Common HIV/AIDS Clinical Symptoms among HIV-Positive Pregnant Women under ARV Therapy: Clinical Indicators for Non- Adherence to Treatment

Article by Admirabilis Kalolella
Ifakara health institute, Dar es salaam, Tanzania
E-mail: kalolella@hotmail.com

Abstract

The objective of this study was to assess adherence to option B+ ARV triple therapy and describe common HIV/AIDS clinical symptoms as indicators of non-adherence among women giving birth in Dar es Salaam Tanzania. We analyzed the prevalence of non- adherence through clinical assessment of common HIV/AIDS symptoms, indicators of non-adherence to treatment.

The cross section method, clinical assessment and self-report interview was used to identify clinical symptoms related to HIV/AIDS. The study analyzed symptoms with higher frequency of occurrence and were termed as common HIV/AIDS clinical symptoms, and were established as indicators of non-adherence. Women with three or more of these symptoms were identified as non- adherents to ART. The study also analyzed the relationship of demographic variables and adherence.

Result. Among the 105 HIV infected women under triple therapy, 63(60%) of them developed at least three HIV/AIDS related symptoms indicating that they were not adhering to the treatment, while 42(40%) adhered to the ARV therapy prescribed. The Adherence to ART Indicators tool was established presence or absence of persistent clinical symptoms of; fatigue, night sweat, muscle ache and frequently fever, extreme and unexplained tiredness, pneumonia, recurring fever, profuse night sweats, and rapid weight loss. Demographic variables were not significant related to adherence.

In conclusion, the majority of HIV infected pregnant women receiving B+ ARV triple therapy developed common HIV/AIDS clinical symptoms, indicating they were not adhering to treatment.

Keywords: *Clinical assessment, non-adherence to ART, HIV infected pregnant women, HIV/AIDS symptoms, B+ ARV triple therapy, PMTCT.*

Background

Following new recommendation of preventing mother to child transmission of HIV (PMTCT) by WHO, Tanzania started implementing new B+ ARV triple therapy for HIV infected pregnant women as part of antenatal services (Ngarina et al., 2014). Nearly 86% of HIV-positive pregnant women in Tanzania receive ARV triple therapy (Ngarina et al., 2014; Avert, 2016). For the past few years Tanzania has been implementing this new option with all PMTCT centers practicing the option B+, whereby pregnant women of gestation age of 34 weeks and above are being treated with Zidovudine + Lamivudine + Nevirapine /Nelfinavir (Tanzania PMTCT, 2016; Ngarina et al., 2014). The new regime is faced with the challenges of non- adherence (Ngarina et al., 2014; Tanzania PMTCT, 2016). The current methods to detect non-adherence, the laboratory detection of viral load and CD4 count are expensive, unaffordable, and invisible to our clinics, particularly the rural antenatal clinics with inadequate resources and unequipped laboratory facilities. Detecting non adherence using visible and affordable method of assessing HIV/AIDS clinical indicators is critical in order to fight mother to child transmission of HIV.

The maternal treatment using Antiretroviral therapy (ART) has been associated with significant increase of CD4 counts and reduction of viral load, resulting into improvement of maternal health and suppression of maternal HIV/AIDS related symptoms (Kilewo et al., 2009; WHO, 2015; Suksomboon et al., 2007). The ART reduce viral load through suppression of viral replication, which reduces number of

virus in the blood plasma and improve health status of pregnant mother (Siegfried et al., 2011; WHO, 2015; Suksomboon et al., 2007). Reduced virus in blood offer protection of transmission of HIV infection from a mother to a new born (Siegfried et al., 2011; Moodley & Wennberg, 2005; Tanzania PMTCT, 2016).Women that adhere to ART do not develop opportunistic infections clinical symptoms, while the absence of clinical symptoms is the indicator of adherence to treatment (WHO, 2015; Tanzania PMTCT, 2016; Hill et al., 2013). The non-adherence to ARV among pregnant women increases chances of HIV transmission to unborn babies, while improved maternal health offers fetus protection from being infected with HIV during pregnancy and delivery (Hill et al., 2013; Kilewo et al., 2009; Kowalska et al., 2003; Suksomboon et al., 2007).

The economic hardship, hopelessness, poverty and lack of motivation discouraged women to continue taking ARV therapy (Ngarina et al., 2013; Ngarina et al., 2014). Weaning of the child for some, and stigma for others intimidated to continue with recommended regime of B+ triple therapy, while fear to disclose HIV status when taking drugs increased barriers to ART adherence (Ngarina et al., 2013; Ngarina et al., 2014; Tanzania PMTCT, 2016).

Describing and establishing common HIV clinical symptoms, indicators tool of non-adherence of ARV therapy among pregnant women will empower health care workers (HCW) to increase identification of non- adherence for immediate attention. These clinical symptoms will form a non- adherence clinical indicators tool that can easily be used by any trained health care staffs in replacement of the current expensive laboratory method. Any trained health care staffs, even these with the lowest education, which are common staffs available in antenatal clinic in resource poor countries, can use the tool. With this tool, the identification of non-adherence will be affordable and visible method to be practiced by any HCW at any level, even these with the lowest health care educations, which are common HCW placed in antenatal clinics in resource poor countries. The HCW can clinically diagnose non- adherence and provide appropriate care before the HIV is advanced to AIDS stage, risk factor for HIV transmission (WHO, 2015; Ngarina et al., 2014; Tanzania PMTCT, 2016). The Adherence to ART Indicators tool to detect non- adherence among pregnant women is crucial to prevent transmission of HIV from mother to child.

The objective of this study was to assess the adherence to B+ ARV triple therapy and describe common HIV/ AIDS opportunistic infection clinical symptoms as indicators of ART adherence among HIV infected women giving birth in Dar es salaam, Tanzania.

Procedures and method

The cross sectional descriptive study design was used to collect data from HIV infected women immediately or few hours after giving birth in Dar es Salaam municipal hospitals providing obstetric services. Municipal hospitals were selected based on attendance of pregnant women in these facilities for delivery services. The selected area and facilities have higher numbers of pregnant women infected with HIV giving births. This study was part of an assessment of prevalence of HIV infection.

Participants were obtained from labor/maternity wards among women who just completed giving birth. The antenatal card of all women delivered was scrutinized for HIV test results. Women who tested HIV positive based on information on antenatal card were eligible for this study. The HIV infected woman was approached by a study staff to determine her eligibility and recruited into the study if she was eligible. All participants with medical conditions that needed emergency medical care and those vomiting, unable to speak and in severe illness were excluded from the study. All interested patients were directed to interviewers for the consent process. Informed consent was administered in local language and these consented were asked to undergo clinical assessment and self-report interviews. The clinical assessment and self-report interview were used to identify and disclosure of opportunistic infections symptoms indicators of non- adherence and determine HIV/AIDS progress and severity (HIV stages).

The checklist for clinical symptoms of opportunistic infections and HIV/AIDS stages was prepared based on WHO guideline (WHO 2015; WHO, 2007). With regard to this study, the study staff filled a checklist of HIV/AIDS related opportunistic infection symptoms that were persistent during pregnancy

period till delivery. Study staffs grouped these clinical symptoms in to their respective stages. The information on demographic variables was also collected. The first part of the checklist collected information on the demographic characteristic; age, marital status, education level, and maternal characteristic of number of births. The second and third part was checklist for symptoms of opportunistic infections of early and late stage of HIV/AIDS respectively. Each question of the second and third part of the checklist form was marked as "Yes" if HIV/AIDS related opportunistic infection symptom was present or "No" if there was none.

Ethical consideration

The approval to conduct this research was obtained from the Medical Research Coordinating Committee of National Institute for Medical Research (NIMR Tanzania), while informed consent was sought from women to participate in the study.

Data analysis

The data analysis was conducted using SAS software version 9.4. The study assessed the prevalence of opportunistic infection clinical symptoms as indicators of non-adherence to B+ ARV triple therapy in HIV positive women. The woman was considered as not adhered to ARV therapy during antenatal period if she presented or reported at least three persistent opportunistic infection clinical symptoms (from any HIV stage) at delivery (WHO, 2015; WHO, 2007, UNAIDS 2012; Tanzania PMTCT, 2016).

The following opportunistic infection clinical symptoms and their respective stages were analyzed; Clinical symptoms in early HIV stage (WHO clinical stages 1 and 2) were; fever, chill, night sweats, rashes, productive cough, muscle aches, sore throat, fatigue, swollen lymph nodes, mouth ulcers (WHO, 2015; WHO, 2007, UNAIDS, 2012). Clinical symptoms in late HIV stage (WHO clinical stages 3 and 4) assessed were; rapid weight loss, recurring fever and profuse night sweats, extreme and unexplained tiredness, prolonged swollen lymph glands in the armpits, groin or neck (lymphadenopathy), diarrhea that lasts for more than a week, sores of the mouth, anus, or genitals, pneumonia, red, brown, pink or purple blotches on or under the skin or inside the mouth, nose or eyelids, depression, memory loss, and other neurological disorders, Kaposi's sarcoma or lymphoma (WHO, 2015; WHO, 2007, UNAIDS, 2012).

Frequency table was used to describe prevalence and percentage of women with at least three clinical symptoms and adherence, while cross tabulations were used to analyze if opportunistic infection clinical symptoms were associated with demographic variables; age, marital status, education status and number of births. The Chi- squire was used to test the significance of association and differences of categorical data. The differences or association of HIV/AIDS symptoms and demographic variables were considered significant if the P- values <0.05.

Results

The HIV positive women under ART triple therapy were screened for presence or absence of opportunistic infection clinical symptoms that defined adherence status. The information on the demographic backgrounds and maternal characteristics was also collected and included for data analysis.

Among 105 HIV positive women that were receiving triple therapy at antenatal clinics, 63(60%) develop at least three or more symptoms of HIV, and thus did not adhere to the ART, while only, 42(40%) adhered to the ARV therapy prescribed (Table 1). The study indicates the common symptoms among women who did not adhere to the ART were; fatigue 46(43.8%), night sweat 43(40.9%), muscle ache 41(39%), and frequently fever 39(37.1%) (Table1). These symptoms were grouped as early HIV clinical conditions. The late HIV stage symptoms that were common among them; Extreme and unexplained tiredness 43(40.9%), pneumonia 37(35.2%), recurring fever and profuse night sweats 33(31.4%), rapid weight loss 27(25.7%) (Table1).

Based on HIV stages, among 63 women that did not adhered to ART 27 (42.8%) had presented with only early HIV stage symptoms, and 4 (6.3%) showed late HIV stage symptoms only, while 32 (50.7%) developed symptoms of both HIV stages (Table 1).

Among women enrolled, 22 (20.9%) were aged between 18-25 years, 79 (75. 2%) aged between 26-40, and 4 (3.8%) were women between the age of 41-44, while 18 (17.10%) stayed without a partner, and 87(82.8%) were living with their partners (Table 2). The data indicates that 19(18.1%) had delivered once, 76(72.3%) delivered between 2-4 times and 10(9.5%) of them had 5-9 births. More than half 62(59%) of them achieved primary level education, while 28(26.6%) completed secondary level education, 13 (12.3%) had not attended any formal education or school, and only 2(1.9%) are college graduate (Table 2). The non-adherence was more observed in women age 26-40 (44.7%), compared to other age groups of; 18-25 (14.2%) and 41-44 (0.95%), although the difference is not significant (Table 2). Women with primary level education were more found with non-adherence symptoms (35.2%) than groups of women from other education levels of; college (1.9%), secondary education (15.2%) and these with no formal education (7.6%) (Table 2), the difference was not significant. The participants that were living with their partners were observed with more none- adherent symptoms (49.5%) compared to women who were living without their partners (10.4%), the difference was not significant (Table 2). The none- adherence to ART was more in women with 2-4 birth (44.7), while other groups of single birth, none –adherence was 10.4% and women with 5-9 births was 4.7%. The observed differences were not significant (Table 2).

Women age 26-40 reported more symptoms of both HIV stages (23.8%) than other age groups of; 18-25 (18.1%) and 41-44 (3.86%), although the difference is not significant (Table 2). Women with primary level education were more found with symptoms of both stages (17.1%) than women from other education levels of; college education 0.95%, secondary level 7.6%, and these with no formal education (4.7%) (Table 2), the difference was not significant. The participants that were living with their partners had more symptoms under both HIV stages (25.7%) compared to women who were living without their partners (4.7%), the difference was not significant (Table 2). The HIV positive women with 2-4 birth developed more symptoms of both HIV stages (24.7) than groups of single birth and women with 5-9 births (2.8%) (Table 2). The observed differences were not significant.

Discussion

This study was conducted in high HIV transmission area where almost 7% of pregnant women are infected with HIV (PMTCT Tanzania, 2016). In the study areas all pregnant women were initiated with ARV (B+) Triple therapy from antenatal clinics at 34 weeks of gestation period (PMTCT Tanzania, 2016).

Among 105 HIV positive women that were screened for adherence, more than half (60%) of them did not adhere to B+ARV triple therapy based on opportunistic infection clinical symptoms. This indicates that the non- adherence to ART is overwhelming as barrier to continue with ARV increases and motivations to use the ART decreases (Ngarina et al., 2013; Ngarina et al., 2014). These women who did not adhere to ART presented with either early, late or both HIV stage symptoms. The most common HIV symptoms that were found among women that did not adhere to ART were; fatigue, night sweat, muscle ache and frequently fever. These symptoms are early HIV opportunistic infection indicators of non-adherence. Other common symptoms developed by these women were; extreme and unexplained tiredness, pneumonia, recurring fever, profuse night sweats, and rapid weight loss, which are late HIV opportunistic infection indicators of non- adherence. These collections of common HIV symptoms can be used as Adherence to ART Indicators tool for identification of pregnant women non adherents to ART at antenatal clinics

More than half of women with non-adherence (50.7%) showed opportunistic clinical signs of both early and late HIV stages. This show that more women are developing AIDS symptoms, which may increase transmission rate in the country (WHO, 2015; WHO, 2007, UNAIDS 2012). The presence of late HIV stage symptoms is a red flag indicating escalating advancement of HIV infection among pregnant women that pose threat in fight against AIDS.

The non-adherence was more observed in women with primary level education, the lowest education available in the country. The low level education may probably have affected the ability to understand the importance of ART. The low education level may have coupled with fear to disclose HIV status, poverty and economic hardship that discouraged long-term adherence (Ngarina et al., 2014; Ngarina et al., 2013; Tanzania PMTCT, 2016).

The participants that were living with their partners had more non- adherent symptoms compared to women who were living without their partners. This phenomenon may have been contributed by women living with partners not able to take drug to prevent their HIV status to be known to family members including their partners (Ngarina et al., 2014; Ngarina et al., 2013).

Currently antenatal clinic lacks a thoroughly clinical assessment that is important to identify non-adherence symptoms to strengthen PMTCT services in Tanzania. This study will inform the government on the importance of policy change with respect to antenatal clinics to replace expensive laboratory methods of detecting non- adherence to ART with Adherence to ART Indicators tool. This study will inform HCW to apply Adherence to ART Indicators tool for HIV infected women when providing antenatal services.

Conclusion

The HIV infected pregnant women under B+ triple therapy are not adhering to their ARV therapy during antenatal period because substantial number were found with indicators of non-adherence to treatment. The indicators of non- adherence during pregnancy were; fatigue, night sweat, muscle ache and frequently fever, extreme, unexplained tiredness, pneumonia, recurring fever, profuse night sweats, and rapid weight loss. These symptoms formed Adherence to ART Indicators tool. Demographic variables were not significant related to adherence. This result will inform clinicians on Adherence to ART Indicators tool that will help to quickly identify defaulters of ARV therapy at antenatal clinics and take appropriate health care measure. The study result should be used to address issues and challenges related to non-adherence.

Table 1. The adherence to art and common HIV infections symptoms at delivery

Variable category	Description of variable	Number (n)	Percentage (%)
Adherence status (N=105)	Non- adherence	63	60
	Adherence	42	40
* Common Early HIV stage symptoms (WHO clinical stage 1&2) (n=105)	Fatigue	46	43.81
	Night sweats	43	40.95
	Muscle ache	41	39.05
	Fever	39	37.14
*Common Late HIV stage symptoms (WHO clinical stage 3&4)(N=105)	Extreme and unexplained tiredness	43	40.95
	Pneumonia	37	35.24
	Recurring fever or profuse night sweats	33	31.43
	Rapid weight loss	27	25.71
Women HIV stages (n=63)	Early HIV Stage only	27	42.8
	Late HIV (Advanced AIDS) stage only	4	6.34
	Both stage	32	50.79

 *Please note that women may present with more than three HIV symptoms

Table 2. The ART adherence status and HIV stages based on demographic background and maternal characteristics (n=105)

Variable	Women adherence to ART based on demographic variables.					P values	HIV stages among women with none – adherence.			
	Demographic variables			Women adhered to ART n (%).	Women not adhered to ART n (%)		1st stage symptoms only. n (%)	2nd stage symptoms only. n (%)	Both stages. n (%)	P Value
	Response	n	%							
Age group	18- 25	22	20.95	7(6.67)	15(14.29)	NS	7(6.67)	1(0.95)	7(6.67)	NS
	26-40	79	75.24	32(30.48)	47(44.77)		19(18.1)	3(2.86)	25(23.81)	
	41-44	4	3.81	3(2.86)	1(0.95)		1(0.95)	0(0)	0(0)	
Education level	College	2	1.9	0(0)	2(1.9)	NS	1(0.95)	0(0)	1(0.95)	NS
	secondary	28	26.67	12(11.43)	16(15.24)		7(6.67)	1(0.95)	8(7.62)	
	Primary	62	59.05	25(23.81)	37(35.24)		16(15.24)	3(2.86)	18(17.14)	
	None	13	12.38	5(4.76)	8(7.62)		3(2.86)	0(0)	5(4.76)	
Marriage status	No Partner	18	17.14	7(6.67)	11(10.47)	NS	5(4.76)	1(0.95)	5(4.76)	NS
	With partner	87	82.86	35(33.33)	52(49.52)		22(20.95)	3(2.86)	27(25.71)	
Maternal characteristics (Number of Births)	1	19	18.1	8(7.62)	11(10.48)	NS	7(6.67)	1(0.95)	3(2.86)	NS
	2-4	76	72.38	29(27.62)	47(44.76)		18(17.14)	3(2.86)	26(24.76)	
	5-9	10	9.52	5(4.76)	5(4.76)		2(1.9)	0(0)	3(2.86)	

References

[1].Avert (2016). HIV and AIDS in Tanzania; UNAID gap report; Global information and education on HIV and AIDS Retrieved on 15february, 2016 from. http://www.avert.org/professionals/hiv-around-world/sub-saharan-africa/tanzania).

[2].Calvert C, Ronsmans C. (2015). Pregnancy and HIV disease progression: a systematic review and meta-analysis. Journal of Tropical Medicine and International Health, 20(2):122-45. Retrieved June 5, 2016, from PubMed.

[3].Kilewo Charles, Katarina Karlsson, Matilda Ngarina, Augustine Massawe, Eligius Lyamuya, Andrew Swai, Rosina Lipyoga, Fred Mhalu, Gunnel Biberfeld. Prevention of Mother to Child Transmission of HIV-1 through Breastfeeding by Treating Mothers with triple Antiretroviral Therapy in Dar es Salaam, Tanzania: The Mitra Plus study. Journal of Acquired Immune Deficiency Syndromes. 2009, 53: 406-41.

[4].Kowalska A, Niemiec T, El Midaoui A, Burkacka E. Effect of antiretroviral therapy on pregnancy outcome in HIV-1 positive women. Med Wieku Rozwoj. 2003 Oct-Dec; 7 (4 Pt 1):459-68.

[5].Kupka, R., Kassaye, T., Saathoff, E., Hertzmark, E., Msamanga, G. I. And Fawzi, W. W. (2009). Predictors of stillbirth among HIV-infected Tanzanian women. Journal of Acta Obstetricia et Gynecologica Scandinavica, 88: 584–592. Retrieved June 5, 2016, from PubMed.

[6].Moodley J, Wennberg JL. HIV in pregnancy. Curr Opin Obstet Gynecol. 2005 Apr; 17(2):117-21.

[7].Ngarina Matilda, Rebecca Popenoe, Charles Kilewo, Gunnel Biberfeld, Anna Mia Ekström. Reasons for poor adherence to antiretroviral therapy postnatally in HIV-1 infected women treated for their own health: experiences from the Mitra Plus study in Tanzania. BMC Public Health. 2013, 13:450.

[8].Ngarina M, Tarimo EAM, Naburi H, Kilewo C, Mwanyika-Sando M, Chalamilla G, et al. (2014) Women's Preferences Regarding Infant or Maternal Antiretroviral Prophylaxis for Prevention of Mother-To-Child Transmission of HIV during Breastfeeding and Their Views on Option B+ in Dar es Salaam, Tanzania. PLoS ONE 9(1): e85310. doi:10.1371/journal.pone.0085310.

[9].Reitter A[1], Stücker AU, Linde R, Königs C, Knecht G, Herrmann E, Schlößer R, Louwen F, Haberl A. Pregnancy complications in HIV-positive women: 11-year data from the Frankfurt HIV Cohort. HIV Med. 2014 Oct; 15 (9):525-36. doi: 10.1111/hiv.12142. Epub 2014 Mar 6.

[10]. Siegfried N[1], van der Merwe L, Brocklehurst P, Sint TT. Antiretrovirals for reducing the risk of mother-to-child transmission of HIV infection. Cochrane Database Syst Rev. 2011 Jul 6; (7):CD003510. doi: 10.1002/14651858.CD003510.pub3.

[11]. Suksomboon N, Poolsup N, Ket-Aim S. Systematic review of the efficacy of antiretroviral therapies for reducing the risk of mother-to-child transmission of HIV infection. J Clin Pharm Ther. 2007 Jun; 32(3): 293-311.

[12]. Tanzania PMTCT. National resource centre for prevention of mother to child HIV transmission (2016). Retrieved June 15 2016 from http://pmtct.or.tz/pmtct-tanzania/pmtct-in-tanzania/.

[13]. UNAIDS .2012. Joint United Nations Programme on HIV/AIDS (*Global report: UNAIDS report on the global AIDS epidemic 2012.* Retrieved May 17, 2016, from

[14]. http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2012/gr2012/20121120_UNAIDS_Global_Report_2012_with_annexes_en.pdf.

[15]. WHO (2007). Who case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children. Retrieved June 15 2016 from http://www.who.int/hiv/pub/guidelines/HIVstaging150307.pdf.

[16]. WHO (2015) Guideline on when to start antiretroviral therapy and on pre Exposure prophylaxis for HIV (pdf). Retrieved June 15 2016 from http://www.who.int/hiv/pub/guidelines/clinicalstaging.pdf).