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EASTERN OF ROMANIA**

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ADHERENCE TO ANTIRETROVIRAL THERAPY IN HIV/AIDS INFECTED INDIVIDUALS: REASONS FOR NON-ADHERENCE IN THE HIV- POSITIVE POPULATION OF THE NORTH- EASTERN OF ROMANIA

Maria Alexandra LARGU¹, Liviu OPREA², Carmen MANCIUC³

Abstract

Adherence to antiretroviral therapy is one of the main focuses regarding HIV/AIDS in the world at the present time. Numerous studies have identified a wide arrange of factors influencing adherence, from psychological aspects such as depression or poor self-efficacy, to medical aspects such as treatment fatigue, pill burden, side-effects, and also social support, stigma, discrimination, lack of knowledge or lack of access to medical care. The research aims to highlight the main reasons HIV-positive patients from Moldova have for non-adherence to antiretroviral therapy. After studying retrospectively psychological evaluation records of patients hospitalized in the HIV/AIDS Regional Center Iasi, between January 2013 and January 2015, we identified the main reasons invoked for non-adherence: fear of disclosure, related to the possibility of being rejected and stigmatized; "treatment fatigue", manifested through forgetfulness, postponing, due to the emotional impact of taking medication; self-management and self-efficacy, or lack of, enhanced also by the lack of proper information or understanding of the disease; medication side-effects; and also, in some cases, poor economic status, substance abuse, depression. The unique characteristics of the HIV-positive population in Romania make adressing problems of adherence a complex process. Having a holistic approach on the difficulties patients face in taking their medication may facilitate intervention and enhance adhrence, proving beneficial for both the individual and the community.

Keywords: HIV/AIDS, adherence, antiretroviral therapy, Romanian pediatric cohort, treatment fatigue, stigma.

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Introduction

In the era of highly active antiretroviral therapy (HAART), HIV has become a chronic disease, with an increasing life expectancy and a higher level of quality of life. An ideal viral and immunological status, with a low HIV viral load and a high number of CD4 blood cells, assures the individual a higher quality of life (Hughes, Jelsma, Maclean, Darder, & Tinise, 2004; Jelsma, Maclean, Hughes, Tinise, & Darder, 2005). This is provided and sustained by the constant administration of the antiretroviral therapy (ART). This makes antiretroviral treatment (ART) and especially adherence to ART critical for people living with HIV/AIDS (PLWHA). According to the Joint United Nations Program on HIV/AIDS (UNAIDS) GAP Report (published in 2014) more than 35 million people in the world were living with HIV in 2013. In the same year, approximately 2.1 million were newly infected with HIV, and around 12.9 million (37% of the total infected) had access to antiretroviral therapy. Despite of this high addressability, in the year 2013 1.5 million people died from AIDS, due to different infectious diseases and organ failures caused by late diagnosis or non-adherence to ART (UNAIDS, 2014).

Adherence has been defined as “the act of following a course of medication in exactly the manner prescribed” (Paparizos et al., 2013). However, many of the HIV-infected persons that are prescribed antiretroviral drugs stop taking them, for various reasons. In literature, non-adherence to antiretroviral therapy is found to be conditioned by a number of psychological, social, economical, and medical factors.

One recurrent reason for non-adherence cited by patients in in-depth interviews is *forgetfulness*. Patients report to have forgotten to take their daily doses, or taken them at a different time than usual (Amberbir, Woldemichael, Getachew, Girma, & Deribe, 2008; Hansana et al., 2013; Meena et al., 2014; Mitiku, Abdosh, & Teklemariam, 2013; Okoronkwo, Okeke, Chinweuba, & Iheanacho, 2013; Oku, Owoaje, Ige, & Oyo-Ita, 2013; Talam, Gatongi, Rotich, & Kimaiyo, 2008). This forgetfulness is associated with “treatment fatigue” (Tabatabai et al., 2014) and also with low self-efficacy (Dima, Schweitzer, Diaconit, Remor, & Wanless, 2013). “*Treatment fatigue*” is defined as “pill burden”, “loss of desire to adhere to the regimen” and “resistance to taking medicine” (Claborn, Meier, Miller, & Leffingwell, 2014; Merzel, VanDevanter, & Irvine, 2008; Molassiotis et al., 2002). It is an emotional response to taking any pill and is an effect of the life-long pill administration specific a chronic disease such as AIDS (Tabatabai, et al., 2014). *Self efficacy* is first conceptualized by Alfred Bandura (Bandura, 1997). He describes it as a person’s confidence on their capacity to carry out behaviors necessary to reach a desired goal. However, the connection between self-efficacy and adherence to antiretroviral treatment has not been sufficiently explored.

Some studies have shown that lower levels of adherence are registered in the case of patients with emotional distress (Dima, et al., 2013). *Depression* is the most cited psychological impairment in connection to living with HIV/AIDS, sometimes associated with *anxiety* (Belenky et al., 2014; Degroote et al., 2013; Morrison et al., 2014; Reisner et al., 2009). Low adherence is also found to be influenced by *traumatic* events such as sexual and physical abuse or the loss of a

parent or sibling. The psychological processes associated with trauma, especially post traumatic stress disorder (*PTSD*), are shown to impact ART adherence (Keuroghlian et al., 2011; Whetten et al., 2013). *Substance abuse* is also considered in literature as a predictor for non-adherence (Reisner, et al., 2009). Illegal drug use, especially the use of injecting drugs, is associated with refusal of treatment (Shigdel, Klouman, Bhandari, & Ahmed, 2014) or suboptimal adherence (Jiamsakul et al., 2014).

Also related to the psychological determinants of ART adherence, some studies discuss the importance of *social support*. *Family support* is shown to be beneficial in the process of coping with the disease (Katz et al., 2013; Okoror, Falade, Olorunlana, Walker, & Okareh, 2013; Slomka, Lim, Gripshover, & Daly, 2013). Being open about the disease within the family environment encouraged patients to take their antiretroviral medication in a correct manner (Molassiotis, et al., 2002; Obirikorang, Selleh, Abledu, & Fofie, 2013; Reisner, et al., 2009; Sanjobo, Frich, & Fretheim, 2008; Wasti, Simkhada, Randall, Freeman, & van Teijlingen, 2012). However, the psychological mechanisms behind the role of family support in coping have yet to be researched thoroughly. The importance of *peer support* has been discussed in relation to revealing the diagnosis. A comprehensive study on disclosing HIV status (Chaudoir, Fisher, & Simoni, 2011) highlights the importance HIV-positive people give to being able to talk about their disease. The sense of being accepted encourages patients to disclose their diagnosis to close friends and reduces stress associated with taking pills in a social context (Watt et al., 2009). The fear of being rejected by peers generates anxiety and reduces likelihood of taking pills correctly (Kumarasamy et al., 2005; Lyimo et al., 2014; Talam, et al., 2008; Van Tam, Pharris, Thorson, Alfven, & Larsson, 2011). Support and acceptance from *the medical staff* have also been cited as important for coping with HIV/AIDS and for adhering to therapy (Katz, et al., 2013; Root & Whiteside, 2013; Slomka, et al., 2013), but have yet to be investigated in detail.

Literature has identified one of the most common reasons for not taking medication as fear of *social stigma and rejection*. Katz et al. (Katz, et al., 2013) reviewed 75 studies on adherence to ART in HIV-positive individuals and concluded that stigma is one of the main effects of social discrimination that compromises adherence. It does so by threatening the individual's access to social support, which is one of the main pillars that sustain long term coping with HIV (Slomka, et al., 2013). Stigma is manifested through negative attitudes towards people living with HIV/AIDS (PLWHA), whether in their family or community or even in health care facilities (Monjok, Smesny, & Essien, 2009; Root & Whiteside, 2013). In qualitative and quantitative studies regarding barriers to antiretroviral medication adherence, PLWHA often revealed that privacy issues due to fear of stigma are among the top reasons for not taking medication (Bezabhe et al., 2014; Biadgilign, Deribew, Amberbir, & Deribe, 2009; Kumarasamy, et al., 2005; Merten et al., 2010; Reisner, et al., 2009; Sanjobo, et al., 2008; Talam, et al., 2008; Van Tam, et al., 2011; Wasti, et al., 2012).

Spirituality and religion are influential in supporting coping mechanisms that aid psycho-social adjustment and mental health (Lyimo, et al., 2014). Studies

often cite support from a certain religious group or from a spiritual belief as vehicles through which patients receive guidance and help (Giday & Shiferaw, 2010; Ross Michael, 2007; Wasti, et al., 2012). However, qualitative interviews with HIV-positive patients revealed that religious customs (such as fasting during certain religious dates) have a negative impact on ART adherence by preventing them from taking pills regularly; this was shown to be common in Orthodox Christians, Hindus and Muslims (Bezabhe, et al., 2014; Giday & Shiferaw, 2010; Wasti, et al., 2012). Another phenomenon related to both religion and cultural aspects is described by Ross et al. (Ross Michael, 2007) as “*folk epidemiology*” – the mixture of myths and religious beliefs in the general population’s information about HIV. The authors cited myths such as “religious and cultural rituals can remove HIV/AIDS”, or “being a member of a certain religion protects against HIV/AIDS”, that encourage HIV-positive people to refuse taking ART or to engage in risk activities. Other studies show similar beliefs, such as the fact that dinking holy water or simply praying to be a cure for HIV/AIDS (Bezabhe, et al., 2014; Wasti, et al., 2012).

Even though we live in an era of technology, where information circulates freely through different means, *lack of knowledge* about HIV/AIDS is still cited as a common reason for non-adherence. This situation is more common in rural areas and in cases of illiterate patients (Belenky, et al., 2014; Ramchandani et al., 2007; Tomori et al., 2014). A particular case regarding lack of information on the topic of HIV/AIDS is that of young people who have been living with HIV since childhood and have found out about their diagnosis in adolescence. They are often deprived of details concerning the disease (Tomori, et al., 2014) or have distorted perceptions due to the inability to communicate on the topic (Denison et al., 2015; Sanjobo, et al., 2008).

In many of the low income countries of Asia, Latin America and Africa, the main barriers in adherence to ART were poor *living conditions*, which reflected in food insecurity or lack of money for transportation to the medical clinic (Root & Whiteside, 2013). Of the two, *food insecurity* was often evoked in relation to the act of swallowing the pills. Taking ART reportedly increased appetite and led to a strong sensation of hunger in the absence of food. Also, ART side effects such as nausea and diarrhea were enhanced by a poor diet (Kalichman & Grebler, 2010; Musumari et al., 2013; Palar, Martin, Oropeza Camacho, & Derose, 2013; Weiser et al., 2010). This led to the patients’ decision to stop taking pills or to take them only when food was available.

Having no money was cited as a common reason for non-adherence. Even though antiretroviral therapy is offered free of charge to HIV infected individuals from almost all countries in the world, studies have shown that additional costs, such as transportation to a clinic for getting the medication, were a barrier to adherence (Kumarasamy, et al., 2005; Meena, et al., 2014; Musumari, et al., 2013; Tabatabai, et al., 2014; Wasti, et al., 2012). In a study that took place in Guatemala, Campbell et al. reported that less than 50% of the PLWHA interviewed had sufficient economic resources to always reach the medical facilities for appointments or to get medication (Campbell et al., 2010).

Also from an economical point of view, many participants in the qualitative studies have pointed out that *having a job* with a strict schedule prevented them from going to doctors appointments and picking up treatment from clinics. A busy work schedule (Okoronkwo, et al., 2013; Oku, et al., 2013) and having a job requiring traveling (Mitiku, et al., 2013; Talam, et al., 2008) were often cited as reasons for not taking ART on time; authors often cited the complaints PLWHA had regarding the schedule on which medical facilities functioned, which forced them to go during work hours (Palar, et al., 2013). Another factor to be considered is discrimination at the work-place, a behavior reported by patients to be a reason for not taking pills during work hours (Rao, Angell, Lam, & Corrigan, 2008).

The specific characteristics of the antiretroviral treatment may also influence patients' adherence. One highly emphasized aspect is the physical discomfort due to the body's response to certain antiretroviral co-formulations. In a study regarding PLWHA in Estonia, Laisaar et al. cited results from a series of focus-groups in which patient described the most common ART *side-effects* they experienced (Laisaar, Uuskula, Sharma, DeHovitz, & Amico, 2013). These were dizziness/vertigo, feeling sick, psychological effects, and to those, other studies added itching, skin rash, gastrointestinal symptoms such as vomiting and diarrhea, pain and/or numbness and insomnia (Amberbir, et al., 2008; Bezabhe, et al., 2014; Caulbeck et al., 2009; Dima, et al., 2013; Giday & Shiferaw, 2010; Laisaar, et al., 2013; Meena, et al., 2014; Molassiotis, et al., 2002; Monjok, et al., 2009; Shigdel, et al., 2014; Wasti, et al., 2012). Patients also report other aspects of physical distress, apart from the reaction to antiretroviral therapy, the most common being neurocognitive complaints (Degroote et al., 2014; Degroote, et al., 2013). Faced with one or more of these symptoms, patients often decide to skip doses or to stop treatment completely. Fewer are the studies that indicate as a reason to stop therapy the fact that patients feel better or very good (Benea Otilia, 2011).

Also regarding therapy, one study cited a *distrust* patients in sub-Saharan Africa have in Western medicine, and their inclination towards traditional medicine for a cure for AIDS (Merten, et al., 2010). There is little research on this aspect of adherence in relation to cultural beliefs.

The HIV-positive population in Romania

In Romania, the main feature of the HIV positive population is that it is made up 90% of young people infected nosocomially in 1988-1989, also known in literature as the "pediatric cohort". These people have been diagnosed with HIV at age 3-6 and have been living with the infection their entire childhood. They have a history of multiple antiretroviral regimens, having grown up alongside the evolution of highly active antiretroviral therapy (HAART). Growing up with HIV involved being taken care of and strictly monitored by family, medical staff and social services. It meant facing the stigma and discrimination that the Romanian post-communist society associated with HIV and AIDS. All these medical and social aspects impacted the psychological development of HIV-positive youth.

Another part of the HIV population in Romania consists of newly diagnosed cases, with a shift in the average age over 30 years. Statistics show that in the North-Eastern part of the country the main mode of transmission is through heterosexual intercourse, while in the South new cases are recorded especially among intravenous drug users and the homosexual population (MSM). These patients have different characteristics than the “pediatric cohort”, having new-generation antiretroviral regimens and new information regarding HIV/AIDS.

Material and method

The research aims to highlight the main reasons HIV-positive patients from Moldova have for non-adherence to antiretroviral therapy. We studied retrospectively psychological evaluation records of patients hospitalized in the HIV/AIDS Regional Center Iasi, between January 2013 and January 2015. The patients’ files, developed by psychologist in the psycho-social services, are completed after semi-structured clinical interviews. They contain a section in which aspects of adherence to therapy are noted - the number of discontinuations, reasons for non-adherence, and details on how the treatment is administered. From these files we extracted the reasons evoked by patients for discontinuing treatment, as well as for disorganized or random administration. We selected the psychological files of patients who were receiving antiretroviral therapy for at least 6 months, excluding new cases diagnosed or with less than 6 months of treatment. We chose this exclusion criterion because the first 6 months of treatment involve the body accommodating to ART and can be characterized by interruptions that may be justified by medical reasons, not by the patient’s choice. We also excluded files for patients that are in hospice placement centers and patients with severe mental disabilities, in which cases therapy is administered by caregivers.

Results

Participant characteristics

During the two-year period, we evaluated 116 files as follows: 61 in 2013, 53 in 2014 and two in 2015. Patients were 52.5% men and 46.5% women. They came from all over the Moldavia region, with a higher percent Iasi (32.7%) and Suceava (23.5%); we also identified a case from the Republic of Moldova. Regarding HIV status, 31.03% of patients were in stages A1, A2, B1, B2 of HIV infection, at the time the files were filled in, while the majority (68.96%) was in the AIDS stage (acquired immune deficiency syndrome), with 42.24% of the total in the final stage of the disease (C3).

Reasons for non-adherence

All the 116 evaluated patients have reported voluntary interruptions of treatment during their lifetime, with durations ranging between 1 day and 4 years. Of these, 100 still report a low level of adherence, identifying one or more of the following: not taking a dose in the last week, skipping more than 5 doses in the last month, not taking any medication for a certain period of time. Below, we present the main reasons patients gave for not taking ART.

Fear of disclosure

Fear of unintentional disclosure was a recurrent reason for non-adherence. Having their diagnosis made public in their community, family or workplace meant, for most participants, being rejected and stigmatized. As described by one 24 year-old man, having the people in his village know about his HIV status meant “they wouldn’t even want to come close to me or my family”. Taking pills in public means, for some patients, being exposed to questions about the nature of their illness. Some patients refuse to take their ART in social settings, and so they miss doses. A 36 year-old woman living with AIDS for 3 years reported: “I had to tell them [her co-workers] I have a heart disease and I have to take pills for that”.

Another fear that prevents patients from taking their ART regularly is that of being rejected by friends or loved ones. Almost all of the patients whose files we evaluated reported to have hidden their HIV status from their close friends or partner at one point in their lives, because “who would want to be with a sick person” (22 year-old woman). In some cases, even though the partner was aware of their diagnosis, both male and female patients (especially from the “pediatric cohort”) reported having stopped taking pills when moving in together.

“Treatment fatigue”

We evaluated a number of behaviours as being manifestations of treatment fatigue. One of the most frequent was forgetfulness. Some patients described often forgetting to take their medication, if they were out of the house or engaged in an interesting activity. One 28 year-old man reported: “A few years ago I would forget to take my pills at night, because I was watching football games or movies with my friends. My best friend would remind me by asking me repeatedly what time it is, so the others wouldn’t know”. Another behaviour specific to treatment fatigue is postponing. “I would think...I’ll take it later”, one 24 year-old female patient said, “and later I would find something to do, and I would say I’ll take the next dose, but then there was always something keeping me from it”. The emotional weight of taking pills is also a reason for postponing: “I couldn’t take it [the treatment] anymore. I thought ... if I ever see a pill again I would vomit. I felt I was going crazy” (29 year-old woman).

Self-management and self-efficacy

Lack of self-management was identified as an important reason for non-adherence especially in the cases of youth turning from adolescence to adulthood, leaving their families or the placement centers. Being able to keep up with the pill schedule in their new lifestyle was a challenge for some patients. Some reported having to go to high school or to university in another city, and finding it “hard to remember to take pills, to find ways to keep them so that no one would ask questions” (24 year-old man). One 22 year-old woman who grew up in foster care and later moved in with some friends said: “I would get so distracted with talking, and going out, or cooking, or cleaning, that I would forget for days. When she [her foster mother] would call and ask if I took the pills I would remember”.

One very common aspect was lack of proper information or understanding of the disease. Patients often evoked feeling fine as a reason for not taking ART, and feeling ill as a reason to take it, as one 45 year-old man, living with HIV for 7 years, explains: “I would think ... why do I have to take the pills if I am not sick? I feel fine, I look fine... If I were sick, I understand, but I feel ok”. Not being told about the disease in childhood, or not having it been explained, represented a barrier to adherence, especially in patients with lower education levels. “They never told me what it was for [the pill] so I would throw it away and just say I took it” (man, 24 years-old). “I took it on and off for all my life. Now I know I should take it every day to get better but it’s hard” (woman, 25 years-old).

Medication side-effects

Patients consider that some side-effects that antiretroviral therapy has, especially during the first few weeks of administration, are too severe to continue taking pills. One 48 year-old woman said “I felt so sick ... I was dizzy and nauseous, and I couldn’t work, I couldn’t do anything. So I stopped taking them [the pills]”.

Other reasons for incomplete adherence

Other reasons for incomplete adherence included not having food to take the pill with, and not having money to come to the hospital to take the medication. One patient repeatedly said “How can I take the pills if I have nothing in my stomach? It would make me feel even more sick”. Two patients who admitted to substance abuse reported forgetting to take medication during the times they were “high”, and also forgetting “to take the pill box with me, or I didn’t even care about the pills”. Some patients reported that feeling depressed made them “not want to fight anymore” or “not care about what happens” if they didn’t take medication. One patient explained: “We are all going to die some day ... so I don’t care ... I don’t want to complicate my life with taking pills like a sick person ... I want to believe I am healthy”.

Discussions

The main reasons for non-adherence evoked in psychological interviews by the patients in the N-E part of Romania were similar to those found in literature, with some exceptions. The main two reasons that emerged from interviews were fear of disclosure and “treatment fatigue”. Fear of disclosure prevented patients from taking their medication in public or in social situations. It was especially salient in young people who were or intended to engage in a relationship. Fear of rejection by the partner, as well as by the community, were strong reasons to skip doses. These motives appeared in all categories of HIV-positive people, regardless of age, gender, living situation or time of infection. “Treatment fatigue” was, however, more common in the youth from the “pediatric cohort”. Their lifetime-long contact with the medical environment and with antiretroviral drugs has left an impact on their reaction to treatment. This caused, in many cases, a form of rejection towards therapy, and also generated difficulties in managing treatment away from home. Literature has strongly highlighted economical difficulties as a reason for skipping doses. In Romania, however, medication is free, and the economical and social services support HIV-infected individuals. Our study revealed only two complaints regarding poor access to hospitals and to therapy.

A surprising result of our research was the absence of religious aspects within the reasons for non-adherence. The literature review revealed a large number of studies in which persons from different religions stop taking their medication in order to pursue religious rituals. The patients in the Iasi Regional Center seem to take their medication, despite fasting or engaging in other forms of religious behaviour.

We also observed no relationship between traumatic events and adherence. Knowing the patients’ history from interviews and medical records, we identified several cases in which young women went through sexual and physical abuse. However, none of them emphasized those moments as being factors for non-adherence, nor were they among those diagnosed with or accusing depression.

One result that we found interesting is regarding self-management and self-efficacy. The patients whose files we studied identified transitioning from adolescence into adulthood as a challenge regarding adherence to antiretrovirals. They have mentioned their need to be reminded to take ART and their difficulty in adapting to a life where they have to keep track of their adherence.

Implications for further research

Several aspects of adherence that emerged in this study are, as we consider, keys for future research. A connection between self-efficacy, self-management and adherence might be further explored. Also, the motivation behind skipping doses and postponing might be explored in relation to both “treatment fatigue” and social aspects.

Limitations

This study took place in the Iasi HIV/AIDS Regional Center, participants coming from the North-Eastern part of Romania. We cannot extrapolate the findings to other persons living with HIV/AIDS in Romania or in other parts of the world. Truth is also a factor to be taken into consideration: having evaluated patients' self-reports on adherence, we can only assume that these are truthful. Despite the limitations, we consider the findings in this study as being of value.

Conclusion

Adherence to antiretroviral therapy has been widely explored and research has shown that a variety of factors are influential in this process. The way in which the individual refers to ART is first and foremost related to the psychological aspects regarding HIV/AIDS. Of these, the concept of self-efficacy seems to have a great deal of impact on the individual's behavior. Both in literature and in patients' reports, it is connected to forgetfulness and treatment fatigue, as a result of life-long pill administration. Exploring psycho-emotional trauma, anxiety and depression, and also addictions and risk behaviors, may offer a comprehensive image of the HIV-positive individual's psycho-emotional profile. Apart from the psychological aspects, research has shown that socio-economical factors, such as poor living conditions and lack of money, religion, stigma and discrimination, as well as medical factors regarding the body's reaction to treatment, impact adherence to ART. In the North-Eastern part of Romania, some of these factors have a significant impact on HIV-positive patients' adherence. The importance adherence has in the HIV-positive patient's life makes research on this topic essential to for both the individual and the community.

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