Original Article

Determinants of Optimal Adherence to Antiretroviral Therapy among People Living With HIV/AIDS Registered for Antiretroviral Therapy in Zimbabwe

L Gonah[1], A Mukwirimba[2]

[1]*Midlands State University, Faculty of Medicine, Gweru, Zimbabwe*

[2]*University of Zimbabwe College of Health Sciences, Department of Community Medicine, Harare, Zimbabwe*

ABSTRACT

Background: Successful Antiretroviral therapy (ART) was shown to rely on high levels of medication adherence to enable maximum and durable viral suppression for the prolongation of life among people living with HIV/AIDS.

Objective: The study sought to determine individual and environmental factors that influence optimal adherence to antiretroviral therapy among HIV/AIDS patients registered at Morgester hospital.

Materials and methods: The study was a cross sectional study. Out of 515 registered patients, a sample of 330 HIV/AIDS patients on ART meeting the eligibility criteria was obtained from people seeking services from the Opportunistic Infection (OI) clinic at Morgenster hospital. Adherence was determined using the self-report 9 Item Morisky Medication Adherence Scale (MMAS) with scores ranging from 0 to 13 where a score of 11 corresponds to 95% level dose adherence.

Results: The level of drug adherence (corresponding to 95% dose adherence) was 65% (n=215) among the study participants. Distance from the health institution, medication side effects and adolescence were associated with non-adherence ($p = 0.029$, $p= 0.019$ and $p= 0.001$ respectively). Demographic variables including sex, marital status, employment status and level of education had no association with non-adherence. Access to health education on the benefits and risks of non-adherence, and participation in ART support groups were seen to promote ART adherence among the study participants.

Conclusions: More research and interventions are required focusing on reasons and challenges of non-adherence to ART among adolescent HIV/AIDS patients, especially the social determinants of health surrounding ART adherence.

INTRODUCTION

Zimbabwe, among many other Sub-Saharan countries, has been highly affected by a huge HIV/AIDS burden. It was estimated that 1 242 768 people were HIV positive by the end of 2012.[1] The most affected group of people were those within the age range 15 to 49 years with an HIV prevalence of 14.9%. In 2012 the number of people estimated to have died due to HIV/AIDS in Zimbabwe was 45 621, thus indicating the serious impact the condition still has.[1] The World Health Organization 2010 guidelines recommended antiretroviral therapy (ART) for people with CD4 cell count less than or equal to 350, and patients with comorbid Tuberculosis and HIV irrespective of their CD4 cell count.[2] Evidence shows ARV therapy being able to lower an individual's viral load and allowing the body to restore some of its immunity.[2]

ART coverage in Zimbabwe for eligible individuals was standing at 78% for adults and 42% for children at the end of 2011.[1] Advancement has been made in coverage, however high level adherence is necessary in maintaining viral suppression and therefore reducing mortality. A

Key words: *Optimal adherence; antiretroviral therapy (ART); HIV/AIDS*

study conducted by Attaron in 2007 showed that viral efficacy or effective suppression is better achieved when people on ART adhere to their doses at least 95% of the time.[3]

Morgenster hospital is a mission hospital situated in Masvingo rural district, to the south of Masvingo city in Zimbabwe. Through its Opportunistic Infection (OI) clinic, the hospital provided an average of 3689 people with anti-retroviral drugs per month in 2012.[4] However, an early warning indicator survey among 210 participants to assess patient factors associated with HIV Drug Resistance at the hospital, from the year 2011 to 2012, showed 'On time drug prescription' being below 46% against the recommended levels of 90% and above.[4] This could be an indication of patients going for some time without drugs or that they were not properly adhering hence having drugs even after the refill period. There are increased chances for viral failure, and attack from opportunistic infection increases when patients do not adhere properly to their medication.

This study sought to identify individual and environmental factors influencing adherence to ART to give an insight on ART adherence in the unique context of Zimbabwe.

METHODS

Research design

This was a descriptive cross-sectional study involving HIV positive patients attending for services at Morgenster Mission Hospital's OI clinic.

Participants and setting

A sample of 330 subjects participated in the study. Study participants consisted of HIV/AIDS male and female patients aged 18 years and above, and registered for ART services at Morgenster hospital's OI clinic, for six months or more, by the time of study. Sampling of study participants was done through the use of an existing HIV register for people living with HIV/AIDS. Out of 513 registered patients, 340 were eligible for, and willing to participate in, the study. Of these 340 eligible participants, 10 participated in the pretest survey, and were therefore excluded from the actual study, leaving the sample size at 330 participants. All the participants were met during their visit to the OI clinic for their ART-related needs/appointments.

Morgenster mission hospital is a Reformed Church of Zimbabwe institution situated some 27 kilometers in a rural setting, to the south-east of Masvingo city, in Masvingo province of Zimbabwe. The hospital represents a district hospital for Masvingo district. Among services offered by the hospital's OI clinic is ART initiation of HIV patients registered at the centre, as well as for those registered at 12 other surrounding rural health centers/clinics, through their outreach program. Through the Community Based HIV/AIDS Program the clinic also performs follow up visits to defaulting HIV/AIDS patients.

Data collection tools

Data was collected using the 9-item Morisky Medication Adherence Scale (MMAS), and a semi-structured interviewer-administered questionnaire. Fluent English and Shona (native language in Masvingo province) language speakers trained on quantitative research methodology participated in data collection.

Self-reported adherence for study participants was determined using the 9-item MMAS, which has scores ranging from 0 to 13 points.[5] The scale has 9-items, where responses to the first 8 items get a score of 1 point per item for an adherent behaviour. The 9th item is scored 1- 5 points, where 1indicates the least adherent behaviour and 5 the most adherent behaviour, thus giving a summary score range of 1 – 13 points. Participants obtaining a total score of 11 and above on the scale were classified as adherent, corresponding to 95% dose adherence, while those scoring less than 11 were classified as non-adherent.

MMAS adherence scoring

ITEM (Question number)		Yes	No
1. Have reminder systems for medicines		1	0
2. Have sometimes forgotten medications		0	1
3. Have forgotten medicines when traveling		0	1
4. Consider it a difficult treatment		0	1
5. Have reduced doses without the doctor's knowledge		0	1
6. Have forgotten medicines during the last 2 weeks		0	1
7. Took medicines yesterday		1	0
8. Have had treatment interruptions because he/she considers the infection under control		0	1
9. Difficulty in remembering treatment	Never	5	
	Occasionally	4	
	Sometimes	3	
	Usually	2	
	Always	1	

Additional data was collected through a semi-structured, interviewer-administered questionnaire consisting of both closed and open-ended questions, and designed to investigate the individual and environmental factors influencing optimal adherence to ART among the respondents. Before the actual data collection, the questionnaire intended for use was pretested and modified according to the pretest responses.

Procedure

Ethical approval for the study was obtained from the Joint Parirenyatwa Hospital and College of Health Sciences Research Ethics Committee (JREC), Reference number: 53/13. Clearance and permission to proceed with the study was sought and obtained from Masvingo Provincial Medical Director and from the Medical Superintendent for Morgenster hospital. Permission to use MMAS was obtained from Morisky. Written informed consent from participants was sought from every participant prior to each questionnaire survey session. Privacy and confidentiality of participants' information and responses were maintained by removal of personal identifiers on data collection and entry, and use of password protected storage of electronic data base.

Data analysis

Quantitative data was cleaned and entered into Epi-Info Statistical package software for data analysis. Univariate and multivariate logistic regression analyses were performed to compare the differences between patients in the adherent and non-adherent groups with respect to various independent variables measured in the study.

RESULTS

A total of 330 subjects participated in the study. The mean age of participants was 38.85 years (standard deviation 10.66). Most participants were in the age category of 20 - 29 years, and 30 – 39 years, each category constituting 35% of the sample size. The 40 years and above age category constituted 25% of the sample size, whilst adolescent participants (18 – 19 years) made up 5% of the sample size. The adolescent age category was considered separately since their characteristics are unique, and hence factors influencing their adherence to ART could also differ in some respect from those in other age categories. More women (60%) were part of the study compared to male participants (40%). Concerning marital status of the study participants, 55% were married with the rest (45%) being single, divorced, separated or widowed. The majority of participants were unemployed (64%), though most (75%) had attended school up-to secondary/high school/tertiary level. Christianity was the main religion followed by most study participants (88%).

Adherence for study participants determined by MMAS resulted in 65% (n=215) of participants being classified as adherent and 35% (n=115) as non-adherent.

Individual MMAS questions and summary score for study participants, n=330

MMAS ITEMS		No. OF PATIENTS	PERCENTAGE
1. Have reminder systems for medicines		257	77.88%
2. Have sometimes forgotten medications		82	24.85%
3. Have forgotten medicines when traveling		45	13.64%
4. Consider it a difficult treatment		32	9.70%
5. Have reduced doses without the doctor's knowledge		18	5.45%
6. Have forgotten medicines during the last 2 weeks		20	6.06%
7. Took medicines yesterday		325	98.48%
8. Have had treatment interruptions because he/she considers the infection under control		10	3.03%
9. Difficulty in remembering treatment	Never	215	65.76%
	Occasionally	79	23.94%
	Sometimes	33	10%
	Usually	3	0.91%
	Always	0	0
Summary score	5 - 8	24	Mean summary score is 11.67
	9 - 10	91	
	11 - 13	215	

Factors influencing ART adherence

We performed univariate analysis, using X^2 tests, and multivariate analysis, using the final binary logistic regression model, in analysing individual and environmental factors influencing optimal adherence to ART. The odds ratios from the final binary logistic regression model were adjusted for participants' age, sex, and marital status, level of education, occupation and religion.

Table 1: Participant characteristics in the adherent and non-adherent to Art groups, and the binary logistic regression analyses of factors influencing non-adherence to ART

	*ART adherence									
	Total (n=330)		Non-adherent		Adherent			Adjusted		
Participant characteristics	n	%	n	%	n	%	P	OR	95 CI	P
Age in years										
18 - 19	17	5.0	14	4.0	3	1.0	0.003	2.30	1.90, 5.43	0.001
20 - 29	115	35.0	43	13.0	72	22.0		1.0		
30 -39	115	35.0	38	12.0	77	23.0		1.0		
40 and above	83	25.0	20	6.0	63	19.0		1.0		
Total			115	35.0	215	65.0				
Sex										
Female	198	60.0	62	19.0	136	41.0	0.203	1.23	0.91, 3.20	0.100
Male	132	40.0	33	10.0	99	30.0	0.110	1.25	0.77, 4.13	0.150
Marital status										
Single/widowed/divorced/	149	45.0	43	13.0	106	32.0		1.0		
Married	181	55.0	44	13.0	137	42	0.230	2.31	0.93, 3.41	0.121
Occupation										
Unemployed	211	64.0	51	15.0	160	49.0	0.100	2.41	0.71, 2.91	0.311
Employed	119	36.0	35	11.0	84	25		1.0		
Level of education										
None/Primary	82	25.0	26	8.0	56	17.0	0.052	3.30	0.88, 4.12	0.221
Secondary/high/tertiary	248	75.0	60	18.0	188	57.0	0.070	1.80	0.83, 3.52	0.110
Religion										
African tradition	36	11.0	0	0.0	36	11.0		1.0		
Christian	291	88.0	84	25.0	207	63.0		1.0		
Muslim	3	1.0	1	0.3	2	0.7	0.001	1.02	0.91, 1.85	0.165

+Univariate analyses to compare the differences between patients in the non-adherent ans adherent group using cross tabulations and the X^2 Tests
Values for the Odds Ratio were obtained from the final binary logistic regression model, which was adjusted for participant's age, sex, marital status, occupation, level of education and religion.

Individual factors

Participants' demographic characteristics (age, sex, marital status, occupation, level of education and religion) were analysed to see if they had a significant relationship with non-adherence. Of all the demographic factors, there was a statistically significant association between adolescence and non-adherence (p=0.001). Five per cent (5%, n=17) of the 330 individuals who participated in the study were adolescents in the 18 – 19 years age group. The level of non-adherence among these adolescents was exceptionally higher (82%, n=14) compared to other age categories (OR 2.31, 95%CI 1.90-5.43). All other demographic characteristics measured under the study did not have a significant relationship with ART adherence.

ART is associated with various side effects. For assessment in this study, side effects were classified as non-serious/manageable (including nausea, diarrhoea, headaches, and occasional dizziness) or unbearable/serious (for example, swelling of the face, mouth, lips, tongue, and bleeding). The extent of side effects experienced by participants (manageable vs. serious) significantly influenced adherence to ART. The proportion of participants who reported to experience unbearable side effects from ART drugs was higher among the non-adherent group (62%) compared to the adherent group (38%). Participants who reported to experience serious side effects form ART were 2.8 times more likely to not adhere to their HIV treatment compared to those who reported to experience manageable side effects (OR 2.8 95%CL 1,52-3.20).

Cross tabulation of experiencing serious side effects and adherence n=330

Experience serious side effects	Adherence		p=0.019
	Non adherent	Adherent	
Yes	80	40	
No	35	175	

Concerning knowledge related to ART and HIV, nearly all the participants (99%) reportedly knew that treatment on antiretroviral therapy was lifelong with only a single individual unsure of the fact. Ninety-eight percent understood how their medication worked, that is in suppressing the virus and allowing the immune system to recover. A significant proportion (8%) thought they could discontinue their ART treatment when they felt well, most of which were those from the non-adherent group (5%) compared to the adherent group (3%).

In cases where they could miss the usual time to take their drugs, 78% (n=258) of the participants indicated that they could take their drugs within the recommended 4 hour period after the usual time, and 5% reported that they could not do so, whilst 17% were unsure of what to do once they had missed taking their drug on time. Again most of those who could not take their drug within 4 hours after the usual time or were unsure of what to do once they miss taking their drug on time, were from the non-adherent group (4% and 15% respectively).

The majority of participants (83%) knew that mothers could breastfeed their babies whilst on ART; most of the remaining 17% who did not share this knowledge were from the non-adherent group (11%).

Knowledge on the possibility of viral resistance to drugs if one did not adhere to his medication as prescribed stood at 97% (n=320) for the whole study sample. The distribution of the remaining proportion of those who did not know about drug resistance among the adherent and non-adherent groups was 1% and 2% respectively. There was no association between knowledge on non-adherence causing viral resistance and non-adherence (p=0.059)

Concerning alternative treatment, the majority (97%) reported to never have stopped taking their ART medication for alternatives such from faith or traditional healing. A slightly higher proportion of the adherent (97.3% of 215) compared to 96.2% (of 115) of the non-adherent reported that they had never stopped due to trial of these alternatives.

Individuals reporting alcohol consumption made up 15% of the study participants. There was no association between alcohol consumption and ART adherence (p=0.066).

Environmental factors

Distance from the hospital was assessed to see if it had a significant relationship with ART optimal adherence. Distance had a statistically significant relationship with adherence (p=0.001). The risk of non-adherence was 2.5 times higher among participants who lived beyond 10km radius from the hospital compared to those who lived within 10km radius.

Cross tabulation of distance to the hospital and adherence to ART medication, n= 330

DISTANCE FROM HOSPITAL	ADHERENCE		p= 0.001
	Non-adherent (n)	Adherent (n)	
Greater than 10km	60	40	
Less/equal to 10km	55	175	
Total	**115**	**215**	

Forty per cent (40%, n=132) of the participants expressed facing difficulties in travelling to the hospital for their ART appointments/needs. Of these, 30% (n=99) lived beyond the 10km radius from the hospital. A significant proportion of participants (67%) who lived beyond 10 km radius from the hospital fell in the non-adherent category.

Concerning the modes of transport to the hospital, there were only two options reported: via public transport or on foot. A smaller proportion of participants (43%, n=142) relied on public transport as their usual mode of transport to get to the hospital, compared to the remainder (57%,

n=188) who reportedly relied on foot. Mode of transport was not significantly associated with ART adherence (p=0.201).

A large proportion of the study participants (73%) reported to never have received at least one support visit from health workers within the last six months prior to the study. The proportion of participants who had not received a support visit from healthcare workers was higher among non-adherent group (80.8%, n=93) when compared to that among the adherents (70.3%, n=151).

Participants reported that privacy and confidentiality concerning their personal information and health statuses were well respected by healthcare workers during consultation at the OI clinic. Most participants (90%)indicated that they always had enough privacy and confidentiality accorded to them during consultation or counselling, while the remaining 10% reported that they did not always get that respect all the time.

Concerning support groups for HIV/AIDS treatment, only a smaller proportion (38%) belonged or was part of a support group by the time of the study. Of the 215 participants in the adherent group, 35% (n=75) belonged to a support group, whilst 46% of the 115 participants in the non-adherent group belonged to a support group for HIV/AIDS treatment. Participation in a support group for HIV was associated with adherence to ART (p=0.012).

Waiting time was assessed to see if it had a significant influence on adherence to medication among the study participants. The mean waiting time was 107.95 minutes (standard deviation 101.9162). There was no significance difference on waiting time between the adherent and non-adherent groups. Again, the association between waiting time and ART adherence was not statistically significant (p=0.201).

Participants who reported to have treatment partners made up a majority of the study sample (82%), while the remaining 18% reportedly had no treatment partners. Out the 215 participants in the adherent group, 83.8% (n=180) reported to have treatment partners, compared to 76.9% (n=88) of those in the non-adherent group which had treatment partners.

Higher proportions in both the non-adherent and the adherent group, 76.9% and79.7% respectively, had at least some form of a reminder to remind them when time for taking medication was due. Common reminders reported were cell phone alarm, radio news hour time, or a family member.

Disclosure of HIV status was predominant in the study population with the majority of the participants (95%, n=314) having disclosed their HIV statusesto someone that could be a family member, close relatives or the community. The proportional distribution ofthe 95% to the adherent and non-adherent groups was 72.6% and 27.4% respectively. The remaining 5% had not disclosed their status to anyone, 4% of which fell in the non-adherent group.

DISCUSSION

Based on the self-report 9-item MMAS, our study found an adherence level of 65% (n=215) among the study participants, which is lightlylower compared to a Swedish study on prevalence of adherence using the same instrument and obtained 68% adherence.[6]Successful ART relies on high levels of medication adherence to enable maximum and durable viral suppression for the prolongation of life among people living with HIV/AIDS. However, the level of adherence found among the study participants in our study is an indicationfor the existence of various individual and environmental factors that could possibly influence ART adherence.

Individual factors significantly influencing optimal ART adherence among study participants included adolescence, medication side effects and general knowledge surroundingHIV/AIDS and ART. Adolescent participants of ages 18 – 19 years were found to be 2.3 times more likely not to adhere to their medication compared to other age categories measured under the study. UNICEF found that the leading cause of death among adolescents in Africa is HIV/AIDS.[7, 8] In Zimbabwe, the HIV/AIDS mortality rate among adolescents has tripled over the last decade, and was found to be higher compared to other age categories.[1, 7, 9]This, together with the high default cases rate observed

among Zimbabwean HIV/AIDs infected adolescents, would justify the need for future research studies to focus on reasons for poor ART adherence among this population, including those aged from 10 to 19 years.[7] The observed high levels of non-adherence among adolescent participants in our study can be due to various possible reasons. The issue of disclosure of the child's status, by parents or guardians, to the child could be a contributing factor. As is the usual case in Zimbabwe,for those children who could have acquired the virus through mother-to-child transmission, most of them spent their early lives directed by their parents/guardians to take medication for a condition they do not even know.[9] In most instances, disclosure to the child about their status is usually done late and/or abrupt/accidental thus causing bitterness/panic/fear/emotional distress among these adolescents, possibly making them more rebellious to comply with medication. Further inquiry on adherence challenges among adolescentsliving with HIV/AIDS is required to inform strategies in addressing the problem.

Participants who reported to experience serious or unbearable side effects, including such as swelling of the face, mouth, lips, tongue, and bleeding, were found to be 2.8 times more at risk ofnon-adherence to ART compared to those who reported experiencing non-serious/manageable side-effects (nausea, diarrhoea, headaches, and occasional dizziness). Although the issue of serious medication side-effects contributing to poor adherence is real and irrefutable, successful HIV/AIDS control programmes have emphasised on the importance of patient education and positive healthcare worker-patient communication/relationships.[7,8,9,10] As found in the study, access to health education on HIV/AIDS and ART adherence among the participants was found to improve knowledge and correct myths and misconceptions, and subsequently improve adherence to ART. People living with HIV/AIDS need to be well informed about living with the virus and encouraged to report to the healthcare worker whenever they experience ART-related side-effects, during all appointments with the healthcare providers.Astudy on predictors of adherencefound a strong association for side effects as primarily influencing adherence(p=0.001), thus supporting our study finding that ART-related side-effects is one of the important factors contributing to non-adherence.[11]

Distance from the hospital was found to be a significant determinant of ART adherence in our study (p= 0.001). Lovett-Scott & Pratherdescribes access to healthcare as (i) "being able to get to and from services (ii) having the ability to pay for the services, and (iii) getting needs met once in the system".[12]According to the Alma Ata declaration on primary healthcare of 1978, [13] everyone must live within 10km radius from the healthcare centre to ensure easy access to healthcare services. In our study, a significant proportion of participants (30.3%) lived beyond the 10km radius from the hospital, and 40% reported facing difficulties in travelling to the hospital for their ART related appointments. Given that the study area is predominantly ruralwith less to no reliable transport system, the possibility of participants missing appointments or getting to the hospital on foot becomes very high. Even if there might be a reliable transport system, most may not even afford transport costs to and from the healthcare centre. The ART outreach program by Morgenster only covers rural health centres which again were less accessible by participants, in terms of distance, compared to Morgenster hospital. Various social determinants of health interconnect and interrelate to form inequities in HIV/AIDS outcomes within and between countries. Adherence levels are likely to be different between rural and urban areas of the same country due to the influence of such determinants of health as geographical location. Barriers to ART adherence among people living with HIV/AIDS in Zimbabwe need to be explored in greater detail. Future studies are required that will assess the influence of social determinants of HIV/AIDS outcomes, and how these can be addressed to ensure health equity in Zimbabwe.

Since ART is a lifelong intervention for people living with HIV/AIDS, its effectiveness and success relies on variousmotivational, promotional and educational strategies to ensure high levels of medication adherence.[7, 14, 15]Besides the individual and environmental factors already discussed, other important factors

motivating/reinforcing ART adherence identified in our study include support visits by healthcare workers, patient participation in HIV/AIDS management support groups, use of reminders, treatment partners, and disclosure of HIV status to a friend/family member. These together with ensuring universal access to Information, Educational and Communication (IEC) materials on HIV/AIDS and ART among people living with HIV/AIDS are promising strategies to ensure high levels of ART adherence.

Treatment partners play a supportive role in improving and maintaining adherence.[16]Their involvement as part of patient counselling, acting as reminders to patients, assisting in reporting clinical symptoms and collection of refills shows their importance. Referred to as treatment 'buddies' in a Zambian study, their involvement in patient antiretroviral treatment reduced by half the odds of patient non-adherence to ART.[16]

Reminders are an important aspect of treatment. Various forms exist from pill boxes, alarms and even treatment partners, all being useful especially to forgetful individuals. A study conducted in South west Ethiopia found an association, with an odds ratio of 3, between memory aids and adherence.[17]

As supported by Wag & Wu[18] in their study where regular visits by health workers had association with ART adherence, home visits from health workers is important for consistency in adherence. Regular healthcare worker visits are important in that they create an opportunity for important challenges related to ART faced by the patient to be identified and addressed on time.Again, disclosure plays a pivotal role as a gateway to social support.[19]

Limitations

Adherence measure used in the study was based on self-report, which is prone to reporting bias by participants. Also, there was possibility for recall bias in instances where participants were asked to recall certain past incidents/events during data collection.

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