ANTIRETROVIRAL MEDICATION ADHERENCE AMONG PATIENTS WITH HIV/AIDS AT A COMMUNITY MEDICAL CENTER IN VIETNAM

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ABSTRACT

Introduction: Non-adherence to antiretroviral (ARV) medications is a common issue worldwide and in Vietnam. **Purpose:** To assess patients' adherence to ARV medications and to determine factors associated with adherence among patients with HIV/AIDS in Ho Chi Minh City (HCMC). **Methods**: A cross-sectional study was conducted on 360 outpatients being on ARV therapy at a community medical center in HCMC from 15th March to 20th June in 2020. We invited patients aged 18 or above who have been on ARV treatment for at least 6 months to participate in the study. Data was collected through patient interviews and medical records. Medication adherence was assessed regarding timing of medication administration and dosing adherence using Morisky Medication Adherence Scale-8-item Questionnaire (MMAS-8). Factors associated with optimal adherence were identified by multivariable logistic regression model. **Results**: The median age of 360 patients was 38 (33 - 43), 72.5% were male. The proportion of optimally adherent patients was 56.4%. Factors associated with better adherence were increased age, stronger belief in medications, and adherence aids use. Factors associated with poorer adherence were alcohol consumption in the previous 30 days, concerns about side effects, twice-daily ARV therapy, and undesirable effects in the previous 3 months. **Conclusion**: Optimal adherence to ARV medications among HIV/AIDS patients was relatively limited. To improve medication adherence, health workers may need to simplify ARV regimens and counsel patients more intensively (especially for the younger) about the effectiveness of ARV medications, alcohol intake reduction and the use of adherence aids.

***Keywords**: HIV/AIDS, medication adherence, ARV, MMAS, BMQ*

I. INTRODUCTION

AIDS (Acquired Immunodeficiency Syndrome) resulting from HIV (Human Immunodeficiency Virus) has long been a great public health problem across the world, which has immensely affected sociocultural, economic, and secure status. In Vietnam, HIV infection rates increase over the years, with about 10,000 newly detected HIV cases and 2000 - 3000 patients dying of AIDS-related diseases annually [8].

Thanks to the introduction of antiretroviral (ARV) medication in the 1990s, HIV infection has been converted from a life-threatening disease into a chronic manageable illness. Although antiretroviral (ARV) therapy cannot cure HIV/AIDS, it is expected to inhibit viral replication and facilitate the immune system's recovery, thereby minimizing HIV transmission in community [1]. In order to achieve the full benefit of ARV treatment and virological success, patients' adherence to ARV medications plays a key role. Besides contributing to therapeutic failure, non-adherence raises the risk of mutation and development of drug-resistant-virus strains which could be widely spreadable in community [2]. However, adherence to ARV medications is still a burning issue for many

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nations across the world, with only 62% of patients achieving at least 90% adherence to ARV therapy [15].

Community Medical Center of District 8 is one of the big clinics of Ho Chi Minh City, managing about 2500 HIV outpatients. Given that medication adherence is paramount to treatment success, and there has been limited evidence about it at this center, this study's purposes were to assess the adherence to ARV regimens and to identify factors associated with adherence among individuals with HIV/AIDS in Community Medical Center of District 8 in HCMC.

II. METHODS

1.1. Study design and participant recruitment

A cross-sectional study was implemented at the Community Medical Center of District 8 in HCMC from 15th March to 20th June in 2020. HIV-positive outpatients aged 18 or over being on ARV treatment for at least 6 months were eligible for the study. Patients were excluded if they were pregnant, or had been involved in other studies that could influence medication adherence in the past 6 months.

The sample size was calculated with a 95% confidence level, a margin of error of 0.05 and a proportion of 0.741. This was the prevalence of optimal adherence reported in a previous study by Bach Xuan Tran on 295 individuals with HIV in Vietnam [17]. The sample size needed was at least 295 participants.

1.2. Data collection and assessment

Study data was gathered through structured face-to-face interviews with patients and medical records review. The average interview duration per participant was 20 minutes. Data collected comprised socio-demographic characteristics (age, gender, highest level of education, marital status, and employment status), alcohol consumption, history of illicit drug use, treatment information (ARV regimen, dosing frequency, and adverse reactions), patients' perception of the quality of healthcare services and support, patients' beliefs about medications, and medication adherence.

Current alcohol consumption was documented if the patient has consumed any alcohol beverage (beer, liquor, wine…) in the previous 30 days.

Patients' beliefs in their medication were evaluated by The Beliefs about Medicines Questionnaire (BMQ) - Specific. This scale has 10 items and is divided into two sub-scales, 5 items each, namely "Necessity" and "Concerns". While the former assesses patients' beliefs about their benefits from adhering to prescribed medications, the latter explores patients' perception of the risk of adverse reactions from prescribed medications. Each item has a score range of 1-5, corresponding to the perception of "totally disagree" to "totally agree". The overall score of each sub-scale is the sum of the scores of five items [14].

Medication adherence was classified into optimal and sub-optimal and was assessed in terms of both dosing and timing adherence. Dosing adherence was assessed by Morisky Medication Adherence Scale-8-item Questionnaire (MMAS-8) [14]. The first seven items are yes-no questions while the item eight is a five-point Likert response scale. In the first seven items apart from item five, each "no" answer is scored as 1 and each "yes" response is rated as 0. For item eight, "never/seldom" response is rated as 1, the other responses are rated as 0. As a result,

MMAS-8 total scores vary between 0 and 8, with higher score denoting better adherence. In the case of HIV/AIDS, a maximum total score (eight) was chosen as a cut-off due to more stringent adherence requirement [3]. Regarding timing adherence, taking ARV medications within one hour around the time prescribed was associated strongly with viral suppression [7, 18]. Therefore, patients were considered optimally adherent if they got an eight score in MMAS-8 and reported taking ARV medication within one hour before or after the time prescribed.

All scales used in the study have been translated and validated in Vietnamese research context [14].

1.3. Statistical method

Statistical Package for the Social Sciences (SPSS) software version 20.0 was used for data entry, coding and analysis. Mean, median, and percentage were calculated using descriptive statistics. Multivariable logistic regression, with elimination technique of backward stepwise, was performed to explore the associations between medication adherence and investigated factors. An association was considered statistically significant if *p*-values of ≤ 0.05.

1.4. Ethical considerations

The study's ethical approval was obtained by University of Medicine and Pharmacy at Ho Chi Minh City (Number: 216/2020/HĐ-ĐHYD). All participants were given clear explanation about the study's background, objectives and informed consent procedure through both oral and written communication. Participants had the right to refuse or stop interview at any time of the study. All information related to participants was coded and kept confidential. Data regarding adverse reactions and patients' current ARV regimens could only be extracted from medical records with patients' permissions.

III. RESULTS

Table 1 describes general characteristics of study participants. The median age was 38 (38 - 43). Of the 360 respondents, 72.5% were male, 79.7% had a job, 41.1% lived with their spouse/partner and 40.8% had an education level of high school or higher. In terms of alcohol/drug use, nearly half (44.7%) told that they drank alcohol in the previous month while a quarter admitted having ever used illicit drugs in their entire life.

Table 1. Characteristics of respondents (N = 360)

Characteristics		Number of respondents	Percentage of sample (%)
Socio-demographic			
Age	18 - 29	60	16.7
	30 - 39	150	41.7
	40 - 49	124	34.4
	≥ 50	26	7.2
Gender	Male	261	72.5
	Female	99	27.5
Employment status	Unemployed	73	20.3
	Employed	287	79.7

Characteristics		Number of respondents	Percentage of sample (%)
Marital status	Single/divorced/separated/widowed	212	58.9
	Living with spouse/partner	148	41.1
Education	< High school	213	59.2
	≥ High school	147	40.8
Risk behaviors			
Alcohol use (last month)	No	199	55.3
	Yes	161	44.7
Ever used any illicit drug	No	270	75
	Yes	90	25
Treatment characteristics			
ARV dosing frequency	Once daily	321	89.2
	Twice daily	39	10.8
ADR in the previous 3 months	No	321	89.2
	Yes	39	10.8
Patients'perception on healthcare service and supports			
Satisfaction with healthcare workers' counseling	No	73	20.3
	Yes	287	79.7
Use of adherence aids	No	156	43.3
	Yes	204	56.7
Type of adherence aids	Mobile phone alarm	170	47.2
	Reminded by relatives	30	8.3
	Other*	4	1.1

**Pillbox, Calendar*

Regarding treatment characteristics, most of the respondents (89.2%) were prescribed once-daily ARV regimens and did not have any ARV adverse reactions in the prior 3 months.

When it comes to healthcare services and support, the majority of respondents felt satisfied with the counseling from healthcare workers (79.7%). More than half (56.7%) applied some strategies to remind them of taking their medications. The most common aid was alarm set on mobile phone (83.3%), followed by reminder from relatives (14.7%). Other aids such as pillbox use or calendar marker only accounted for 2.0%.

Table 2. Results of BMQ-Specific

BMQ	Median (IQR1 - IQR3)
Specific-Necessity	25.0 (22.0 – 25.0)
Specific-Concerns	8.0 (5.0 – 10.0)

Table 2 presents the beliefs of participants about medications assessed by the BMQ-Specific tool. The median scores of BMQ Specific-Necessity and BMQ Specific-Concerns were 25.0 (maximum score) and 8.0 respectively. These results demonstrated that the majority of patients were aware of the importance and necessity of ARV medicines but there were some still worried about undesirable effects brought by ARV medicines.

Table 3. Level of ARV adherence (N = 360)

	N	%
Timing adherence		
Yes	259	71.9
No	101	28.1
MMAS-8 Score		
8	260	72.2
< 8	100	27.8
Optimal adherence		
Yes	203	56.4
No	157	43.6

From Table 3, the percentages of patients getting an MMAS-8 score of eight and taking medications at the right time as recommended were 72.2% and 71.9% respectively. As a result, there were 56.4% of patients achieving optimal adherence (those who satisfied both criteria above).

Table 4. Individual answers to the eight-item MMAS-8 Questionnaire (N = 360)

MMAS-8 items	n (%)
1. Do you sometimes forget to take your medicine? (yes)	68 (18.9)
2. Thinking over the past 2 weeks, were there any days when you did not take your medicine? (yes)	18 (5.0)
3. Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when you took it? (yes)	2 (0.6)
4. When you travel or leave home, do you sometimes forget to bring along your medicine? (yes)	21 (5.8)
5. Did you take all your medicines yesterday? (no)	2 (0.6)
6. When you feel like your symptoms are under control, do you sometimes stop taking your medicine? (yes)	3 (0.8)
7. Do you ever feel hassled about sticking to your treatment plan? (yes)	29 (8.1)
8. How often do you have difficulty remembering to take all your medicine? (Once in a while/sometimes/usually/all the time)	14 (3.9)

Adherence assessment using MMAS-8 also provided several reasons for suboptimal adherence among patients with HIV/AIDS (Table 4). The most prevalent justifications were unintentional ones. Specifically, 18.9% of patients forgot to administer medicines, 5.8% forgot to bring the pills when traveling or leaving home. Intentional reasons were picked in 9.5% of the patients, including 8.1% felt hassled about sticking to their treatment plan and only 1.4% cut back or stopped taking medicine after feeling better or worse when they took it. Besides, two other reasons were sleeping through dose caused by alcohol (six cases) and hospitalization (two cases).

Table 5. Factors associated with optimal adherence to ARV medication among HIV patients (N = 360)

Factors		p	OR	95% CI
Age		**0.045**	1.034	1.001 - 1.068
Gender	Female*			
	Male	0.209	1.482	0.802 - 2.737
Employment status	Unemployed*			
	Employed	0.446	0.780	0.411 - 1.478
Education	< High school*			
	≥ High school	0.735	0.911	0.530 - 1.564
Alcohol use (last month)	No*			
	Yes	**< 0.001**	0.328	0.196 - 0.547
Ever used any illicit drugs	No*			
	Yes	0.314	0.746	0.422 - 1.319
BMQ Specific-Necessity		**0.033**	1.090	1.007 - 1.181
BMQ Specific-Concerns		**0.004**	0.915	0.861 - 0.972
Satisfaction with healthcare worker's counseling	No*			
	Yes	0.833	0.939	0.525 - 1.681
Use of adherence aids	No*			
	Yes	**0.008**	1.920	1.186 - 3.108
ARV dose frequency	Twice daily*			
	Once daily	**0.014**	2.599	1.212 - 5.576
ADR in the previous three months	No*			
	Yes	**0.020**	0.408	0.192 - 0.867

***** Reference group

Table 5 shows the association of surveyed characteristics with ARV adherence in the multivariable analysis. The higher likelihood of sub-optimal adherence was found among people who consumed alcohol in the previous 30 days, got high BMQ Specific – Concerns Score, administered twice-daily ARV therapy, and experienced undesirable effects over the past three months. Factors associated with better adherence included: older age, higher BMQ Specific - Necessary score and adherence aids use. On the contrary, we did not observe any statistically significant associations between adherence and gender, employment, education, history of illicit drugs as well as satisfaction with healthcare worker's counseling.

IV. DISCUSSION

The current study found a prevalence of optimal adherence to ARV medications among HIV-infected people at the Community Medical Center of District 8 in HCMC of 56.4%. Compared to other previously published studies, our result was lower than those of Tran Xuan Bach (2013) [17] with 74.1%, Chesney with 50-70% [4] but higher than Mai Thi Hue (2017) with 45.5% [12].

The variation among these studies could be explained by several reasons. First, these listed studies were conducted in various locations with heterogeneous socio-economic contexts. Second, the tools used for adherence assessment as well as the recall periods were different across the studies. In more detail, the MMAS-8 scale in this study

evaluated adherence within two weeks before the interview (mentioned in item two) whereas the Visual Analog Scale (VAS) chose a prior month or the Adult AIDS Clinical Trial (AACTG) Questionnaire assessed in a four-day period. Furthermore, Mai Thi Hue's and our studies [12] were implemented in the context when every patient diagnosed with HIV/AIDS has been encouraged to be treated with ARV medications as soon as possible regardless of their viral loads. Therefore, more asymptomatic patients were included, and they were more likely to lack motivation of adherence in comparison with those who were apparently clinically symptomatic.

The multivariable regression analysis found out six factors associated with adherence (Table 5).

Age: In our study, each year increment in age was associated with 3.4% higher odds of optimal adherence (p = 0.045), which was in line with American setting [4]. This might be originated from older people's better awareness of their ailments and benefits of good adherence to ARV medications. Additionally, the elderly generally have a more stable daily routine and often stick their medication usage to a specific activity (such as before going to sleep or after eating).

Alcohol consumption: Drinking alcohol in the preceding 30 days negatively affected patients' adherence to ARV medications (OR = 0.328, 95% CI: 0.196 – 0.547, p < 0.001). Our findings were consistent with several previous studies in both Vietnam [5] and foreign countries [9] [10]. Alcohol might affect medication adherence in several ways. First, excessive alcohol consumption reduces patients' cognitive ability leading to missing doses or even forgetting medical appointments. Moreover, some patients intentionally skipped doses after consuming alcohol due to their fear of adverse interactions between alcohol and ARV medications [10].

Beliefs about medication: The results explored that patients were more likely to be well adherent if they obtained a higher Necessity score but a lower Concerns score, which was in agreement with studies of Peyre M. in 2016 [16] and Fall E. in 2013 [6]. Intentional sub-optimal adherence typically resulted from patients' beliefs and perception about ARV therapy. The more they believed in the necessity of ARV medications, the higher motivation they had to adhere to their regimens. At the same time, the fear of ARV medication's adverse reactions could make patients feel cautious taking medicines and try to skip doses to avoid potential undesirable effects [11].

The use of adherence aids: Similar to a previous study from three metropolitan areas of Vietnam (2013) [11], our study found that patients using reminder supports had higher likelihoods of better ARV adherence compared with those who did not (OR = 1.920, 95% CI: 1.186 – 3.108, p = 0.008). Timing adherence in ARV treatment can be as essential as dosing adherence, especially in HIV/AIDS treatment. This is one important point that healthcare workers should highlight when counseling patients about treatment plans. Appropriate reminding methods tailored to individuals can also be discussed to improve adherence.

ARV dosing frequency: In our study, patients taking once-daily ARV regimen had 2.6-fold higher odds of optimal adherence (p = 0.014). This result was in line with a meta-analysis of Nachega J. B in 2014 involving 6312 HIV patients (OR = 2.55, 95% CI: 1.23 – 3.87, p < 0.001) [13]. Apparently,

simplified ARV therapy with fixed timing every day would reduce patients' confusion and make it easier for them to remember to take medicines as prescribed.

ARV medication's adverse reactions: Aligned with prior studies [5] [9], we explored the association between ARV medication's undesirable reactions and patients' adherence. Over three months prior to the interview, those who suffered any adverse effects had their odds of adherence declined by nearly 60% compared to those who did not (OR = 0.408, 95% CI: 0.192 – 0.867, p = 0.020). ARV medication's adverse drug reactions can range from mild to severe extent that requires regimen modifications. These reactions might bring about unpleasant feelings for patients, interfere with their daily routine and cause them to skip doses. Therefore, before initiating ARV therapy, patients should be counseled about potential adverse reactions and simple ways of managing these symptoms [12].

The current study has some strengths. Firstly, data was collected from two sources (direct interview and medical records), hence ensuring validity. Secondly, all the assessment instruments used in our study were validated in Vietnam context, so the results could be highly reliable. Finally, face-to-face interview could enhance patients' understanding of the questions and enable patients to share more about their drug administration.

However, there were some limitations to consider. The cross-sectional design could not determine cause-effect relationships. Additionally, self-reported measurement tended to overestimate actual adherence due to recall bias and social desirability bias. To reduce this risk, the interviewers were trained to give patients clear explanation about the study's purposes and anonymity assurance before joining the interview.

V. CONCLUSION

The optimal ARV medication adherence prevalence among HIV/AIDS patients was rather low (about a half). Some measures explored from the study could be applied in clinical practice to enhance ARV treatment adherence in Vietnam namely simplifying ARV regimens (using fixed-dose combination or once-daily regimens); counseling patients more intensively (especially for the younger) about the benefits of ARV medications, alcohol intake reduction and the use of adherence aids.

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