ARTICLE

Factors associated with poor adherence to anti-retroviral therapy in patients attending a rural health centre in South Africa

V. G. Bhat · M. Ramburuth · M. Singh · O. Titi · A. P. Antony · L. Chiya ·
E. M. Irusen · P. P. Mtyapi · M. E. Mofoka · A. Zibeke · L. A. Chere-Sao ·
N. Gwadiso · N. C. Sethathi · S. R. Mbondwana · M. Msengana

Abstract South Africa has a very high HIV disease burden and proper patient adherence to anti-retroviral therapy (ART) is crucial in achieving optimal treatment outcomes. Factors influencing adherence include demographic and psychosocial factors, medication-related issues and other patient-related matters. This study was carried out in order to determine factors associated with poor compliance to anti-retroviral (ARV) medications in a rural setting. This interview-based descriptive and analytical study was carried out in a health centre where 168 patients who received ARVs were interviewed with pre-structured questionnaires, which covered various important compliance-related aspects. The results showed that 37.5% of the patients were non-adherent. Amongst men, poor adherence was seen in those who were single (48.9%), with tertiary education (60%), in those who consumed alcohol regularly (47.1%) and in those who were unemployed (56.1%). Higher rates of non-adherence in women was associated with being single (36.5%) and in those who used alcohol (60.7%). Medication-related adverse effects were reported in 47% of patients, notably, neuropathy, headache, nausea, loss of memory, diarrhoea and fatigue. Common reasons for missing doses were: being away from home (57.1%), simply forgot (41.3%), side effects (50.8%) and being too busy (49.2%). Poor adherence to ART is an important concern relating to HIV management in our setting and needs to be addressed with more patient-oriented interventions.

V. G. Bhat (✉)
Department of Medical Microbiology, Faculty of Health Sciences,
Walter Sisulu University,
Pvt. Bag X1,
Mthatha, ECP, South Africa
e-mail: vivekbhat2005@yahoo.com

M. Ramburuth · M. Singh · O. Titi · A. P. Antony · L. Chiya ·
E. M. Irusen · P. P. Mtyapi · M. E. Mofoka · A. Zibeke ·
L. A. Chere-Sao · N. Gwadiso · N. C. Sethathi ·
S. R. Mbondwana · M. Msengana
MBChB-3 COBES Group, Walter Sisulu University,
Mthatha, ECP, South Africa

Introduction

More than 5 million people live with HIV/AIDS in South Africa and there is a high prevalence of 18.2% (Stats SA 2006 estimates) of the condition in adults [1]. According to the South African UNGASS Country Progress Report (UNGASS 2008), by the year 2007, 889,000 people needed treatment, of which 488,739 (55%) had enrolled and 371,731 (42%) had initiated on an anti-retroviral therapy (ART) programme (approximately 55% women and 45% men). This service was mainly rendered by public sector accredited service points providing "comprehensive HIV and AIDS services" from 362 public sector health facilities, located in more than 80% of the 254 local municipalities and metropolitan areas [1]. These community clinic-based programmes effectively integrate comprehensive HIV care and treatment into primary health care [2].

Combination therapies now constitute standard anti-retroviral (ARV) treatment regimens. The successful implementation of an ART programme is dependent upon achieving effective control over the viral load [3] in the treatment population and proper adherence to ART is among the most important determinants to successful outcome [4]. In fact, individual treatment success can be seriously compromised and drug resistance may develop if adherence is less than 90% [5]. Various factors can affect patient adherence to ART, thereby, influencing treatment outcomes. The age, education, employment status, income, family type, distance from the clinic and availability of

transportation, cost of medication, discomfort with disclosure of HIV status, inadequate knowledge about the disease and medication, use of alcohol and drugs, religious and spiritual beliefs, presence or absence of AIDS symptoms, levels of health education and healthcare satisfaction, and the presence of co-morbid conditions are among the various patient-related correlates which may influence ARV adherence in patients, as described in various studies [4, 6–9]. Although community ART distribution may decrease stigma, it may hinder some individuals from seeking treatment because of the fear of losing anonymity and, thereby, reduce compliance [2]. The complexity of multiple drugs (too many pills) and dosing may also lead to the undermining of treatment adherence [8, 10], which may further be compounded by undesirable adverse effects [9, 11, 12]. Social and psychological support are also very important motivating factors for treatment adherence [13].

In addition to the above, social, historical and geographical contexts also have a bearing on adherence rates to ART programmes [14], especially in the context of rural South Africa. Although many studies on ARV adherence have been described in developed countries [6] and in sub-Saharan Africa, there is a paucity of studies carried out in rural South Africa, especially the Eastern Cape. The Ngangelizwe community area, with a population of about 82,300, is located 3 km from Mthatha. In 2008, approximately 2,125 patients received ART from the health centre. This study was carried out to determine factors associated with poor compliance among patients on ART in this setting.

Methods and design

This is an interview-based descriptive and analytical study. The study was carried out as a component of the Walter Sisulu University, Faculty of Health Sciences' Community Based Education and Service (COBES) programme, which seeks to familiarise medical students with community-specific medical conditions and related issues and also initiate them into research. Patients attending the Ngangelizwe health centre ARV clinic for ARV medication were selected and included in the study. Questionnaires were used to interview the subjects and were designed to cover important demographic parameters, including age, sex, education, family type, employment and income, levels of medication adherence, reasons for missed doses, adverse effects and other aspects related to medication compliance. A total of 168 men and women in the age group 18–62 years volunteered to be interviewed. The study was performed during the period May–September 2009. The subjects were interviewed face-to-face in the clinic and the pre-structured questionnaires filled in. Informed consent was obtained from all participants and full confidentiality

and anonymity was ensured. Data were assimilated from the questionnaires and the results were entered into MS Excel sheets and Microstat statistics software by Ecosoft was used to analyse the statistical significance of various parameters on compliance.

Results

There were 168 respondents; 67 (39.9%) men and 101 (60.1%) women. The important demographic features are listed in Table 1. Most of the respondents were in the age group 18–48 years. The mean age of the sample was 33.9 years, with a median of 34 and a standard deviation (SD) of 8.5. The majority of those interviewed had secondary education (68.5%). About three-quarters of the respondents were married and most of them were cohabiting. A high proportion of the respondents were unemployed (62.5%), 73.8% (124 out of 168) of the respondents said that their HIV status was known to others, usually some family member or close friend, and almost 95% felt that social support was an important factor motivating them toward treatment adherence.

A total of 37.5% reported to having been poorly compliant with their medication at some time, with men (41.8%) showing greater non-compliance than women (34.5%), but this was not statistically significant. Non-compliance was highest in the age group 18–28 years (65%) and lowest in those >48 years of age (12.5%). The relation between adherence and some important demographic parameters are summarised in Fig. 1. Amongst men, poor adherence was seen in those who were single (48.9% NC=non-compliant), with tertiary education (60% NC), those who consumed alcohol regularly (47.1% NC) and in those who were unemployed (56.1% NC). In contrast, married (22.2% NC), employed men (16.7% NC) and teetotallers (25% NC) showed better medication adherence. Amongst women, higher rates of non-adherence was associated with being single (36.5% NC) and in those who drank alcohol (60.7% NC). No person in the study group had ever discontinued the ART for any reason. Of those who were poorly compliant, 48% missed the doses only sometimes (once or twice a month); the remaining missed them more regularly (more than twice a month). Most of them seemed to have missed the doses within the last month (Fig. 2).

A total of 79 (47%) patients (comprising 54 women and 25 men) reported experiencing some symptoms or side effects which they attributed to the medication. However, only less than half of these cases (40.5%) admitted to having missed doses due to side effects. The common perceived symptoms/side effects that were attributed to the medication by the respondents were pain, numbness or

Table 1 Demographics (*n*=168)

|	Men (*n*=67)	Women (*n*=101)	Total (*n*=168)	Percentage
Age group (years)				
18–28	19	21	40	23.8
29–38	31	48	79	47
39–48	13	28	41	24.4
>48	4	4	8	4.8
Education				
Primary	9	22	31	18.5
Secondary (high school)	48	67	115	68.5
Tertiary (university etc.)	10	12	22	13.1
Employment				
Employed (with job)	15	21	36	21.4
Self-employed	9	16	25	14.9
Pensioner	2	0	2	1.2
Unemployed	41	64	105	62.5
Living with				
Parents/spouse/relatives etc.	57	85	142	84.5
Alone	10	16	26	15.5
Martial status				
Single	45	82	127	75.6
Married	18	18	36	21.4
Divorced	4	1	5	3

tingling sensations in the hands and feet (20.8%), fatigue (19.6%), loss of memory (17.9%), headache (15.5%) and dizziness (15.5%), loss of appetite (14.3%) and weight loss (14.3%) (Table 2). Some of the symptoms—peripheral neuropathy, loss of memory and fatigue—were seen to be occurring more commonly in women compared to men (about two-thirds of those with these symptoms were women). However, symptoms most frequently associated with non-adherence included diarrhoea (70.6%), nausea/vomiting (64.7%), hair loss (69.2%) and depression (68.4%). There

were various reasons cited by the patient for non-adherence (Table 3), the most common among these being that they were away from home (57.1%), side effects (50.8%), too busy (49.2%) or simply forgot to take the medicines (41.3%).

Discussion

In a country where the prevalence of HIV is very high, and the disease presents a heavy burden on public health

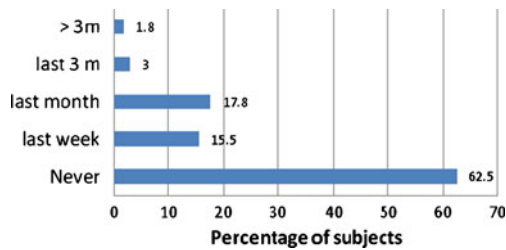**Fig. 1** Relationship of demographic parameters to non-compliance (NC)
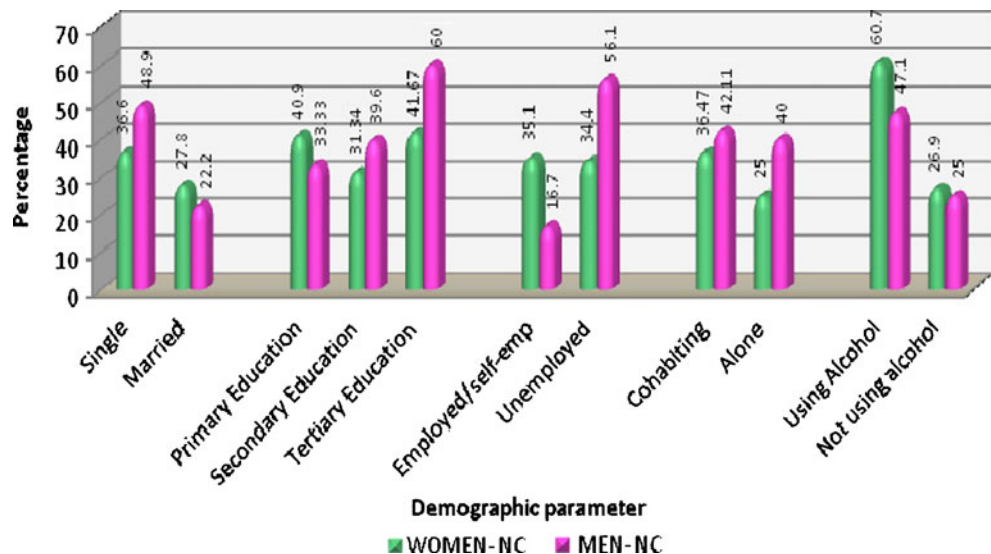
Fig. 2 Time interval since last missed dose

resources, as in South Africa, it is particularly important that optimal treatment outcomes are achieved in order to realise the long-term goals of public health programmes. It is in this context that treatment adherence assumes importance, because it is a key variable not only in determining the efficacy of treatment, but also in preventing the virus from developing resistance to ARVs [15]. Although the challenge of promoting treatment adherence, which is essential for maintaining viral suppression [16], has received increased attention in recent years, it is a matter of concern that rates of adherence still remain sub-therapeutic [17].

In our study, the percentage of patients who were fully adherent was 62.5%. In comparison, another study in South Africa has reported higher adherence rates of 79% [18]; studies in other parts of the world have shown rates ranging

Table 2 Perceived symptoms due to anti-retroviral (ARV) medications

Symptoms	Percentage	Percentage non-adherent because of symptom
Fatigue, lower energy	19.6	48.5
Fever, chills or sweats	9	40.6
Dizziness	15.5	42.3
Pain, numbness or tingling sensations in the hands and feet	20.8	45.7
Loss of memory	17.9	36.7
Nausea, vomiting	10.1	64.7
Diarrhoea	10.1	70.6
Depression, sadness	11.3	68.4
Anxiety	11.3	57.9
Sleep disorders	8.9	40
Skin rash, itching etc.	8.3	50
Cough, breathlessness	13.1	45.5
Headache	15.5	50
Loss of appetite	14.3	54.2
Bloating, gas, abdominal pain	11.9	45
Muscle, joint pain	7.7	53.8
Sexual dysfunction	8.9	40
Weight gain	13.1	40.9
Weight loss	14.3	45.8
Hair loss or other hair changes	7.7	69.2

Table 3 Common reasons for missed doses

Reason	Percentage
Away from home	57.1
Busy with other things	49.2
Forgot	41.3
Too many pills	23.8
Symptoms/side effects	50.8
Did not want others to notice	19
Change in daily routine	23.8
Fell asleep during dose time	30.2
Ran out of pills	33.3
Felt better	9.5

from 59% in Manipur [12] and 60.4% in Bangalore, India [7] to 79% in a Kenyan study [19]. Most patients seemed to have missed their doses within the last week or the past month, but this could also reflect that recent events are more easily remembered and recollected. In another study, 47% of young respondents reported adherence difficulties at some point during the course of their treatment, with 35% acknowledging treatment discontinuation [11]. In our study, none of the respondents reported to having discontinued the treatment for a prolonged period for any reason.

Various studies have reported reasons for poor adherence in different parts of the world. Factors influencing adherence include demographic and psychosocial factors, medication-related issues and other patient-related matters. In our study, we found no significant gender differences with respect to medication adherence ($p=0.15$). Gender differences with respect to adherence were not noted in most other studies [8, 18, 20]. The age of the patients has also not seemed to correlate with adherence in many studies [8, 21, 22]. However, in this study, we noted that the adherence percentage was lower in the 18–28 years group as compared to older age groups. Other studies have shown a lower cumulative mean adherence at 2 months in younger patients [19] and a higher mean age for adherent patients [23].

Among other demographic factors, we found that married people tended, in general, to be better compliant ($p=0.008$) than their unmarried counterparts. This effect was more pronounced in women than in men. Also, the percentage of adherent patients was better among people who were living with some family member, though it was not statistically significant. It is probable that married people and people living with a family member may tend to have a greater sense of security, of togetherness and cooperation, which may motivate better compliance, but this has not been substantiated in other studies [21, 22]. Although all of the subjects expressed their unhappiness about living with the disease, most had learnt to accept their HIV status and felt that such social support in the form of

family and friends helped them adhere to medication. Acceptance of HIV status, social support networks and lifestyle changes [24], and faith in God and medicine have been associated with a better therapeutic relationship with ARVs and an expression of hope [15].

Employed men showed better compliance than their unemployed counterparts in our study ($p<0.001$). The reason for this may be that employed people might be relatively more motivated with a general sense of greater hope and a positive outlook towards life. The majority of participants in this study were from a relatively disadvantaged socio-economic background with high unemployment rate. However, employment and levels of income have showed no clear correlation to adherence in other studies [4, 7, 21]. Similarly, educational levels were also not correlates of adherence in many studies [7, 21]; however, other investigators showed that higher education was associated with better adherence [25, 26]. Surprisingly, in our study, we found that people with tertiary education were less compliant than those with primary ($p=0.04$) and secondary education ($p=0.016$). Patient-related behaviour like alcoholism has also been associated with a negative influence on adherence [4, 23, 25]; this was also noted in our study ($p<0.001$). Some patients agreed that they felt the use of alcohol made them more vulnerable to forgetting to take their medicines. Regular screening for the use of alcohol and specific alcohol interventions may be effective in decreasing its use and improving adherence and treatment outcomes among HIV-infected persons who have a history of hazardous alcohol use [27].

Amongst the important predictors of adherence are medication-related issues, particularly the perceived adverse effects of the ARV medication. The complicated multi-drug ARV regimens with varying dosing schedules, dietary restrictions and adverse effects make adherence a difficult task [20]. The findings listed in Table 2 are the perceived symptoms/side effects which the patients attributed to the ART. It is possible that some of these may not necessarily have been adverse effects of the medication, but may be related to the disease itself. However, in our study, almost 60% of the patients who experienced side effects still managed to adhere to the medication. Side effects were generally not a deterrent to continuing treatment in another South African study [24]; however, lack of information and continued unpleasant side effects can cause patients to adjust the medication dose or even discontinue treatment [28]. Among those who admitted to being affected by the side effects, maximum association to non-adherence was seen with diarrhoea, nausea, vomiting, depression and hair loss. We found that women were more compliant than men in general, in spite of side effects.

Common reasons mentioned by patients for missing the scheduled doses have included reasons such as "fell asleep", "simply forgot", "was depressed", "busy with other things", "ran out of pills", "was travelling", "side effects" and "did not want people to see", among others [7, 26, 29]. The efficacy of treatment has also had a conflicting effect on adherence in different studies, with reasons like "felt that medicine had no effect" and "felt better" also being among the reasons for missed doses [26]. Most of these were also mentioned by patients in our study. The significant number of patients "who did not want others to see" highlights the underlying problems such as fear of stigmatisation and discrimination, as also reported in another South African study [24]. Stressful life events such as serious illness or death of a family member, loss of job or income etc. may also impact adherence adversely; however, none of our respondents came up with any such issue [30]. In our study, reasons such as "being away from home", "fell asleep" and "to avoid side effects" were more common reasons among men, whereas "busy with other things" and "feeling depressed" was more common among women. Symptoms like depression have been shown to be independent predictors of HIV disease progression and mortality [31]. Treatment literacy and proper advice regarding the importance of continuing treatment would play an important role in this context in promoting adherence [24].

Interestingly, although many people in this region do take recourse to traditional medicines/healers, as some of the respondents did also in the case of HIV infection, none of them believed that these could cure the HIV infection. On the other hand, a significant number (38%) of the respondents believed that modern medicine could cure HIV/AIDS. It is possible that this belief, at least in part, could encourage people to check their status and seek medical intervention.

The health centre where this study was conducted distributes ARVs twice a week, and some patients felt the need to increase the frequency of ARV dispensing days, so that patients have more flexibility vis a vis their other commitments and, thereby, influence adherence rates.

The enhancement of adherence may also be achieved by certain interventions. Ensuring patients' adherence by means of fewer pills and simpler dosing schedules will promote adherence and help minimise the emergence of resistance to ARVs [13]. Individual counselling and social support from family and friends and health care workers play an important role in encouraging adherence [8, 15]. Drug readiness and compliance may be further enhanced by the motivation and support provided by community health care workers [32] and "treatment buddies" and the use of devices like mobile phones [33]. Patients must be encouraged to report any side effects to the clinician and should not discontinue the treatment by themselves. The development of a directly observed therapy adherence intervention for certain groups has also been proposed [11]. More

studies need to be conducted in South Africa to give a wider perspective of factors influencing ARV medication adherence among patients, so that relevant public health programmes can institute necessary interventions to address this important issue.

Limitations

One limitation of this type of self-reported adherence study is the risk of recall anomalies, including some patients overestimating their adherence levels willfully or otherwise. However, the lack of a gold-standard method for assessing adherence does not make things easier [10]. Apprehensions about confidentiality may also hinder free and full participation. The sampling was confined to patients attending one health centre and can limit the generalisation of findings. In addition, adherence being a dynamic phenomenon, a single assessment might be insufficient to optimally characterise adherence in this population.

Conclusion

A significant number of respondents were not fully compliant with the anti-retroviral (ARV) regimen in this study. Patients who were unemployed, unmarried and those consuming alcohol were found to be less compliant than their counterparts. "Being away from home", "being preoccupied with other things", "having side effects" or "simply forgot" were the common reasons for missing doses. Diarrhoea, nausea, vomiting, depression and hair loss were among the perceived adverse effects most frequently associated with non-compliance. Poor adherence to ARVs is an important concern relating to HIV management in our setting and needs to be addressed with greater patient-oriented interventions.

Conflicts of interests No conflicts of interests are declared.

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