhabitants and artisans. Ilo and Adeyemi (2010) in their own opinion submit that information is the most potent weapon available for the prevention and cure of HIV and AIDS.

HIV is endemic in Nigeria, thus to control the disease, all need to know as much as possible about the disease. There is no better way to start the education than from the basics which is access to information. As for those living with HIV, comprehensive and up-dated information is an essential part of a healthy life which is available as they access HIV care. In the year 2014, the Joint United Nation Programme on HIV/AIDS (UNAIDS) established a new target for HIV treatment for 2020, that by the year 2020, 90% of all people will know their HIV status, will receive sustained antiretroviral therapy and will have viral suppression. Considering this study, achieving these goals is possible with increased level of awareness of individuals as posited by Onyeonoro et al. (2014).

HIV/AIDS has affected the wellbeing of the people negatively. More cases of new infections are reported in hospitals (UNAIDS, 2015). The acronym has received popular attention, that it is now a household name by members of the public. The problem of HIV/AIDS has invaded virtually all facets of human endeavor (homes, schools, work place, even churches and mosques). With a grim picture of the disease not only at the global or continental frontiers but, also at the national level, the spread of HIV/AIDS may continue like wildfire. As HIV/AIDS is devastating people of productive age, the world may experience years of economic depression resulting from the scourge of HIV/AIDS, which has no cure for now (Dehne and Riedner, 2005; Wilson et al., 2011; Adekeye, 2010).

Abia et al (2012) has noted that the increasing incidence and prevalence of HIV/AIDS in Nigeria (urban as well as rural) has raised the question of whether the heightened level of awareness, education and information on HIV/AIDS has not yielded sufficient dividend in the prevention and the control of the disease.

Increasing awareness on the effects of HIV/AIDS must be sustained especially as the statistics on HIV/AIDS is currently alarming and demoralizing. The channel of communication and knowledge about the virus and the disease is as important as the means of controlling its spread, especially where the population is socially active as Nigeria's population.

The role of mass media in information dissemination cannot be ignored. The mass media is a large-scale organization which use one or more of these technologies, radio, print and TV to communicate with large numbers of the people within the population.

In recent years, with the advent of Global System of Mobile Telecommunication (GSM); the incidence of HIV/AIDS is bound to increase especially as more people are acquiring the GSM facility with the attendance networking of people; Abia et al. (2012) has noted that

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the advent of internet software phones compounded networking of people, as amorous episode of raw sex are downloaded into phones. Some of these images are transferred from phone to phone as video clips through Bluetooth. Internet has its own negative impact as pornography; scam and other forms of vices are committed through the internet. Television and radio preceded the internet as electronic forms of mass media dissemination in Nigeria. This study therefore determined community awareness and sources of information on HIV/AIDS among market women in Ibadan, Oyo State.

Considering the aforementioed, this study therefore focused on assessing the awareness level of women in informal sector on HIV/AIDS with special focus on market women in Ibadan, Nigeria and their sources of information on HIV/AIDS.

Findings of this study will be valuable in formulating HIV/AIDS preventive strategy among women in market place and contribute to existing knowledge on status of HIV/AIDS in informal sector.

METHODOLOGY

Study design

This involves a cross-sectional survey adopting the quantitative method of data collection.

Study area

Ibadan is the capital city of Oyo State and the third largest metropolitan area, by population, in Nigeria, after Lagos and Kano, with a population of over 8 million, and the largest metropolitan geographical area.The principal inhabitants of the city are the Yorubas.

There are eleven Local Governments in Ibadan Metropolitan area consisting of five urban local governments in the city and six semi-urban local governments in the lesser city.

There are major markets in Ibadan like Bodija market, Oja-Oba market, Oje market, Gbagi market, Sasa market and Dugbe market to mention but a few. Most of the markets in Ibadan are typical of open markets in African setting with many small sheds/shelter and few concrete built shops in urban and sub-urban areas, but rural areas are typical with sheds and shelters made from palm fronts and roofing sheets. Buying and selling activities take place every day of the week in merely all the market within the metropolis. These markets operate business during the day from about 8:00 am till late in the evening.

Study population

Study population included market women; these included registered member of the market women association of the Ibadan chapter.

Sampling technique

Multi-stage sampling technique was adopted. Stage A: Three LGAs (two urban and one semi urban) were randomly selected from the 11 LGAs in Ibadan metropolis, this include Ibadan North, Ibadan South East and Akinyele local government areas. Stage 2: One major market from each LGA was selected: Bodija, Oja-Oba and Sasa markets. Stage 3: Stratified random sampling technique was adopted for administration of the structured questionnaire to the market women. The collection of data in the market was organized in such a way that people selling the same kind of goods are grouped together or with shops arranged next to each other. This arrangement was therefore used as strata for the market and adopted in selection of the traders for the questionnaire administration. Women in the following five sections of the market were randomly sampled: (a) Perishable goods section (vegetables, meat, fruits, etc); (b) Staple food stuff section (rice, beans, millet, corn, yam, etc); (c) Provision section (can food, soup seasoning, juice drinks, wine, etc); (d) Cosmetics section (body cream, soap, detergents, etc); and (e) Cloth and clothing material section. Twenty (20) women were sampled from each of the listed sections in each market making a total of hundred (100) women per market.

Data collection

Data was collected with a semi structured interviewer administered questionnaire. The questionnaire consisted of 5 sections namely: Socio-demographics, awareness on HIV/AIDS, knowledge on HIV/AIDS, sources of Information on HIV/AIDS, and attitude about HIV/AIDS and voluntary counseling and testing services.

Data analysis

The filled questionnaires were checked for completeness daily before data were entered into the computer. The fields were checked and validated before analysis. Descriptive statistics were computed using Epi-info Version 7.0 to generate frequency tables, charts, proportions and means to describe the data.

Ethical considerations

Approval for the study was obtained from the Ethical Review Committee of Oyo State Ministry of Health.

Informed consent

Written informed consent was obtained from the respondents.

RESULTS

Socio-demographic characteristics of respondents

Table 1 shows the socio-demographic characteristics of respondents. Findings indicated that more than half of respondents were between the ages of 30 years old and 49 years old. More than two-thirds were Muslims, almost nine out of ten (87%) were married. With regards to their education, more than half (55.6%) completed primary education, about a fifth (17.6%) completed secondary education while 2% had OND/NCE (Ordinary National Diploma/Nigeria Certificate in Education) and 1% had higher education. Almost a quarter (24%) had no formal education. Almost all (95.6%) of the respondents were traders with about 3% who were students.

Awareness and Knowledge of HIV/AIDS

Most of the respondents (78%) had heard of HIV/AIDs,

Table 1. Socio-demographic characteristics of respondents.

Background Information		Frequency (n=300)	Percentage
Age (years)	20 - 29	27	9.0
	30 - 39	88	29.3
	40 - 49	72	24.0
	50 - 59	50	16.6
	60+	55	18.3
Religion	Christian	55	18.3
	Muslim	236	78.6
	No response	6	3.1
Marital status	Married	260	86.7
	Single	9	3.0
	Divorced	6	2.0
	Widowed	25	8.3
Education	No formal education	72	23.4
	Primary School Leaving Certificate	167	55.6
	WAEC	53	17.6
	OND/NCE	5	1.6
	BSc/HND	3	1.2
Occupation	Trading/business	287	95.6
	Student	9	3.0
	No response	4	1.4

as shown in Table 2. However, of those that ever heard of HIV, only 31% ever accessed HIV screening and 68% had not. Most of those that had not accessed the screening (55%), did not do so because of fear of death or testing positive followed by about one-third who were afraid of stigmatization. One-fifth just did not want to test or screen for HIV.

Knowledge of mode of transmission

Majority of the respondents (92%) correctly mentioned sexual intercourse as mode of transmission followed by sharing blades/needles (82%), breastfeeding (78%), mother-to-child transmission (73%), and blood transfusion (65%). More than two-fifth wrongly mentioned sharing toilet as mode of transmission, followed by more than a third (35%) that mentioned eating together, sharing market stall (31%), handshake (30%), and sharing the same bed (28%) (Figure 1).

Attitudes towards modes of transmission of HIV/AIDS

The respondents were asked about their attitude towards HIV transmission, as shown in Table 3. The respondents were asked about the perception with regards to isolating an infected person as a means of preventing HIV infection. More than a quarter (28.3%) agreed that an infected person be isolated while more than two-fifth (43.3%) indicated that an infected person should not be isolated and 28.4% were undecided. Seven in ten (71%) indicated condom use as means of preventing HIV infection while 7% disagreed and almost a quarter (21.7%) were undecided.

Furthermore, seven in ten (70.6%) agreed that discouraging sharing of blade could prevent HIV infection, 6% disagreed and 23.3% were undecided. More than seven in ten (71%) agreed that abstinence from pre-/extra-marital sexual intercourse could prevent HIV infection, 7.3% disagreed and 20% were undecided.

Source of information on HIV/AIDS

Figure 2 shows respondents' sources of information about HIV. More than three-quarter heard about HIV from the radio. Almost two-fifths (36%) heard from hospitals, more than two-third (77%) heard on television, little above half (54%) read from posters and 18% heard from home.

DISCUSSION

Awareness on HIV/AIDS

The findings of this study indicate that most of the

Table 2. Awareness on HIV /AIDS and accessing HIV screening.

Variable	Frequency	Percentage
Ever heard of HIV/AIDs		
Yes	234	78.0
No	66	22.0
Total	**300**	**100.0**
Ever done HIV Test		
Yes	73	31.3
No	161	68.7
Total	**234**	**100.0**
HIV/AIDS has no cure		
Yes	101	43.0
No	133	57.0
Total	**234**	**100.0**
HIV/AIDs is a white man's initiative to discourage sex		
Yes	146	62.6
No	88	37.4
Total	**234**	**100.0**
HIV/AIDs victim can live long on a special type of drug and hygienic condition		
Yes	112	47.6
No	122	52.3
Total	**234**	**100.0**
Reason for not tested		
No response	88	54.7
No opportunity	8	4.9
Do not just want to test	6	3.8
Fear of stigma	19	11.8
Fear of death	40	24.8
Total	**161**	**100.0**

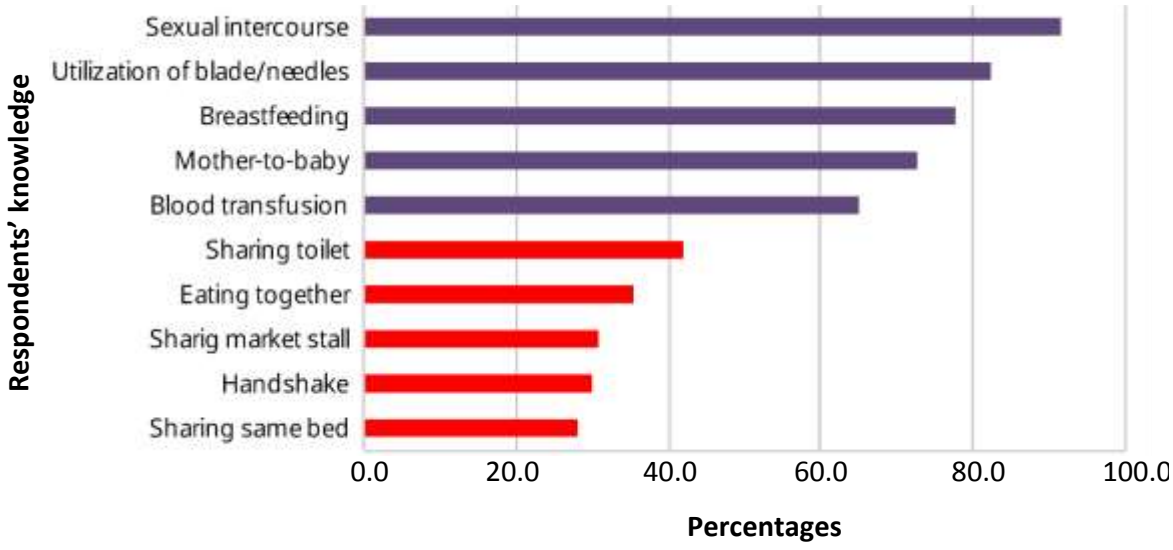

Figure 1. Distribution of respondents' knowledge of modes of transmission of HIV.

Table 3. Attitudes towards modes of transmission of HIV.

Variable		Frequency (n=300)	Percentage
Isolate HIV/AIDS patients	Agreed	85	28.3
	Disagreed	130	43.3
	Undecided	85	28.4
Use of condom	Agreed	212	70.6
	Disagreed	23	7.7
	Undecided	65	21.7
Discourage sharing of blades	Agreed	212	70.6
	Disagreed	18	6.1
	Undecided	70	23.3
Abstinence from pre-extra marital sex	Agreed	218	72.7
	Disagreed	22	7.3
	Undecided	60	20.0

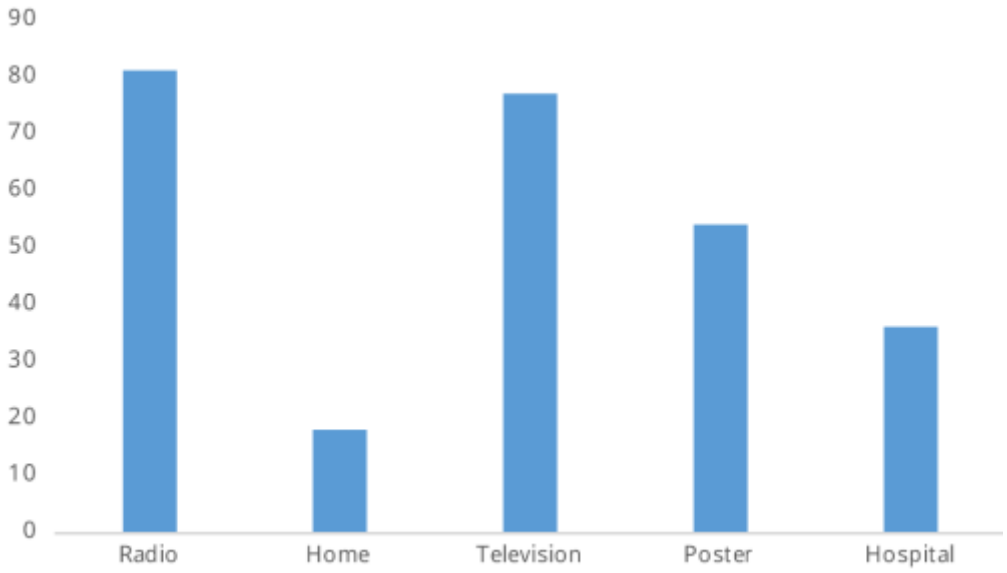

Figure 2. Distribution of respondents' sources of information about HIV/AIDS (n=234).

respondents were aware of HIV/AIDS, this is in line with findings from Ebonyi among women farmers conductd by Egbo and Chukwu (2015). This also implies that most of the informal sectors are aware of the existence of HIV/AIDS. Screening for HIV/AIDS was low among the women in this study and this was based on so many reasons, but the major reasons were fear of death and stigmatization. This finding is similar to what was reported by Ilo and Adeyemi (2010) where three-fifths of the respondents said they did not screen for HIV/AIDS because of fear of death and stigmatization. Others just did not want to know their status, which maybe because they felt that their friends would look down on them if they tested for HIV (Mwangi et al., 2014).

Knowledge on mode of transmission of HIV/AIDS

Most of the market women in this study had good knowledge on the mode of transmission of HIV/AIDS. Among different options given, many of these women knew that HIV can be contracted through sexual intercourse and sharing of sharp objects. This is in line with findings of Ilo and Adeyemi (2010) where 80.1% of market women in Ogun State understood that HIV/AIDs can be transmitted through sexual intercourse. A small percentage of market women had poor knowledge of the mode of transmission by choosing to share of toilets, sharing same market stall, sharing same bed and hand shake as means of transmission. The findings from this

study differ from findings of Babalola and Babalola (2013) where women's perception of HIV/AIDS, indicated that one cannot get HIV/AIDS through sharing of food (78%) and 60.0% disagreed that HIV/AIDS could be transmitted through sharing of toilet. The difference in these findings indicates that information available to market women on HIV/AIDS is still not enough and there is need for more sensitization among these groups of people.

Attitude towards HIV/AIDS

The attitude of market women in this study towards HIV/AIDS was good. The results showed that majority of these women agreed that an HIV infected person should not be isolated and condoms should be used as means of prevention. This is in support of what was reported by Ilo and Adeyemi, 2010 in Ogun State where most women indicated they have relevant information on prevention practices against HIV/AIDS. The finding from this study is also similar with findings of Babalola and Babalola, 2013 where 64.0% of the women affirmed that male condom can prevent unplanned pregnancy and sexually transmitted infections.

Source of information on HIV/AIDS

The most important source of information on HIV/AIDS among the market women in this study was the radio. The implication of this finding is that the radio remains a strong channel of communication to reach out to members of the public. The benefit of the radio over any other medium is that it required no full knowledge on how to read and write before accessing or receiving it is contents. Abia et al 2012 has listed radio as a strong channel of mass communication. It reaches the widest audience with a single signal. It carries the persuasive force to modify a person's behavior because of it acceptability and coverage. A radio gadget is affordable since a radio set could be acquired at less than 2000 naira ($7). However, this is different from findings of Ilo and Adeyemi, 2010 in Ogun State where the hospital was reported as the best source of information for nearly 30% of respondents. Although the percentage is almost the same for women who chose hospital as their source in this study, this difference may be because of difference in the structure of health care system between the two States. When the women in Ogun State go for ante-natal cases and health challenges, they receive hand bills, posters, etc., and listen to talks organized for women in the hospital.

Conclusion

The study assessed the level of awareness and sources of information on HIV/AIDS by women trading within the selected markets in Ibadan. Many of the market women have heard of HIV/AIDS and their main source of information on HIV/AIDS was radio. Most of the sampled women were aware that HIV/AIDS is contacted through sexual intercourse, and that a person should abstain from unprotected sex by using condom. Most of the respondents have not had HIV/AIDS test done for the fear of death and stigmatization. This may suggest that discrimination of people living with HIV/AIDS still exists among the market women. Although HIV prevention programmes are expanding, they are not keeping pace with the epidemic, yet. This is a challenge in Nigeria with an estimated population of 3.2 million people living with HIV and adult coverage being only 51%, a lot still has to be done to achieving the 90-90-90 target to help end the AIDS epidemic by 2030.

In reaching out to the populace, consideration needs to be given to the source of acquiring information about the disease. Radio and television are the major sources of information gathering and dissemination. To control the spread of HIV/AIDS requires reaching out to a wider number of people. The source that is most affordable, accessible and acceptable is the radio, followed by the television. These sources cannot be ignored if we want to achieve rapid reduction in the spread of the virus through behavior modification by health education and achieving the expected 90% level of individuals knowing their HIV status and been placed on treatment.

Repeated jingles on radio and television have the persuasive force of modifying our negative behavior (especially loose sexual behavior). The wave of conduct over condom is to be reinforce using radio and television as channels of communication. However, other channels of communication must be explored.

Recommendations

Based on the findings from this study, the following recommendations are made:

1. There is need to plan and implement new strategies of educating women particularly in market places such as distribution of flyers and erecting bill boards at strategic locations.
2. More awareness on HIV/AIDS should be incorporated into talks on radio as this is the most important source of information to the market women; since there is still a high level of stigmatization and discrimination of people living with HIV/AIDS by the market women.
3. There is a great need to educate the market women on the importance of voluntary HIV testing.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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academicJournals

Vol. 9(9), pp. 187-193, September 2017
DOI: 10.5897/JAHR2017.0431
Article Number: 57A9BDA65779
ISSN 2141-2359

http://www.academicjournals.org/JAHR

Journal of AIDS and HIV Research

Full Length Research Paper

Determinant of mortality in HIV infected people on antiretroviral therapy in Southwest Ethiopia

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Received 24 April, 2017; Accepted 29 June, 2017

The introduction of antiretroviral drug has considerably reformed the course of HIV/AIDS from life threatening epidemic to a chronic manageable health problem. Mortality and morbidity associated with HIV/AIDS are changing. The main aim of this study was to assess the potential determinant of death among people infected with HIV and initiated anti-retroviral therapy (ART). A general retrospective cohort method was used on 2655 people undertaking ART at Mizan Hospital from 7 January, 2005 to 8 May, 2013 in Southern Ethiopia. The three age groups: Pediatrics (age under 10 years), teens (age between 11 and 19 years), and elderly (age older than 20 years) was used to stratify the cohort. The usual clinical follow-up registry of the ART clinic was the main data for the study. Kaplan-Meier (KM) method was used to compare the survival experience of patients after initiation of ART. Cox proportional regression model was used to assess determinant of mortality. A total of 2655 patients, consisting of 6.3% pediatrics, 3.3% teenagers and 90.4% elderly were included in the study. The survival probability at the sixth month after initiation of the treatment was 96, 94, 96 and 96% for pediatrics, teenagers and adults, respectively. A low initial CD4 (P=0.001), advanced WHO clinical disease stage (P=0.01), receiving ISONIAZID preventive prophylaxis (P=0.02), tuberculosis coinfection (P < 0.001) and being bedridden (P < 0.002) was an independent determinant of death. The cumulative incidence of mortality rate for HIV patients has been low in this study hence early initiation of the treatment is highly recommended.

Key words: Anti-retroviral therapy, mortality, South Ethiopia.

INTRODUCTION

Occurrence of the Human Immunodeficiency Virus (HIV) epidemic is one of the major challenges that the world has seen in recent past. Millions of individuals have died of HIV in the last thirty years. The large proportion of deaths reportedly occurred in sub-Sahara African countries where antiretroviral treatment was announced recently (Federal Democratic Republic of Ethiopia, 2012). Highly active antiretroviral therapy (HAART)

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pharmacological intervention has inhibitory effects on HIV replication which has revealed positive results on the HIV epidemic. The suppression of viral copying is mainly related to the steady rise in the CD4 count and results in medical stabilization (AIDS Institute, 2013; Organization, 2012b). The antiretroviral therapy (ART) interventions have yielded considerable results. The 2012 World AIDS Day report revealed that there were 700,000 fewer new infections in the world in the year 2011 than a decade ago, with much of the progress supposedly attributed to the ARV therapy (WHO World AIDS Day, 2012).

Evidence showed that untreated HIV infection can lead to higher morbidity and mortality from conditions other than HIV, even at high CD4 counts (AIDS Institute, 2013; Zaidi et al., 2013; Johnson et al., 2013; Andreychyn and Zhyvytsia, 2013). Researchers currently recommend that all patients living with HIV be treated with ART to decrease transmission of HIV from one another (AIDS Institute, 2013; Organization, 2012b). This is due to increasing evidence that patients with well-known HIV infection have benefited from ART at all stages of the disease (Cohen et al., 2011; Organization, 2012a). Decreased viral load which should have reduced transmission risk from ART is now part of the established strategy aimed at dropping HIV transmission (AIDS Institute, 2013; Organization, 2012a).

In Ethiopia, HIV epidemic has remained a major public health problem mainly affecting people of productive and reproductive age (CSA-Ethiopia, 2011). Since HIV cases reported in the mid-1980s in Ethiopia (MOH Guidelines, 2003), both government and non-governmental organizations have shown commitment to prevent its spread and alleviate its impact from the early days of the epidemic. That included expansion of ART provision to health facilities located closer to the communities has improved access to ART for vulnerable groups. In Ethiopia, around two hundred and fifty thousand people living with HIV initiated treatment and nearly two hundred thousands are currently on ART (WHO, 2005). In spite of the courage shown regarding universal access to the treatment, there is a critical shortage of figures about the results of the therapy in the country. Thus, the objective of this study is to examine the survival status and associated factors.

METHODOLOGY

An open retrospective cohort study design was carried out at one ART clinic in Mizan Hospital, on people living with HIV/AIDS (PLWHA) who attend ART follow-up clinic.

Study setting

Mizan Hospital is a general hospital found in Southern Ethiopia, 565 km in southwest Addis Ababa. ART service was introduced in 2003 in the hospital. A total of 2682 patients who started ART was selected using distinctive identification serial number from the ART database and studied.

Data processing and analysis

A secondary data routinely collected for clinical monitoring and evaluation purpose in the hospital was used. The data were fed into an ART register database by a trained data clerk during the follow-up time. Data recording and entry usually starts when patients engaged in HIV- follow-up care in the hospital. The accessed database was retrieved using Microsoft Excel; data were transported to Epi-Info 7 for windows; and the imported data were checked for completeness, cleaned and edited. Twenty-seven data with inadequate information was omitted from the analysis. The data was analyzed using SPSS version 20 for windows.

The survival time was analyzed in months using the time interval between dates of ART started and date of event (death), date of transfer for transferred out (TO), first date of the first missed appointment for lost cases and the date in which patient completed the end of follow up. The data were categorized into three age groups: pediatrics (age younger than 10 years), teens (age 11 to 19 years), and adults (age older or equal to 20 years). The characteristics of the study participants were designated in terms of quantitative value of descriptive statistics for numerical data and frequencies or proportion for nominal data. The actuarial life table method and/or KM approaches were carried out to compare the survival experience of study participants after initiation of ART. The Log rank test was used to test if the detected variance in survival experience in the groups was significant or not. Proportional Cox-regression hazard model was used in identifying potential predictors of mortality.

Measurement

The outcome of interest for the present study was death from any causes that was confirmed through medical registration in the ART clinic. Individuals alive and on the treatment, lost from follow up care, dropped and/or transferred out were seen as censored at the end of the follow-up time.

The study encompasses all patients who initiated the treatment from 2005, regardless of age. For individual patients, the following starting point information was taken: Age at initiation of ART (years), sex (male, female), entry CD4 cell count, baseline WHO medical stage, baseline functional status, date of last visit for clinical care, and date final event took place.

Ethical considerations

Personal identification data was maintained for confidentiality.

RESULTS AND DISCUSSION

The present study included 2655 patients out of 2682 patients who had initiated ART since 2005, irrespective of age. Of the 2655 patients, there were 6.3% pediatrics, 3.3% teenagers, and majority 90.4% were adults. The median interquartile range (IQR) age in year was 30.5 (IQR: 25.5, 35.6) for the adults and 17.8 (15.5, 19), 3(1, 7),

Table 1. Entry basic demographic and clinical characteristics of the study participant, Mizan Hospital, 2005 to 2013.

Characteristics	Age category n (%)			χ^2 p-value
	Children	Adolescent	Adult	
Sex (N =2655)				
Male	98(58.3)	14(16.1)	1111(46.3)	
Female	70(41.7)	73(83.9)	1289(53.7)	0.001
Age (n=2655, Mean (±SD)	4.1(3.1,3.1)	16.8(2.4 18)	31.5 (8.1)	
Base line CD4 (n=2446) median(IQR)=169(91,257)	336(214.5,569)	215(103.5, 270)	162.5(88, 249)	
CD4 0-49	5(4.9)	6(7.3)	264(11.7)	
50-199	17(16.7)	34(41.5)	1137(50.3)	0.001
≥200	80(78.4)	42(51.2)	861(35.9)	
WHO stage at entry (n= 2655)				
Clinical Stage one	11(6.5)	9(10.3)	246(10.2)	
Clinical Stage two	17(10.1)	10(11.5)	398(16.6)	0.105
Clinical Stage three	113(67.3)	58(66.7)	1443(60.1)	
Clinical Stage four	27(16.1)	10(11.5)	313(13)	
Baseline functional status (n=2655)				
Bedridden	29(17.3)	2(2.3)	145(6)	
Ambulatory	113(67.3)	27(31)	570(23.8)	0.001
Working	26(15.5)	58(66.7)	1685(70.2)	
Tuberculosis status (n=2655				
Yes (+ve)	30(17.9)	17(19.5)	533(22.2)	0.364
No (-ve)	138(82.1)	70(80.5)	1867(77.8)	
Isoniazid (n=2655)				
Yes	5(3)	11(12.6)	206(8.6)	0.014
No	163(97)	76(87.4)	2194(91.4)	
Regimen substitution (n= 2655)				
Yes	22(13.1)	19(21.8)	414(17.2)	0.191
No	146(86.9)	68(78.2)	1986(82.8)	
Cotrimoxazole prophylaxis (n=2655				
Yes	149(88.7)	77(88.5)	2131(88.8)	0.996
No	19(11.3)	10(11.5)	269(11.2)	

for teenagers and pediatrics correspondingly. More than half (54%) of participants were females among which 83.9% were found in the teenagers.

The baseline weight at treatment initiation was 50 (44, 56), 51 (45.5, 57) 42 (34.7, 50) and 13 kg (9, 16) for adult, teenagers and pediatrics, respectively. Cotrimoxazole preventive therapy (CPT) was provided to 89% of pediatrics, 87% teenagers and 89% adults. Tuberculosis co-infection was 18, 20 and 22% of teenagers, adolescents and adults, respectively. Regarding the WHO clinical stage of disease, for tuberculosis, majorities in all the age groups; 67% pediatrics, 67% teenager and 60% adults were in Stage three, while 16% pediatrics, 12% teenagers and 13% adults were in Stage four. The CD4 cell count at the time of entry was meaningfully different across the age groups (P=0.001): Pediatric patients still under the treatment at a median (IQR) cells/ml^3 cell count of 367 (240, 726), teenager patients that started at a median (IQR) cells/ml^3 of 198 (101, 271) and adult participants that started at a median (IQR) cells/ml^3 of 160 (IQR85, 245) (Table 1).

The incidence rate of mortality throughout the follow-up

Table 2. Probability estimates of periodic survival of the study participant using actuarial table, Mizan Hospital, 2005 to 2013

Duration (month)	Probability of event free experience at in age groups		
	Pediatric	Teens	Elderly
6	0.94(0.89, 0.97)	0.96 (0.88, 0.98)	0.96 (0.95, 0.97)
12	0.91 (0.86, 0.95)	0.93 (0.83, 0.97)	0.95 (0.94, 0.96)
24	0.91 (0.86, 0.95)	0.90 (0.80, 0.96)	0.94 (0.93, 0.95)
36	0.91 (0.85, 0.95)	0.90 (0.79, 0.95)	0.93 (0.92, 0.94)
48	0.91 (0.86, 0.95)	0.90 (0.79, 0.95)	0.93 (0.92, 0.94)

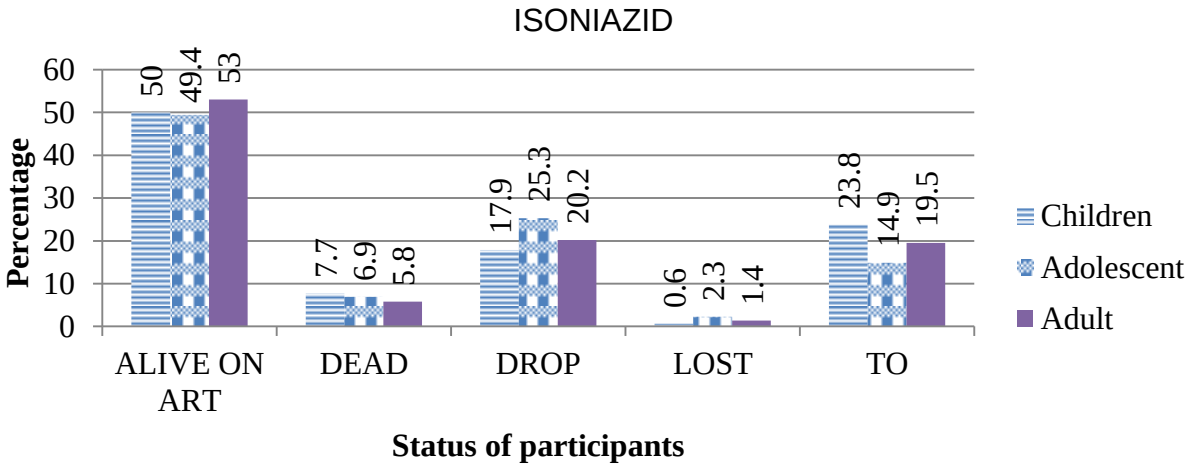

Figure 1. Final events of study participant, Mizan Hospital, 2005 to 2013.

time was 5.8, 6.9 and 7.7% among adult, teenagers and pediatrics, respectively. The failure rate was nearly 18% in children, 20% in adults and 25% in adolescents (Figure 2). The survival probability at the sixth month after the initiation of the treatments was 96 and 94% for pediatrics, 96% for teenagers, and 96% for adults (Table 2).

The trend of clients engaged in ART by the particular year at the study area was shown in Figure 2. The result reveals that children survival rate was 83 months (79, 87), 81 months (75, 86) for adolescent and 89 months (87, 90) for adults. Throughout the follow-up time, there were 159 deaths and 537 dropouts (Figure 1). In Cox regression model, gender, initial CD4 count, functional status and WHO clinical stage at treatment initiation, Isoniazid prophylaxis for tuberculosis co-infection, and age category was considered (Table 3). This model revealed that there is no significant difference between male and female in the risk of death. Progress of participants with advanced disease are as follows: Stage IV had higher risk (HR) (95% CI) 4.5(1.36, 14.88) of death when compared with patient with Stage I; Stage III had HR (95% CI) 3.2 (1.06, 10.23) of dying than Stage I, whereas there are no significant hazard risk differences compared with Stage II. Participants with a history of tuberculosis co-infection had higher risk (HR) (95% CI) 1.25 (1.03, 1.53) of death throughout the follow-up time. Danger of death in patient who did not take Isoniazid prophylaxis lowers by HR (95% CI) 72% on average when compared with taking Isoniazid during the follow-up time.

The HR (95% CI) for bedridden and ambulatory patients were 2.63 (2.05, 3.36) and 1.56 (1.31, 1.86) higher as compared to the working group. Patient ART initiated at CD4 count less than 50 cells/ml^3 were HR (95% CI) 1.977 (1.55, 2.52) when compared with patient ART initiated at CD4 count >200 cells/ml^3.

The result revealed that there was no significant difference in the age groups in crude mortality rate. However, higher proportions of lost to follow-up were seen in adolescent and adult than children. In multivariate analysis, explanatory variables did not reveal significant difference in mortality in all age groups, whereas higher proportion of adolescents was lost to follow up. A study done in Uganda (Bakanda et al., 2011) revealed that

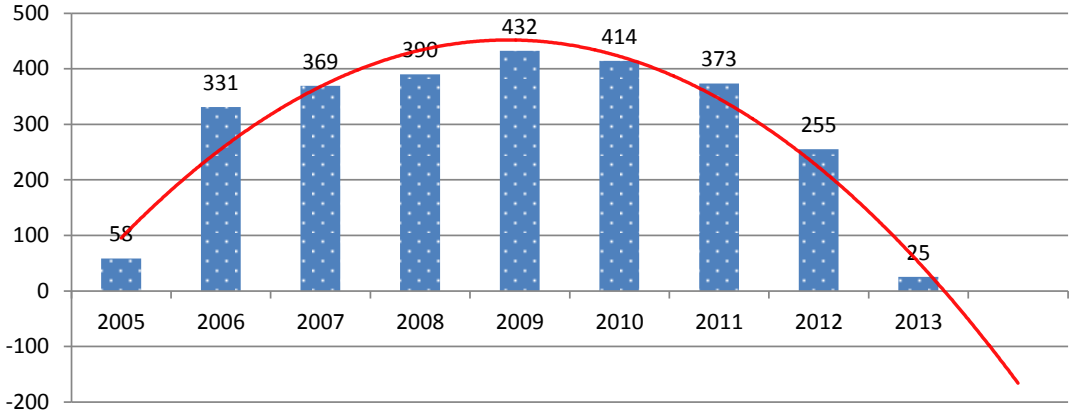

Figure 2. Trends in initiation of ART in study setting (Mizan Hospital, 2005 to May 2013).

Table 3. Cox proportional hazard regression model, predictors of mortality in study participants, Mizan Hospital, 2005 to 2013.

Characteristics	n	AHR (95% CI)	p
Age category	**2655**		
Child ≤10 years)	168	R	
Adolescent (11–19 years)	87	1.879(0.704,5.015)	0.208
Adult (≥20 yrs.)	2400	1.412 (0.789, 2.526)	0.245
Gender	**2655**		
Male	1223	0.987 (0.721, 1.350)	0.333
Female	1432	R	
WHO stage	**2655**		
Clinical Stage one or	266	R	
Clinical Stage two	425	2.142 (0.597, 7.681)	0.242
Clinical Stage three	1614	3.209 (1.060, 10.235)	**0.049**
Clinical Stage four	350	4.506 (1.364, 14.883)	**0.014**
Baseline functional status	**2655**		
Active	1769	R	
Self-helping	710	2.848 (1.939, 4.183)	**0.0001**
Bedridden	176	6.724 (4.253, 10.630)	**0.0001**
Ever ISONIAZID	**2655**		
Yes	222	R	
No	2433	0.205 (0.065, 0.647)	**0.024**
CD4 category	**2446**		
≤50	275	2.262(1.33, 3.82)	**0.003**
50-199	1188	1.414(0.91,2.2)	0.124
≥200	983		
Tuberculosis status	**2655**		
Yes(+ve)	580	1.25(1.027,1.525)	**0.026**
No(-ve)	2075		

there were no significant differences both in mortality and lost to follow-up among the age groups. However, a report from South Africa showed that adolescents had worse outcomes compared to their adult counter parts (Nachega et al., 2009). Likely explanations for this difference may be the sociocultural and other variations in the age groups in different countries.

In this study, risk of death was not related to gender. This is in line with other studies in Ethiopia that revealed gender has no significant effect on mortality (Alemu and Sebastián, 2010; Biadgilign et al., 2012). Contrary to these findings, ample evidences (Bakanda et al., 2011; Tsegaye and Worku, 2011; Assefa and Wencheko, 2012) confirmed male sex as an independent predictor of mortality. These debatable reports may be related to the socio-cultural differences in the study setting.

A patient who initiated ART as bedridden (inability to attain self-care in the daily living) had the shortest survival rate than working (able to perform routine activities). The result is consistent with various reports in Ethiopia (Biadgilign et al., 2012; Tsegaye and Worku, 2011; Assefa and Wencheko, 2012). The study showed that bedridden patients were 6.7 times more likely to die than those patients involved in their everyday activities. CD4 cell counts had a strong influence on the survival experience of patient on ART (Bakanda et al., 2011; Biadgilign et al., 2012; Zachariah et al., 2006). This study draws similar result and conclusion as the above researchers. New findings by other researchers reported that those patients with higher CD4 counts are at low risk for immediate adverse outcomes. There is suggestion in a number of literature that if ART is initiated with higher or normal CD4, both morbidity and mortality will be lessened (Andreychyn and Zhyvytsia, 2013; Kitahata et al., 2009; Hanna et al., 2013). New York report on ART (AIDS Institute, 2013) recommended that all patients with HIV infection be evaluated for initiation of ART regardless of the CD4 count. This is due to growing evidence that HIV patients benefit from ART at all stages of the disease (Cohen et al., 2011; Organization, 2012a). The result is consistent with other study reports from Ethiopia (Alemu and Sebastián, 2010; Biadgilign et al., 2012; Zachariah et al., 2006). WHO staging provides a basis for the development of AIDS defining conditions, characterized by severe clinical manifestation, which leads to gradual deterioration of the immune system. Therefore, it is likely that patients with deteriorating immunity are faced with challenges of survivorship.

This study has shown that patients with history of tuberculosis were 1.3 times at higher risk of mortality than those without a history of tuberculosis during the follow-up period. Similarly, study done by many scholars confirmed that HIV positive tuberculosis patients had shorter survival rate (Shaweno and Worku, 2012; Cavanaugh et al., 2012). The risk of death in patients who did not take Isoniazid preventive therapy lowered by 72% as compared with their counterparts. The result is not consistent with the documents that advocate Isoniazid as being among the preventive therapy which supposedly extends and improves the quality of life for people living with HIV (Vitoria et al., 2010). The possible reason for controversy is that Isoniazid preventive therapy is not universal amongst the cohorts. Only patients suspected for tuberculosis co-infections by health professionals, and in most cases of advanced medical stages are eligible for Isoniazid (FMOH, 2007).

Conclusions

Generally, this study finds out low incidence of mortality though there was high loss to follow-up rate. The likelihood of survival by the sixth month after beginning of ART was highest for adults compared to children and adolescents. Advanced clinical stage, base line functional status, low CD4 cell count, Isoniazid preventive therapy and tuberculosis co-infection were variables that predispose for mortality. HIV infected individual identification and early initiation of ART in the early stage of the disease should be given priority in the treatment modality. Further researches are required to accurately determine the risk factors related to mortality among the HIV patients who are taking ARV therapy.

CONFLICT OF INTERESTS

The author has not declared any conflict of interests.

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academicJournals

Vol. 9(9), pp. 194-201, September 2017
DOI: 10.5897/JAHR2017.0438
Article Number: ED15F9365797
ISSN 2141-2359

http://www.academicjournals.org/JAHR

Journal of AIDS and HIV Research

Full Length Research Paper

Lysine and threonine plasma concentrations in Ivorian patients living with human immunodeficiency virus

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Received 23 June, 2017; Accepted 17 August, 2017

Côte d'Ivoire is one of the most affected countries in West Africa with HIV/AIDS, with a prevalence of 3.4%. Essential amino acids are needed by the organism as they play key roles in the immune system and they are supplied through diet. The objective of this study was to determine the plasma lysine and threonine status for better medical and nutritional management of patients living with HIV. This study involved 254 individuals: 127 HIV positive and 127 HIV negative (serving as controls) after confirmation of their HIV status through an HIV test (test DETERMINE® and GENIE II). Lysine and threonine were assayed using high performance liquid chromatography (HPLC) on plasma and CD4 lymphocyte count by the method of flow cytometry (FacsCalibur) from whole blood containing EDTA. This study showed that deficiency of lysine was more observed in male HIV infected individuals (66.7%) and threonine deficiency in female HIV infected individuals (17.1%) as compared to the controls subject. The amino acid concentrations as a measure of the degree of immunosuppression was significant for lysine (P = 0.0006) and not significant for threonine (P = 0.8640). The deficiency observed in HIV infected patients taking antiretrovirals is therefore probably due to viral infection and insufficient lysine intake in diet. The threonine concentration depends on the health condition of the subject.

Key words: Amino acids, essential, Côte d'Ivoire, HIV-infected patients, lysine, threonine.

INTRODUCTION

Human immunodeficiency virus (HIV) infection is a major public health problem (Alqudah et al., 2016). During HIV infection, activation of immune cells causes an increase in the body requirements of specific amino acid, and affected immune cells require an exogenous supply of certain amino acids (McGaha et al., 2012). In actual fact, HIV infection causes hypermetabolism of proteins and amino acids in the muscles, liver and adipose tissues in patients taking antiretroviral therapy (Zou and Berglund, 2007).

Lysine is an essential amino acid that helps build the body immune system by contributing to the development of antibodies; it has antiviral properties (Lukasheva and Berezov, 2002). A plasma lysine requirements increases in cases of acute infectious diseases which are common in many developing countries (Ghosh et al., 2010).

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Furthermore, lysine deficiency leads to active HIV replication (Butorov, 2013).

Threonine is a key nutrient to the intestine. In the intestine, this amino acid plays a major role in the synthesis of mucin, a glycoprotein required for the protection of the intestinal epithelium (Ruth and Field, 2013). Like mucins, immunoglobulins are globular glycoproteins rich in threonine. Due to the high threonine concentration in immunoglobulins, the deficiency of threonine may affect the production of immunoglobulins (Richard and Galanaud, 1995). During HIV infection, nutritional care and support are very important to prevent the development of nutritional deficiencies and therefore, improve the quality of life of people living with HIV (WHO, 2002).

Few clinical data exist on plasma lysine and threonine profiles in HIV-infected patients (Butorov, 2013). In Côte d'Ivoire, the status of essential amino acids, particularly lysine and threonine in patients living with HIV, is not documented. For better medical and nutritional care for people living with HIV, it is therefore necessary to evaluate the levels of lysine and threonine, the essential nutrients for proper functioning of the living organism.

The objective of this study was to determine the plasma lysine and threonine concentrations and analyze their relationship with the degree of immunosuppression in people living with HIV/AIDS taking antiretrovirals in Côte d'Ivoire.

MATERIALS AND METHODS

Period and study design

The study was carried out in the Clinical and Fundamental Biochemistry Department of the Institut Pasteur of Côte d'Ivoire from December 2014 to November 2016. It was a cross-sectional descriptive study involving a cohort of individuals from whom blood samples were collected. The rapid tests Determine^{TM} HIV-1/2 and *GENIE II* HIV-1/HIV-2 were used for selection of the individuals.

Blood sample collection

Blood samples from HIV positive and negative subjects were required for the various biochemical and serological analyses. Therefore, two blood tubes containing EDTA (Termo, Tokyo, Japan) were used to determine plasma concentrations of essential amino acids (Maeda et al., 2010) and $CD4^+$ T cell count (blood total) in HIV positive subjects, respectively. A tube of blood without anticoagulant (dry tubes) was used to carry out HIV serological tests and biochemical parameters assay. Finally, blood glucose was determined on serum from a tube containing potassium oxalate and sodium fluoride. Blood samples from pregnant women and children, regardless of their serology status were not included in this study.

HIV test and $CD4^+$ T lymphocytes count

For the detection of antibodies anti-HIV, two rapid tests were performed. They were the "Alere Determine^{TM} HIV-1/2 kit" (Alere Medical Co., Japan) which is an immunochromatographic test based on the principle of formation of an antigen-antibody complex revealed after staining (Tang et al., 2008) and the GENIE II HIV-1/HIV-2 kit (BIO-RAD, France) which is a confirmatory immunoenzymatic assay. The principle of this test is based on the detection of anti-HIV1 and anti-HIV2 antibodies directed specifically against antigens (Ouassa et al., 2007; Laforgerie et al., 2010).

The CD4 T lymphocyte count was performed using flow cytometry system on the automated FacsCalibur from the whole blood taken from EDTA tube. The principle is based on the quick analysis of moving particles (cells) in a single file in front of a laser beam (Ormerod and Imrie, 1990).

Indeed, the $CD4^+$ T lymphocyte count was determined by pouring a volume of 20 µL of Tri TEST (CD3, CD4 and CD45) in each Trucount tubes. A volume of 50 µL of whole blood and a lysis solution diluted by 1:10 at a rate of 500 µL was added to each tube. The tubes were then homogenized and incubated for 15 min in the dark. This operation (homogenization and incubating the tubes in the dark) was repeated a second time; then the Trucount tubes were placed on the rack of FacsCalibur device after third homogenization. The mixture was drawn into the flow cytometric counter and the result is shown electronically.

The normal reference values for CD4 count according to WHO are: 600 to 1750 cells/mm^3 (31 to 60%). All HIV-1 infected patients were classified into four groups according to their $CD4^+$ T cells count: no significant immunodeficiency (≥ 500 cells/mm^3), average immunodeficiency (350 to 499 cells/mm^3), advanced immunodeficiency (200 to 349 cells/mm^3) and severe immunodeficiency (< 200 cells/mm^3) (Schneider et al., 2008).

Biochemical analysis

The serum concentrations of creatinine, urea, glycaemia, alanine aminotransferase (ALAT) and aspartate aminotransferase (ASAT) were measured on the COBAS INTEGRA 400 plus controller. It is a spectrophotometer based on the reaction of TRINDER which is an enzyme, and colorimetric method which uses a chromogen whose colour intensity developed is directly proportional to the concentration of the measured substance, was used (Deyhimi et al., 2006).

Plasma lysine concentration and threonine were determined by high performance liquid chromatography (HPLC) according to the method of Teerlink et al. (1994).

Stock solutions of 1000 µmol/L of lysine and threonine as well as the internal standard (L-Norvaline) were prepared in acidified methanol (0.1% HCl). For each amino acid, successive dilutions were made from these solutions to obtain the following concentrations: 5, 10, 25, 50, 100, 200 and 400 µmol/L. These concentrations were selected according to the limits of detection (LOD) and quantification (LOQ), and the physiological concentrations of lysine and threonine in blood plasma. For this analysis, the detection limits of lysine and threonine are respectively 8 and 44 fmol/L. The quantification limits of lysine and threonine are 27 and 146 fmol/L, respectively. A calibration line is made using the entered values for the concentrations of amino acid in the standard. For each of the analysts, the concentrations in the "unknown" samples are calculated separately.

After thawing at room temperature, 200 µL of plasma was introduced into a tube containing an equal volume (200 µL) of acidified methanol (0.1% HCl). The mixture obtained was centrifuged at 3000 rpm for 15 min, and then the collected supernatant was filtered on millipore of 0.45 µm in diameter. 15 µL of internal standard L-Norvaline (400 µmol/L), an equal volume (15 µL) of sample filtrate (plasma, standards or mixed standards) and 60 µL of MilliQ water were added to 270 µL of derivatization reagent (OPA / 3-MPA, pH 10.0). The solution obtained after homogenization was incubated in the Autosampler for 3 min before the injection.

The analysis was carried out with an elution rate of 1 mL/min, a wavelength of 340 nm (excitation) and 455 nm (emission), an analysis time of 25 min, an analysis temperature of 37°C and a gain of 2. The injection volume was fixed at 10 µL of the sample, the standard or the mixed standards from the HPLC injection loop (Waters®, France). The NUCLEOSIL® 100 Å column (150 mm × 4.6 µm x 5 µm particle size) was cleaned with 100% of the mobile phase B (acetonitrile/water v/v) and rebalanced with 100% of the mobile phase A (potassium dihydrogen phosphate buffer, 30 mM, pH 7.0) between two injections. Normal reference values for lysine and threonine are 107 to 244 µmol/L and 74 to 175 µmol/L, respectively (Teerlink et al., 1994).

Statistical analysis

Statistical analyses were performed using Student's t-test for comparison of averages. The correlation between essential amino acid concentrations and $CD4^+$ T lymphocytes count was determined by the Pearson test. A $P < 0.05$ value was considered to be statistically significant.

Ethical considerations

The study was conducted in accordance with the Helsinki Declaration 2000 on HIV and AIDS research conducted in poor countries and in accordance with the local legislation regarding the national program on treatment management for People Living with HIV/AIDS (Decree No. 411 of December 23, 2001). The blood samples were collected from HIV-positive patients monitored at the Institut Pasteur of Côte d'Ivoire (IPCI), a reference center for public health programs in Côte d'Ivoire supported by the global fund for HIV/AIDS/malaria/tuberculosis. However, for research purposes, written consent was obtained from patients for the use of their blood samples taken during biological monitoring.

RESULTS

Background characteristics

This study involved 254 blood samples from 127 HIV-negative and 127 positive individuals. Their ages varied between 26 and 49 years and the average age of infected subjects was 37 ± 0.52 years against 32 ± 0.50 years for the controls. In addition, the HIV serological subtype found was 100% HIV1. Among these 127 HIV positive individuals, there were 70 women and 57 men on antiretroviral therapy (zidovudine + lamivudine + nevirapine).

Determination of biochemical parameters and analysis of amino acid concentrations

Biochemical parameters

The mean values of the biochemical parameters in the HIV-infected and the control samples analyzed were within the normal standard reference values [blood glucose: 4.16 to 6.11 mmol/L; creatinine: 53 to 106 µmol/L; urea: 1.66 to 5.83 mmol/L and transaminases (ASAT): 8 to 49 IU/L; ALAT: 7 to 48 IU/L] and no significant difference was observed in the control samples.

Analysis of the plasma lysine and threonine profile

This study showed a significant increase ($P = 0.0040$) in lysine levels (148 ± 16.32 vs. 92 ± 6.14 µmol/L) and a non-significant decrease ($P = 0.6124$) in the threonine levels (324 ± 42.00 vs. 357 ± 48.06 µmol/L) in HIV positive subjects as compared to the controls subject, respectively. However, threonine levels were higher in the two groups of subjects as compared to normal standard values (control versus infected subject: 357 vs. 324 µmol/L).

Relating to sex: Regarding deficiency, 66.7% (38/57) male HIV-positive had deficiency of lysine as compared to threonine; 0.0% (0/57 HIV-positive) (Figure 1a). On the other hand, in female PLHIV, 37.2% (26/70) had lysine deficiency as compared to threonine; 17.1% (12/70) of PLHIV (Figure 1b).

Regarding excess amino acids, 74.1% (43/57) HIV-positive men had excess threonine and 0.0% (0/57) had excess lysine (Figure 1a). On the other hand, 50.0% (35/70) female HIV-positive have excess threonine and 12.8% have excess lysine (9/70) (Figure 1b). However, excess threonine was 100% in the male control subjects and 50.0% in women against total absence of excess in lysine in both sexes.

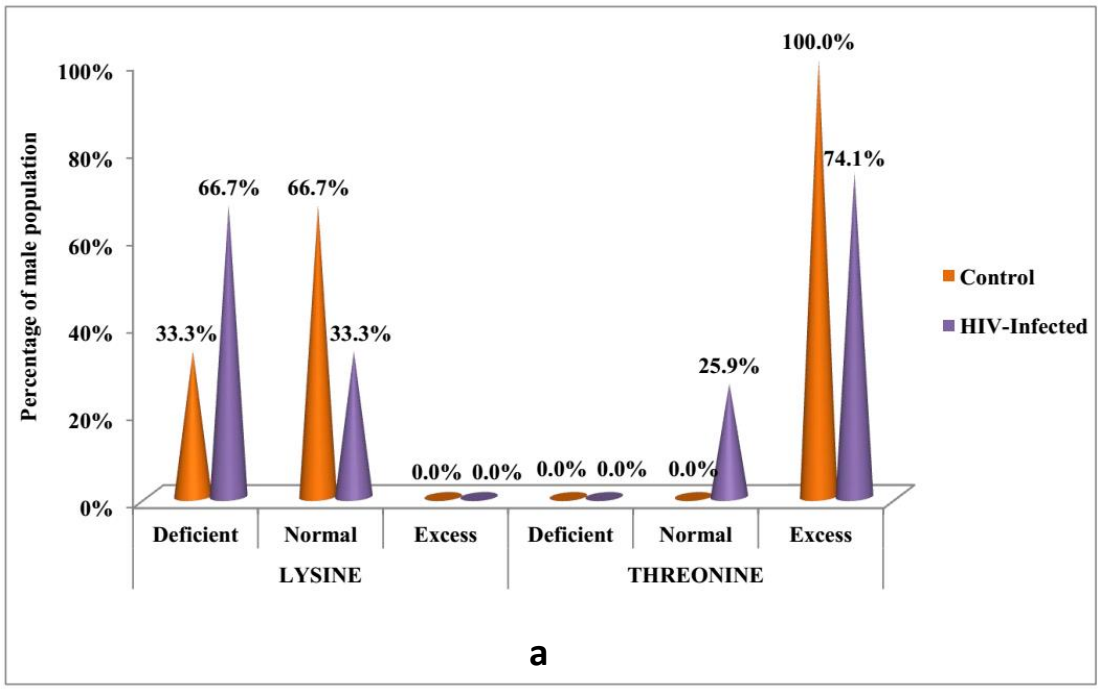
In HIV infected male, mean concentrations of lysine and threonine were significantly lower, 97 ± 3.00 and 329 ± 27.36 µmol/L, respectively, as compared to the control (Table 1). However, in HIV infected females, average concentrations of lysine and threonine were respectively higher (173 ± 19.61 and 320 ± 49.05 µmol/L) as compared to the controls (83 ± 5.27 and 243 ± 36.32 µmol/L) with a significant difference for lysine ($P < 0.0001$) and non-significance for threonine ($P = 0.2101$) (Table 1).

Relating to HIV infection: Concerning lysine, 50.4% (64/127) of HIV-infected patients and 54.3% (69/127) of the control subjects had lysine deficiency. On the other hand, 9 (7.10%) samples from HIV patients had excess of lysine, as opposed to the control subjects that showed no excess in lysine concentration (Table 2).

Concerning threonine, 9.5% of both HIV patients and controls (12/127) had threonine deficiency; however, 61.4% (78/127) of the HIV-infected patients and 72.4% (92/127) of the controls had excess threonine (Table 2).

Finally, the number of HIV infected patients having lysine deficiency (64/127) was higher than those having threonine deficiency (12/127) (Table 2).

Relating to the WHO classification of CD4 lymphocytes: In HIV-infected female who had CD4



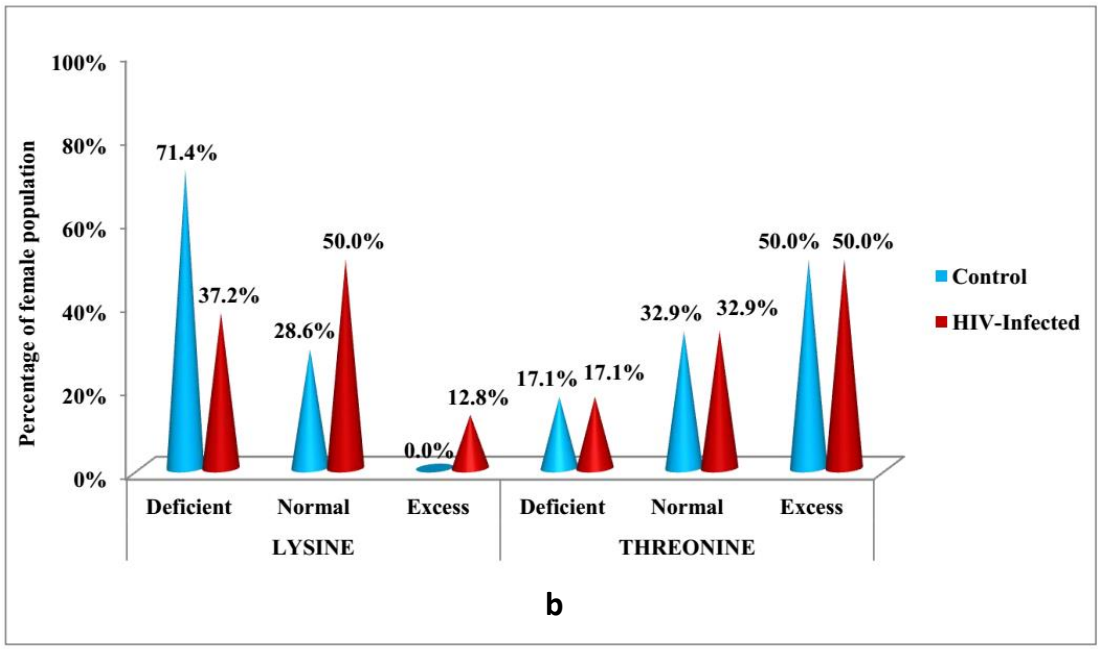


Figure 1. a. Lysine and threonine status of male HIV infected and control population. **b.** Lysine and threonine status of female HIV infected and control population, in the study according to sex.

Table 1. Concentrations of L-lysine and L-threonine in HIV patients and control population according to gender.

Amino acids	Males			Females		
	HIV infected	Control	P-values*	HIV infected	Control	P-values*
Lysine (107-244 µmol/L)	97 ± 3.00	115 ± 4.27	0.0012	173 ± 19.61	83 ± 5.27	< 0.0001
Threonine (74-175 µmol/L)	329 ± 27.36	697 ± 23.31	< 0.0001	320 ± 49.05	243 ± 36.32	0.2101

*The difference is significance at P < 0.05.

Table 2. Mean concentrations of lysine and threonine in HIV infected patients and controls.

Amino acids	HIV infected patients		Control		P value
Reference values (µmol/L)	Mean concentrations (µmol/L)	Population (%)	Mean concentrations (µmol/L)	Population (%)	
Lysine					
< 107	82 ± 4.92	64 (50.4%)	71 ± 10.34	69 (54.3%)	0.3301
107 - 244	172 ± 16.76	54 (42.5%)	124 ± 8.13	58 (45.7%)	0.0522
> 244	427 ± 3.08	9 (7.1%)		0 (0%)	
Threonine					
< 74	61 ± 0.74	12 (9.5%)	27 ± 0.58	12 (9.5%)	< 0.0001
74 -175	124 ± 8.13	37 (29.1%)	75 ± 0.26	23 (18.1%)	< 0.0001
> 175	447 ± 80.51	78 (61.4%)	518 ± 75.23	92 (72.4%)	0.5369

Table 3a. Average concentrations of lysine and threonine in HIV-infected women according to $CD4^+$ count.

$CD4^+$ Range	HIV infected female (n = 70)	Lysine		Threonine	
		Mean concentration (µmol/L)	Chi^2 P*	Mean concentration (µmol/L)	Chi^2 P*
> 500	35	243 ± 27.86	0.00	296 ± 27.86	0.87
499 – 350	17	143 ± 8.09	0.03	443 ± 67.76	0.70
349 – 200	07	104 ± 1.09	0.03	350 ± 3.57	0. 03
< 200	11	87 ± 0.49	0.64	107 ± 0.81	0.18

*Difference is significance at P < 0.05.

Table 3b. Average concentrations of lysine and threonine in HIV-infected men according to $CD4^+$ count.

$CD4^+$ range	HIV infected male (n = 57)	Lysine		Threonine	
		Mean concentration (µmol/L)	Chi^2 P*	Mean concentration (µmol/L)	Chi^2 P*
> 500	20	126 ± 0.83	0.29	473 ± 18.84	0.05
499 – 350	11	96 ± 0.17	0.46	273 ± 6.69	0.38
349 – 200	13	92 ± 0.74	0.85	249 ± 20.42	0.72
< 200	13	83 ± 0.18	0.84	322 ± 1.13	0.47

*Difference is significance at P < 0.05.

lymphocytes >500 and between 350 and 499 cells/mm^3, the amino acid concentrations were normal for lysine (243 and 143 µmol/L, respectively) with a significant difference (P < 0.05) and higher for threonine (296 and 443 µmol/L) with no significant difference (P > 0.05) as compared to the normal reference values (lysine: 107 to 244 µmol/L; threonine: 74 to 175 µmol/L). However, when CD4 lymphocytes count was <200 cells/mm^3 and between 200 and 349 cells/mm^3, these values were lower for lysine (87 and 104 µmol/L, respectively). In the case of threonine, these values were higher (350 µmol/L) with a CD4 range of 200 to 349 cells/mm^3 (P < 0.05) and lower (107 µmol/L) with a CD4 range < 200 cells/mm^3 (P > 0.05) (Table 3a).

In HIV-infected male, mean concentrations of lysine were normal (126 µmol/L) with CD4 range > 500 cell/mm^3 and reduced with CD4 < 500 cells/mm^3 (P > 0.05). The mean concentrations of threonine was high in any CD4 range with no significant difference in all cases (P > or = 0.05) (Table 3b).

Finally, according to CD4 lymphocytes count, the correlation is significant for lysine (P = 0.0006) and not significant for threonine (P = 0.8640) (Table 4).

DISCUSSION

Lysine deficiency was observed in 66.7% male and 37.2% female HIV patients which showed the significant use of lysine by the body in the fight against HIV

Table 4. Correlation between $CD4^+$T lymphocytes cells and plasma amino acids in HIV infected patients.

Amino acids	$CD4^+$ T lymphocytes count	
	Correlation	P value
Lysine	r = 0.840	0.0006*
Threonine	r = 0.056	0.8640

r Value denotes degree of positive or negative correlation; *P denotes statistically significant value; the difference is significant at $P < 0.05$.

infection. This amino acid, like other essential amino acids, cannot be synthesized by the body itself and therefore must rely on adequate dietary intake to function properly. During viral infection (herpes virus, shingles, HIV, etc.), the virus uses the amino acid, arginine in its viral replication process. However, lysine competes with arginine in this process. This competition is expected to slow down viral replication (Walsh et al., 1983) and therefore reduce the synthesis of nitric oxide (NO) which contributes to the establishment of cardiovascular disease (Liaudet et al., 1997). The higher lysine deficiency observed in men may be due to increased uses of this amino acid in the production of various enzymes, hormones and anti-infectious antibodies (Weinert et al., 2013). In general, the deficiencies observed in people living with HIV taking ARV may be therefore due to viral infection and insufficient amount of lysine intake in their diet. Lysine deficiency varies depending on the CD4 count (Butorov, 2013).

In the control population, the opposite was observed: lysine deficiency was more common in women (71%) than in men (33%). Lysine deficiency may occur in situations of intense stress or malnutrition (Thorne-Lyman et al., 2010) which can lead to a decrease in the immune system and disorders such as stunted growth, slow healing of wounds, anemia, reproductive problems, osteoporosis, lipid disorders, diarrhea, anxiety and stress (Smriga et al., 2002; Thorne-Lyman et al., 2010). Generally, deficiency in lysine may be due to several phenomena. It could be either an insufficient intake of lysine-rich diet, which is mostly the case in many developing countries, poor absorption, liver disease, and/or increased lysine utilization or loss in urine during acute and chronic infection (Flodin, 1997), or a lack of signal transduction in vision color. This defect is related to the level of vitamin A (Bhagavan and Ha, 2015). Unfortunately, in Côte d'Ivoire, Boyvin et al. (2013) showed dyslipidemia, phosphocalcic disruption, a link between very high reduction in vitamin A and HIV infection, which is so disastrous for HIV patient.

Concerning excess in lysine level, the absence of excess lysine observed in male PLVIH and the controls population, implied a normal catabolism of lysine by its two main pathways which are: through saccharopine (mainly mitochondrial) and pipecolate (essentially cytosolic and peroxisomal) (Bender, 2012; Hallen et al., 2013). In contrast, the excess lysine found in 13% of female HIV individuals could be due either to hyperlysinaemia, a rare hereditary genetic disease caused by an enzyme deficiency that prevents breaking of lysine (Zhu et al., 2002), and associated with liver and kidney metabolic disorder which is associated with lack of signaling on both catabolism pathways of lysine (saccharopine and pipecolate). With regards to the metabolic disorder, no biochemical disruption of blood glucose, creatinine, urea and transaminases were observed in this study. In the study of Galindo et al. (2016), this same observation was reported.

Concerning threonine, both study populations (controls and HIV infected patients) generally had higher mean concentrations of threonine. Indeed, threonine is a key nutrient to the intestine. An important part of the ingested threonine is absorbed in the distal part of the intestine-the ileum. The remaining part (indigestible threonine) is found at the end of the ileum. Only 40% of the threonine intestinal light reaches the portal vein that collects nutrients from the digestion process. Enterocytes (cells in the wall of digestive tract) use 60% of the ingested threonine, which is two times more than that of lysine (Mao et al., 2011) for the synthesis of endogenous secretions, particularly mucus.

The plasma threonine deficiency observed in 17% of HIV positive patients and the female control population could be due to activation of threonine catabolism and/or synthesis of threonine-rich proteins (Laurichesse et al., 1998). Due to the high threonine concentration in immunoglobulins, threonine deficiency may affect the production of immunoglobulins (Richard and Galanaud, 1995). In actual fact, an infection or inflammation of the small intestine increases the synthesis of intestinal mucin and the use of threonine from arterial but non-luminous supply. This leads to the mobilization of endogenous proteins to meet the increased threonine demand associated with acute intestinal inflammation (Remond et al., 2009).

The absence of threonine deficiency observed in male in both groups (controls and PLHIV) showed the integrity of the intestinal barrier because mucus is an important component of the intestinal barrier that protects the intestine against digestive enzymes, physical damage and infections (Ruth and Field, 2013).

The excess threonine observed in HIV positive patients and the control population was not as a result of the high amount of threonine ingested which could disrupt liver function, causing the formation of excess urea, and consequently the toxicity of ammonia, in actual fact, the biochemical assessment of urea, creatinine and transaminases in this study revealed normal level which is similar to the study of Galindo et al. (2016) on the treatment of naive HIV infected patients.

This excess in threonine reflects the increased and maintained daily use of threonine for the synthesis of proteins in the intestinal wall and plasma proteins in

fighting against infections in HIV and against situations of intense stress and infections in the environment where malnutrition is often encountered, especially in developing countries. Threonine-rich diet intake in these two population groups and particularly in controls population is therefore essential for effective early nutritional management (Faure et al., 2007). Apart from its role as protein depositor, threonine is involved in maintenance processes, such as intestinal mucus renewal and immune protein synthesis (Bishop et al., 2013; Ruth and Field, 2013). In view of the importance of these digestive secretions to the intestines and to the digestive processes, an adequate amount of threonine must be provided by food to allow proper functioning of the digestive tract (Mao et al., 2011). Like mucins, immuno-globulins are threonine-rich globular glycoproteins. A poor and degraded health condition leads to threonine deficiency and must be filled (Nichols et al., 2008). Based on the degree of immunosuppression, no relationship was found between threonine deficiency and lower CD4 count. This confirms that the threonine level depends on the degradation of the health condition of the subject (Faure et al., 2007).

Conclusion

The deficiencies observed in HIV positive patients on antiretroviral therapy are therefore due to viral infection and insufficient nutritional intake of lysine. The threonine level depends on the degradation of the health condition of the subject. Therefore, effective early nutritional management of lysine and threonine is very essential to slow down viral replication in order to achieve a better quality of life for patients living with HIV.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

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