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ORIGINAL RESEARCH

Forgetting to Take Medication, Treatment Adherence and Their Relationship with Viral Load Suppression Among People Living with HIV in the Kilimanjaro Region, Tanzania

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Background: Antiretroviral therapy (ART) adherence is crucial for virological suppression and positive treatment outcomes among people living with HIV (PLHIV), but remains a challenge in ensuring patients achieve and sustain viral load suppression. Despite the recommended use of digital tools medications uptake reminders, the contribution of forgetting to take medication is unknown. This study investigated the contribution of forgetting to take medication on the total missed medication and its effects on detectable viral load (VL).

Methods: This mixed-method research was conducted among children, adolescents, pregnant, and breastfeeding women living with HIV on ART in northern Tanzania. Forgetting to take medication constituted reporting to have missed medication due to forgetfulness. A multivariable logistic regression model was used to estimate the adjusted odds ratio (AOR) with a 95% confidence interval (CI) to determine the contribution of forgetting medication intakes on total missed medication and other factors associated with having a detectable VL.

Results: Of 427 respondents, 33.3% were children, 33.4% adolescents, and 33.3% pregnant and breastfeeding women, whose median age (interquartile range) was 9 (7–12), 18 (16–18), and 31 (27–36) years, respectively. Ninety-two (22.3%) reported missing medication over the past month, of which 72 (17.9%) was due to forgetting. Forgetting to take medication (AOR: 1.75 95% CI: 1.01–3.06) and being on second-line regimen (AOR: 2.89 95% CI: 1.50–5.55) increased the chances of a detectable VL, while females had lower chances of detectable VL (AOR: 0.62 95% CI: 0.41–0.98). The themes on the reasons for forgetting to take medication from qualitative results included being busy with work and the importance of reminders.

Conclusion: Forgetting to take medication is common among PLHIV and an important predictor of a detectable VL. This calls for the use of automated short message services (SMS) reminders or Digital Adherence Tools with reminders to improve and promote good ART adherence among PLHIV.

Keywords: ARV Adherence, forgetting medication, skipping medication, viral load suppression, Tanzania

Background

HIV/AIDS remains a public concern, with an estimated 37.7 million cases worldwide and most (84%) of infections occurring in sub-Saharan Africa.[1] The overall prevalence of HIV in Tanzania stands at 4.5%, but it is lower as 2.6% in Kilimanjaro region.[2,3] In 2020, Tanzania reported an average of 58,000 new infections among people aged 15–49 and 8600 among children aged 0–14 years.[2] Numerous policies have been developed by the government to reduce the HIV epidemic in the country. These include improving access to HIV testing, improving access to Antiretroviral Treatment

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(ART) for people living with HIV (PLHIV), reducing the number of new infections caused by mother-to-child-transmission by promoting prevention of mother-to-child transmission (PMTCT) services, and providing education and protection tools like free condoms.[4] To achieve the global targets of zero new HIV infections and ending the HIV epidemic by 2030, viral suppression among people on ART must be achieved.[5,6]

The World Health Organization (WHO) defines medication adherence, as the extent to which patients follow instructions.[7] Previous studies have shown that good medication adherence can be achieved if one manages to take at least 80% of the medications provided to them.[7] In recent years, the WHO and other studies have recommended taking at least 90–95% of the medication provided to patients to achieve good adherence and better treatment outcomes.[8,9] Poor medication adherence is attributed to many factors, including forgetting medication intake, stigma, depression, and side effects amongst others. Studies have reported forgetting to take medication as the main reason for missing medication intakes and poor adherence. A systematic review that included adults, children, and adolescents reported a 41.1% prevalence of forgetting to take medication among adults, 40.7% among adolescents, and 29.2% among children.[10–13] Several studies in Tanzania have reported that forgetting to take medication is a reason for not taking medication but did not show how much forgetting to take medication contributes to a detectable viral load.[13–15] Other factors termed to be associated with a detectable viral load include stigma, depression, non-disclosure status, longer distance to the clinic, food insecurity, substance abuse, and ART side effects.[16–20]

Several ways to monitor adherence to ART treatment have been implemented, such as pill counts and pharmacy refill counts, but several setbacks have been highlighted, including recall bias and patients' personal barriers.[17] The WHO has recommended tools for enhancing adherence, including the use of Digital Adherence Tools (DAT), which can be used to remind patients in real-time to take medication.[21] Several studies have demonstrated the effectiveness of DAT in improving adherence across different health conditions.[21–23] However, the contribution of forgetting to take medication on viral suppression (detectable viral load) has not been well documented. Understanding the contribution of forgetting to take medication on total missed medication and its subsequent viral suppression or detectable viral load will help to know if currently proposed interventions, such as the use of reminder tools, will help to improve viral suppression. The overall objective of this study was to assess the extent to which skipped medication is attributed to forgetting (or the percentage of forgetting among skipped medication). The secondary objective was to determine the relationship between forgetting to take medication and a detectable viral load. Furthermore, we simultaneously investigated the association between other factors and detectable viral load. Lastly, a qualitative approach was employed to explore the main reasons for missing medication and forgetting medication intake.

Methods

Study Design, Setting, and Population

This was a mixed-methods study which was conducted from September 2021 to March 2022 as part of the REMIND-KID project that used a mixed-methods design to investigate the needs and contents of a customized DAT. We enrolled children, adolescents, and pregnant and breastfeeding women living with HIV attending care and treatment clinics (CTC) in the Kilimanjaro region, which is in Northern Tanzania. We included pregnant and breastfeeding mothers, parents/caretakers of children and adolescents, who were able to read SMS, willing to use DAT, and who were willing to give informed consent or assent. We included pregnant and breastfeeding women aged 15–45 years and <2 years breastfeeding their infants. We also included children aged 0–14 years and adolescents aged 15–17 years with their parents or caregivers. Our participants were required to have a mobile phone for receiving SMS. We selected twenty participants from each group, and they were given a DAT to use for one month.

Sample Size and Sampling Technique

Since there were no previous studies that explored barriers to using DAT among PLHIV, we used an assumption that barriers for using DAT among PLHIV is 50% to estimate the minimum sample size, with $\alpha = 0.05$ and a power of 80% (estimation of single proportion sample calculation). We needed a sample size of 142 participants in each group of children, adolescents, and pregnant/breastfeeding women. The final sample size was 426 participants. We enrolled

participants from all CTC sites involved in the study. Healthcare providers helped identify potential study enrolment participants following defined eligibility criteria.

A sub-sample of 20 participants in each group was purposively selected from the study participants, with a variability in demographic characteristics including rural or urban, facilities, clinic adherence patterns, and viral load to ensure heterogeneity in the use of digital tools. Participants used the device for a period of one month to understand the mechanism of its operation. Total of 60 participants were in-depth interviewed, and 6 Focus group discussion were conducted to understand the context of adherence to treatment, use of the digital tools, contents and experience of DAT and SMS in each group. We believed this sample size would be adequate to reach saturation.[24]

Data Collection

Participants were checked for eligibility by nurse counsellors in the clinics. If eligible, study nurses explained the study well to the participants and asked for informed consent. Adolescents aged 18 years and above and pregnant and breastfeeding women provided written informed consent. For children and adolescents below 18 years of age, we asked their parents for written informed consent, and the children to whom their HIV status was disclosed by their parents were asked to give oral assent. For mature minors, who were adolescents below 18 years but were heads of their households, we asked for written informed consent. We used structured questionnaires for the quantitative survey, which included socio-demographic characteristics, depression assessment, clinical and adherence-related characteristics, and laboratory results of viral load results from the patients. A semi-structured topic guide for in-depth interviews (IDIs) and Focus Group Discussions (FGDs) was developed based on the Sekhon framework.[25] Participants were asked open-ended questions based on the use of DAT and SMS sent as reminders of taking medication and more understanding of the reasons for forgetting to take medication after the completion of one month of use of the device. Further participants were asked about different reasons for missing medication intakes and forgetting to take medication. The qualitative interviews were conducted in the hospital clinic in a private doctor's room. The interviews lasted approximately 40 to 90 minutes. We improved the topic guide based on emerging themes during the interviews. All tools were designed in English and Swahili language, and interviews were conducted by trained research assistants (RA), ie, study nurses in Swahili.

Study Procedures

After informed consent and assent were given, trained research assistants did a survey to investigate the contribution of forgetting to take medication on the total missed medication and its effect on viral load suppression among children and their caretakers, adolescents, and pregnant and breastfeeding women. Twenty participants from each group and were provided with a DAT to use for one month. They received daily short message services (SMS) to remind them to take medication. After that, trained research assistants conducted in-depth interviews (IDI) and focused group discussions (FGD). The in-depth interviews were conducted in controlled environments and lasted for about sixty minutes. Selection of participants for focus group discussions considered matching socio-demographic characteristics to allow better and open discussions. The discussions were led by trained research assistants and lasted for about ninety minutes. The interviews were done in the local language (Kiswahili) and tape-recorded. Interviews were transcribed verbatim and translated to English and were done by a research assistant.

Study Variables

The main outcome variable in this study was a detectable viral load. We defined detectable viral load as copies above 20 per mL of blood. VL was measured using Roche Amplicor 1.5 monitor assay (Indiana USA), and blood samples were collected by trained laboratory scientists following standard of care procedures.

The main independent variable was forgetting to take medication, which was reported as the number of medications missed over the past month due to forgetfulness. We assessed missing medication intakes by asking the patients about the number of pills missed over the past 1 month and the number of pills missed due to forgetfulness. Adherence to ART was assessed by asking the participants the number of times they skipped medications in the month preceding the survey. A respondent was considered to skip medication intake if he/she did not take the required dose/pill on a given day. They

were asked for reasons for skipping medication and if forgetting was among the reasons, participants were required to state reasons for forgetting to take medication.

Depression was measured using a PHQ9 (Patients Health Questionnaire-9) with nine questions and validated to measure depression among people living with HIV and used in sub-Saharan countries, including Tanzania, having a sensitivity and specificity of above 80% (24,25). The responses to these questions were based on a five-point Likert scale, ie, "not at all" as 0, "several days" as 1, "more than half the days" as 2, and "nearly every day" as 3. The total score ranged from 5 to 20, and a score of 0–5, 6–10, 11–15, and 16–20 represented mild, moderate, moderately severe, and severe depression, respectively (24). Participants were also asked whether they had encountered any medication side effects during the last month of treatment.

Socio-demographic characteristics included age, education level, clinic site, and sex. Other independent variables included clinical characteristics such as ART regime, ie, first-line treatment which includes the use of two nucleoside reverse transcriptase inhibitors (NRTI) with one non-nucleoside reverse transcriptase inhibitor (NNRTI) or an integrase inhibitor. Second-line treatment included the use of two nucleoside reverse transcriptase inhibitors (NRTI) and one protease inhibitor. Adherence-related characteristics included any other factors affecting adherence to ART such as medication side effects, knowledge on ART regimes and clinic attendance.

Data Analysis

Before analysis, we checked the data for possible errors, missing values, and duplicates. Quantitative data were analysed using Stata version 15.0 (StataCorp). 2017). We summarized categorical variables such as reasons for missing medication and forgetting to take medication using frequencies and percentages. Numerical variables were summarized using the median and interquartile range. We computed the proportions of viral load suppression for our study participants as the number of participants without a detectable viral load (<20 copies/mL) within the total number of participants enrolled. We computed the proportions of forgetting medication intakes as the number of participants who reported skipping medication intakes due to forgetfulness divided by the total number of participants who skipped medications. We used a classical logistic regression model in the univariate and multivariable analyses to determine the contribution of forgetting medication intakes and other factors associated with a detectable viral load. We included explanatory variables with p-values of <0.2 in the univariable analyses into the multivariable /adjusted analysis. We used stepwise regression to select variables to be included in the development of the final regression model. We interpreted the magnitude of the association using the Odds ratio (OR) and respective 95% Confidence Intervals (CI). We set a statistical significance at a p-value of <0.05.

We analyzed other reasons for skipping medication intakes and forgetting medication intakes from the qualitative data using the thematic framework analysis method. After transcription and translation of the qualitative data, two researchers (NE, RM) created memos of the transcripts to develop initial codes and subthemes. A preliminary codebook was developed based on the memos and codes from the transcripts. We imported translated transcripts, memos, field notes, and the codebook into NVivo software version 12 to organize the data.

Results

Socio-Demographic Characteristics of the Study Participants

A total of 427 participants enrolled from five CTC clinics. We included 142 (33%) pregnant and breastfeeding women, 143 (33%) adolescents, and 142 (33%) children and their caregivers. The characteristics of the study participants are shown in Table 1. Nearly half (48.5%) of the enrolled participants had primary education. Majority (60.2%) were women. The detectable viral load was significantly different between primary, secondary and tertiary education level (28%, 34% and 22%, respectively, p = 0.007). Women had higher proportion of detectable viral load compared with their male counterparts (38% vs 28%, p = 0.04). Children aged 0–8 years had higher proportion of detectable viral load (45.6%) compared to other age groups, 9–14 years and 15–19 years, 22 (26.5 and 31.9%), respectively (p = 0.055). See Table 1.

Table 1 Socio-Demographic Characteristics of the Study Participants (N = 427)

Characteristics	Frequency	Percentage	Undetectable Viral Load (%)	Detectable Viral Load (%)	P-value
Health facility					
KCMC hospital	123	28.7	74 (61.2)	47 (38.8)	0.232
Mawenzi Regional Hospital	112	26.1	79 (70.5)	33 (29.5)	
Kibosho Hospital	44	10.3	34 (77.3)	10 (22.7)	
Pasua Health Centre	73	17.0	51 (72.8)	19 (27.2)	
Majengo Health Centre	77	17.9	53 (70.7)	22 (29.3)	
Age (age in years)					
Children (0–8)	59	13.8	31 (54.4)	26 (45.6)	0.055
Children (9–14)	84	19.6	61 (73.5)	22 (26.5)	
Adolescents (15–19)	143	33.3	96 (68.1)	45 (31.9)	
Pregnant and breastfeeding women (15–49)	142	33.3	103 (73.1)	38 (26.9)	
Education level*					
None	16	3.8	5 (33.3)	10 (66.7)	0.007
Primary Education	205	48.5	145 (71.8)	57 (28.2)	
Secondary Education	155	36.6	102 (66.2)	52 (33.8)	
Tertiary Education	48	11.3	36 (78.3)	10 (21.7)	
Sex*					
Male	145	33.8	88 (62.4)	53 (37.6)	0.040
Female	284	66.2	203 (72.2)	78 (27.8)	
Target group					
Children (0–14)	142	33.3	91 (65.5)	48 (34.5)	0.327
Adolescents (15–19)	143	33.5	96 (68.1)	45 (31.9)	
Pregnant and breastfeeding women (19–45)	142	33.2	103 (73.6)	37 (26.4)	

Notes: *Frequencies do not tally with the total due to missing values.

Forgetting Medication Intakes, Clinical, and Adherence-Related Characteristics of the Study Participants

Ninety-seven (22.3%) participants reported missing medication intakes and seventy-two (17.9%) reported it was due to forgetting. Fourteen (9.8%) caretakers of 142 children forgot to give medication. Among 143 adolescents, 45 (31.5%) reported forgetting to take medication, and among 142 pregnant and breastfeeding women, 14 (9.8%) forgot to take medication. Of those who forgot to take medication, 30 (41.1%) did not achieve viral load suppression.

Sixty-eight participants (16.1%) reported having moderate-to-severe depression. Eight participants (3%) had developed symptoms of HIV disease. Among all participants, 80 (19%) reported having skipped clinic visits in the past six months, and 133 (31%) participants reported experiencing medication side effects. Among all study participants, 131 (31%) had a detectable viral load, 48 (34.5%) were children, 46 (31.9%) were adolescents, and 37 (26.4%) were pregnant and breastfeeding women (Table 2).

Forgetting to Take Medication with Other Factors Affecting Viral Suppression Among Children, Adolescents, Pregnant and Breastfeeding Women

Those who forgot to take medication had higher chances of being unsuppressed (COR: 1.77 95% CI: 1.04–2.99). Participants on second-line treatment had higher chances of being unsuppressed compared to those on first-line treatment (COR: 2.89 95% CI: 1.50–5.55). Compared to undisclosed children, those who were disclosed had lower chances of having an unsuppressed viral load (COR: 0.47 95% CI: 0.26–0.86). Details can be found in Table 3

Table 2 Participant Clinical and Adherence-Related Characteristics (N = 427)

Characteristics	n (%)	Undetectable Viral Load (%)	Detectable Viral Load (%)	P-value
Forgot medication intakes over the past month*				
No	327 (82.1)	233(71.3)	94(28.7)	
Yes	72 (17.9)	30 (41.6)	42 (58.3)	0.032
Skipped medication intakes over the past month				
No	325 (77.7)	232(71.4)	93(28.6)	
Yes	97 (22.3)	4 (4.1)	93 (95.9)	0.055
Depression*				
No to mild depression	353 (83.9)	245 (69.4)	108 (30.6)	0.962
Moderate to severe depression	68 (16.1)	47 (69.1)	21 (30.9)	
HIV clinical stage				
Asymptomatic	417 (97.2)	290(69.5)	127 (30.5)	0.894
Symptomatic and AIDS converted	8 (2.8)		4 (33.3)	
Current ARV regimen				
First Line	386 (89.9)	277 (71.8)	109 (28.2)	0.001
Second line	43 (10.1)	21 (48.8)	22 (51.2)	
Disclosure of HIV status among children*				
No	88 (42.9)	51(57.9)	37(44.1)	
Yes	117 (57.1)	87 (74.4)	30(25.6)	0.013
Years living with HIV [median (IQR)]	6.7 (3.1–10.7)			
Action taken after realizing intakes were forgotten*				
Tell nurse	5 (6.9)	2 (25.0)	3 (75.0)	0.301
Stay quiet	17 (23.3)	8 (47.1)	9 (52.9)	
Take it immediately	24 (32.9)	15 (62.5)	9 (37.5)	
Wait for next dose	27 (36.9)	18 (66.7)	9 (33.3)	
Forgot to attend clinic for prescription refills over the past six months*				
No	375 (89.1)	263(70.1)	112(29.9)	
Yes	46 (10.1)	28(60.0)	18(40.0)	0.165
Skipped clinic visits over the past six months*				
No	78 (18.7)	50(64.1)	28(35.9)	
Yes	347 (81.3)	319 (91.9)	28(8.1)	0.295
Intentionally not taking medication*				
No	399 (95.1)	278(69.7)	121(30.3)	
Yes	21 (4.9)	13 (61.9)	8 (38.1)	0.360
Taking medication on time over the past month				
No	57 (13.3)	34(59.7)	23(40.4)	
Yes	370 (86.7)	240 (64.9)	130 (35.1)	0.099
Knowing importance of Viral suppression				
No	96 (22.9)	71(73.9)	25(26.1)	
Yes	329 (77.1)	224 (68.1)	105 (31.9)	0.236
Ever experienced medicine side effects				
No	284 (68.8)	199(68.9)	90(31.1)	
Yes	133 (31.2)	3 (2.3)	130 (97.7)	0.901
Decide to stop medications after side effects in the past month*				
No	101 (77.4)	73(72.3)	28(27.7)	
Yes	30 (22.6)	2 (6.3)	28 (93.7)	0.200

Notes: *Frequencies do not tally with the total due to missing values.

Table 3 Crude Analysis for Factors Associated with Detectable Viral Load (N = 422)

Characteristics	Total (n)	COR (95% CI)	*P*-value
Demographic Characteristics			
Health facility			
KCMC hospital	121	1	
Mawenzi R Hospital	112	0.66 (0.38–1.13)	0.133
Kibosho Hosp	44	0.46 (0.21–1.02)	0.057
Pasua H Centre	70	0.59 (0.31–1.11)	0.118
Majengo H Centre	75	0.65 (0.35–1.21)	0.177
Age categories			
Children (0–8)	57	1	
Children (9–14)	83	0.43 (0.21–0.88)	0.020
Adolescents (15–19)	141	0.56 (0.29–1.04)	0.070
Pregnant and breastfeeding women (15–49)	141	0.45 (0.23–0.83)	0.012
Education status			
None	15	1	
Primary Education	202	0.19 (0.06–0.60)	0.004
Secondary Education	154	0.25 (0.08–0.78)	0.017
Tertiary Education	46	0.14 (0.04–0.50)	0.003
Sex*			
Male	141	1	
Female	281	0.64 (0.41–0.98)	0.040
Target group			
Children (0–14)	139	1	
Adolescents (15–19)	141	0.89 (0.54–1.46)	0.642
Pregnant and breastfeeding women	140	0.68 (0.40–1.14)	0.142
HIV related characteristics			
Depression			
No to Mild	350	1	
Moderate to severe dep	68	0.71 (0.23–2.22)	0.554
HIV clinical stage			
Asymptomatic	410	1	
Symptomatic to AIDS converted	12	1.34 (0.31–5.68)	0.694
Years positive		0.99 (0.95–1.02)	0.545
Current ARV regimen			
First line	381	1	
Second line	41	2.89 (1.50–5.55)	0.001
Disclosure of HIV status among children* (Yes)	88	0.47 (0.26–0.86)	0.014
Skipped medication over the past month (Yes)	325	1.59 (0.99–2.56)	0.056
Forgot medication over the past month (Yes)	327	1.77 (1.04–2.99)	0.033
Action taken after realizing intakes were forgotten*			
Tell nurse	4	1	
Stay quiet	17	0.37 (0.03–0.37)	0.434
Take it immediately	24	0.20 (0.02–2.22)	0.190
Wait for the next dose	27	0.17 (0.02–1.83)	0.143
Forgot to attend clinic for prescription refills over the past six months (Yes)	45	1.56 (0.83–2.95)	0.167
Skipped clinic visits over the past six months (Yes)	78	1.32 (0.78–2.21)	0.296
Intentionally not taking medication* (Yes)	20	1.53 (0.61–3.84)	0.364
Taking medication on time over the past month (Yes)	363	0.62 (0.35–1.09)	0.101
Knowing the importance of Viral suppression (Yes)	324	1.36 (0.81–2.27)	0.237
Medicine side effects (Yes)	131	0.97 (0.62–1.52)	0.901
Decide to stop medications after side effects in the past month* (Yes)	101	1.73 (0.74–4.07)	0.203

Notes: *Frequencies do not tally with the total due to missing values.
Abbreviations: COR, Crude Odds Ratio 95%; CI, 95% Confidence Intervals.

Reasons for Skipping Medication

The main reason for skipping medication intake was forgetting to take medication (62%). Taking a medication break and having side effects were the least provided reasons for skipping medication intakes (3.3%) (Figure 1). The main reason for forgetting to take medication was the lack of a reminder (39%) and forgetting medication intake due to being stressed 5.9% (Figure 2).

The study's findings revealed several recurring themes from the IDI and FGD. These themes included participants' busy schedules, the absence of reminders, and children's apprehension about disclosing their forgetfulness regarding medication adherence to their guardians. To enhance the clarity of these findings, we present relevant participant quotes that illustrate each theme.

The most crucial reason for forgetting to take medication was being busy with work by most participants. We tried to get a better understanding of what the context of "being busy" was. Adolescents reported several reasons for being busy. Most adolescents reported missing their medication due to their schedules. Being busy included several activities they do

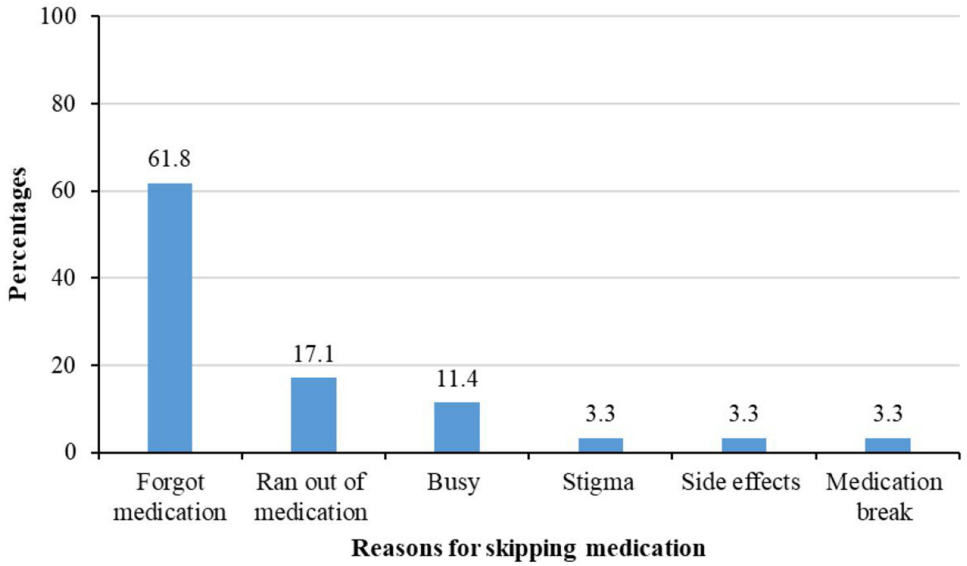

Figure 1 Reasons for skipping medication among those who skipped medication (N = 92).

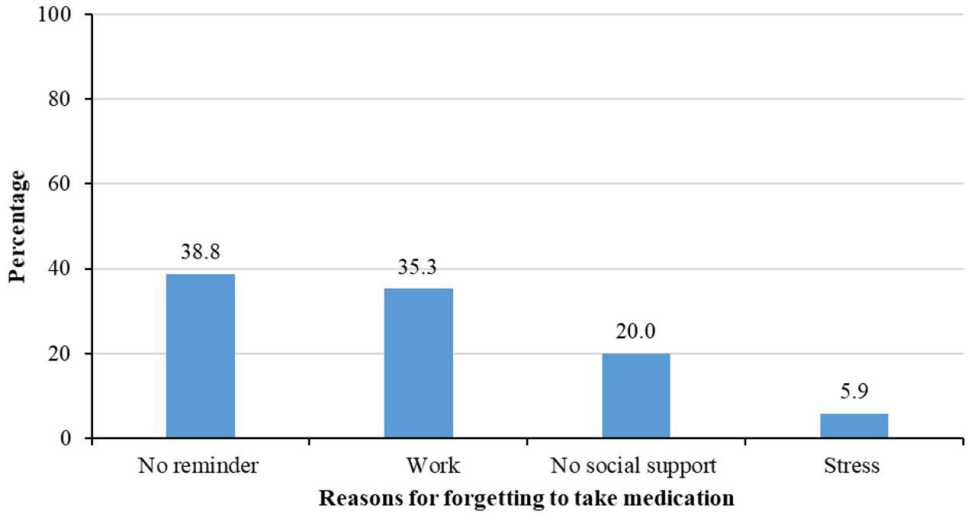

Figure 2 Reasons for forgetting to take medication among those who forgot to take medication (N = 72).

in a day and during the agreed time of medication intake. A male adolescent said the reason for not taking medication included forgetting due to being busy. He said:

> I may forget to take medication once a week and promise myself: 'I will take it tomorrow', and the following day, I may forget. So, I may not take medication multiple times in a month. There was a time I got a job in the city, and it was a very busy job. I never had time for myself, and so I forgot to take medications always.

A female in her 20s also reported forgetting to take medication due to different activities done during the agreed time of intake:

> And you know when you (pause) completely forget. Maybe, if you are with friends, so, when you reach home maybe, or if you are watching football, you can forget. Now you come to remember when you look and see the alarm had rung. So, that is it. But even when I miss, even if I remember later, on that day, even if it is one hour later, I take medication. If I don't remember at all, I won't take the medication.

The Importance of Having Reminders

Participants also reported the importance of having reminders to take medication since missing medication is primarily due to forgetfulness. Further, we found from the interviews that participants appreciate reminders such as SMS reminders or reminders from their guardians. In addition, we saw that adolescents with caretakers were afraid to tell if they forgot to take their medications. This raises concerns, as the caretakers remind them of their medication intakes and monitor their adherence at home. A male adolescent taking medication at 8:00 pm said on the importance of having reminders, such as SMS:

> Because the biggest challenge lies in time. Today you can swallow at 20:00. Tomorrow, you forget to swallow at 21:00. But, if you have reminders, they help.

An adolescent who lives with her grandmother stated she misses medication intake due to forgetfulness, and her grandmother reminds her. She said:

> Aah, sometimes you find I forgot; grandma reminds me of my medication time. Then I take them. Now if I tell her that I forgot yesterday, she will scold me and say: 'Why you forgot to take medications' and another day, I should not repeat.

After adjusting for age, sex, education level, treatment site (CTC), depression, ART regime, HIV clinical stage, number of years living with HIV and skipping clinic visits, forgetting to take medication was still a significant predictor of having a detectable viral load (AOR: 1.75, 95% CI: 1.01–3.06). We also found that being female was protective against having a detectable viral load (AOR: 0.56, 95% CI: 0.36–0.90) and being on second-line treatment increased the chances of having a detectable viral load (AOR: 2.64 95% CI: 1.16–6.02). See Figure 3.

Discussion

The primary goal of this study was to investigate the contribution of forgetting to take medication on the total missed medication and its effects on detectable VL. We observed that 31% of our study participants had a detectable viral load. In our study, forgetting to take medication was defined as skipping medication intake due to forgetfulness. Among all our enrolled participants, 97 (22%) skipped medication intakes, and 72 (17%) forgot their medication intakes. In this study, we saw that participants who forgot to take their medication had higher chances of having a detectable viral load.

The percentage of participants missing and forgetting medication is comparable to other studies. In Guinea-Bissau, the proportion of missed medication intakes over one month of reporting time was 23%.[26] A study conducted in South Africa revealed that 13% of medication doses were missed.[27] This finding is comparable to the proportion of missed medication doses in Guinea-Bissau. It suggests that the factors contributing to poor adherence to medication are consistent across various locations in Africa. We observe a slight difference in the proportions of skipping medication intakes from the ones reported; this could be due to different personal barriers that could contribute to not taking medication by our study participants.[28]

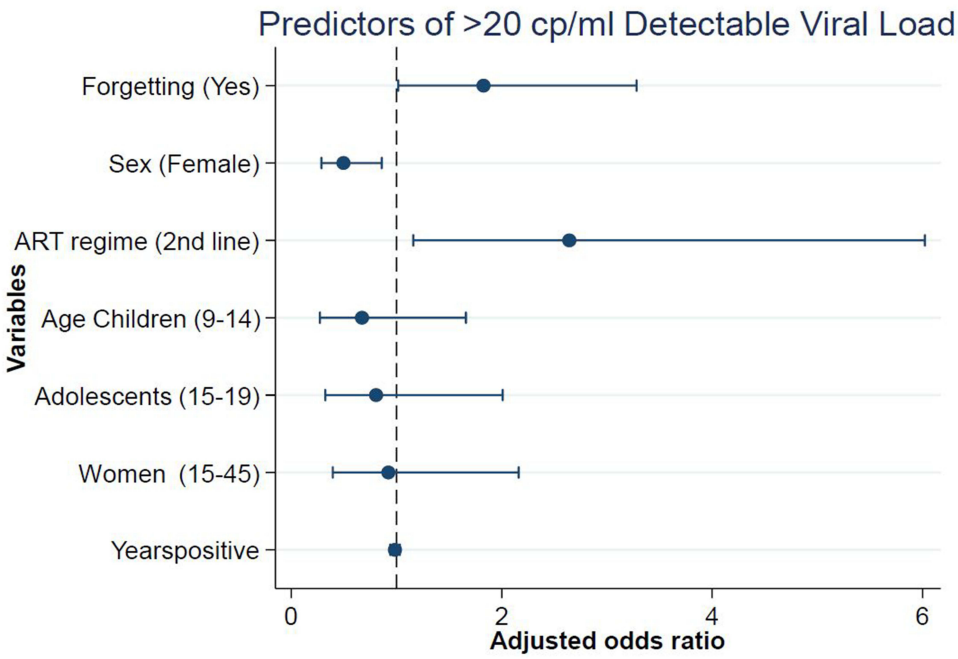

Figure 3 Adjusted analysis for factors associated with a detectable viral load.

Forgetting to take medication proved to be a setback of good adherence in this study. We found that forgetting to take medication increased the chances of having a detectable viral load in our study. Forgetfulness has been a reason for poor adherence, as reported in several studies worldwide.[29–34] There are no reports of reasons for forgetting to take medications in Tanzania. However, in a study among pregnant women on improving adherence, participants reported the usefulness of SMS as a reminder tool for taking their medications.[35] A systematic review also showed that forgetfulness was associated with a 65% contribution to poor adherence among adults, adolescents and children.[10] With most studies reporting different proportions of forgetting medication intakes, to our knowledge, none have shown an apparent effect of forgetting medication with having a detectable viral load.

The reasons reported for forgetting medication intake included being busy, lack of reminders and stress. These reasons are similar to those reported in the USA and India, which also reported other barriers to adherence to ART, such as pills making them sick (perceived side effects) and depression.[36,37] In Uganda, forgetting to take medications was attributed to a lack of family support, family instability, orphan hood and stress.[33,38] Several studies in East Africa have shown that reasons for missing medication intakes (non-adherence to ART) included forgetting, being busy, depression, food insecurity, non-disclosure status and stigma-related factors.[8,39] Among children and adolescents in the Kilimanjaro region, reported reasons for missing medication were forgetting and being too busy with other activities.[40] Further, our study found that having reminders such as using text messages will be a useful tool in reminding our participants of their medication time. This concurs with findings from a systematic review which showed that forgetting to take medication can be solved by using SMS reminders.[10]

Other factors associated with detectable viral suppression included being on second-line treatment and being male. Among HIV-positive pregnant and breastfeeding women in South Africa, it was shown that being on first-line treatment increased the chances of being detectable.[18] This is different from what we found in our study, where those on second-line treatment had a higher likelihood of being detectable Another multisite follow-up study, which included sites from Tanzania, showed that being on second-line ART increased the chances of not being virally suppressed.[28] This could be due to participants being changed to second-line who failed to achieve viral suppression in first-line due to different factors affecting adherence and consequently not being able to become suppressed during second-line treatment as well.

Study Strengths and Limitations

In terms of limitations, our study did not assess the use/abuse of any substances, such as alcohol. However, this could be another reason for forgetting to take medication or poor adherence, as it has been pointed out in other studies.[38,41,42] This study was a cross-sectional study; despite the observed association, we cannot establish a causal relationship between forgetfulness and a detectable viral load. Indeed, detectable viral load can be influenced by several factors besides forgetting medication intake. Further use of self-adherence reports could lead to personal bias of over estimating the rate of adherence of the participant. Also, there could be chances of recall bias since adherence was reported over a month period. The sample size used for different groups could not allow us to perform a stratified analysis to get the factors associated with a detectable viral load in the specific populations used in our study. However, we saw that forgetting to take medication affects all our study populations. Our study had several strengths, which included this being the first study in our setting to explore the contribution of forgetting medication intakes and its association with viral load suppression. We believe this study will enlighten most care providers during care provision among people living with HIV who face difficulty adhering to medication. Also, this study employed the collection of both qualitative and quantitative data, which provides us with more understanding of our findings on the reasons for forgetting medication intakes.

Conclusions

Forgetting is highly prevalent, with more than one-fifth forgetting to take medication. Furthermore, forgetting is a significant predictor of a detectable viral load.

Other variables influencing a detectable viral load included being male and being on a second-line ART regime. Our study determined the reasons why people forget to take their medication, which is powerful information as interventions could be better developed to improve treatment adherence. We recommend using interventions to remind medication intakes, such as automated SMS reminders or the use of DAT to improve and promote good adherence among people living with HIV. These interventions have been shown to be effective tools for reminders through different studies conducted.[21,23]

Abbreviations

ART, AntiRetroviral Treatment; DAT, Digital Adherence Tools; HIV, Human Immunodeficiency Virus; IDI, In-Depth Interview; FGD, Focus Group Discussion; SMS, Short Message Services; PLHIV, People Living with HIV.

Data Sharing Statement

All data generated and analysed during this study are included in this article. Raw data can be accessed by communicating with the author and upon signing of a data transfer agreement form according to the nationals' policy.

Ethics Approval and Consent to Practice Ethical Consideration

The ethical approvals with certificates PG 20/2021 and NIMR/HQ/R.8a/Vol.IX/3825 were obtained from Kilimanjaro Christian Medical University College Research Ethical Committee and the National Institute for Medical Research, respectively. All methods and study procedures were carried out in accordance with the Declaration of Helsinki. Participants provided informed consent prior to study entry after detailed explanation on the study provided by study nurses.

Consent for Publication

The informed consent included consenting for publication of the study findings from the study participants with anonymity of their personal identifiers.

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Tanzania for their endless efforts during the preparation and implementation of the study. The abstract of this paper has been presented in several conferences as a poster presentation. Preliminary results were presented in the INTEREST 2022 conference and the National Institute of Medical Research (NIMR) conference as poster presentations. The abstract has been published by NIMR in a Tanzania Journal of Health Research, 2022, Vol 23, p193. Another abstract poster presentation was done in the AIDS 2022 conference which included final results.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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