REVIEW PAPER

Quality of Life and Adherence to Antiretroviral Drugs

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ABSTRACT

***Introduction*:** Antiretroviral therapy has led to a substantial reduction in HIV-associated morbidity and mortality. Efficacy of antiretroviral treatment in HIV/AIDS is showing inhibition of viral replication and reduction of viral load to a point where viral particles are undetectable in the blood of infected individuals. This has led to the realization that HIV/AIDS is a chronic illness and hence the quality of life of PLWHA needs to be enhanced.

***Purpose*:** The purpose of this literature review is to analyze quality of life and adherence to antiretroviral drugs.

***Method*:** A comprehensive analysis of articles obtained from CINHAL, PUBMED, AIDSLINE, PSYCINFO, and Ohio link was conducted.

***Results*:** Quality of life has received special attention in the last decade because it has been recognized as an outcome of health care and a determinant of disease progression. Quality of life is a complex broad ranging multidimensional concept defined in terms of individual's subjective experiences. The definition by the WHO is more appropriate because it is culturally sensitive. Studies can be undertaken to improve the understanding of quality of life concept itself and the extent to which it is individually, socially and culturally determined. Understanding the dimensions and linkages among the dimensions of quality of life will facilitate the design of optimally effective interventions and organizational structures for quality patient care and also provide information to reveal trends, suggest linkages between practice variations and patient outcomes and identify potentially problematic patterns of care.

Antiretroviral regimens are demanding and difficult, with numerous possible side effects and patients need to take the pills for indefinite periods of time. Efficacy of antiretroviral drugs in HIV/AIDS is showing inhibition of viral replication and reduction of viral load to a point where viral particles are undetectable in the blood of infected individuals. Persons with HIV/AIDS that adhere to medication for at least one year are less likely to experience AIDS related mortality. Hence adherence to antiretroviral regimens is imperative not only for the health of individual patients but also for the health of the public as a whole. Determination of medication adherence leads to development of innovative, effective interventions needed to facilitate behavior change, improve quality of life and prevent resistance to antiretroviral drugs.

***Conclusion*:** The World Health Organization has developed a comprehensive culturally sensitive definition of quality of life. Generally, there is an agreement that quality of life should be measured subjectively from patient self reports and not from clinical assessments. However, there are very few interventions that have been developed to assist persons with HIV/AIDS improve their quality of life. Meanwhile studies on medication adherence have shown that there are three main ways of measuring medication adherence, pill count, self reports and the Medication Event Monitoring System (MEMS) cap. There is need to identify measurement suitable for different economic and

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cultural groups and this will enhance the development of interventions that would apply to each situation appropriately. Zambia can use the empirical evidence on quality of life and medication adherence to identify, develop and implement interventions that would enhance both adherence to antiretroviral drugs and quality of life.

INTRODUCTION

The HIV/AIDS pandemic has become a serious health and economic problem in many countries around the world and more especially in sub-Saharan Africa. By the year 2004, the HIV pandemic had 40 million people globally living with the HIV virus and 70% (26.6 million) of these were in Africa that has only 10% of the world's population [1; 2]. An estimated 22.4 million adults and children were living with HIV in sub-Saharan Africa at the end of 2008 [2]. Zambia, a country in sub-Saharan Africa had an HIV/AIDS prevalence of 16% [3]. The incidence continued to rise with majority of cases converting to AIDS [4, 5;, 6, 4]. In Zambia life expectancy without HIV/AIDS was projected to be 60 years at birth but by 2006, it was projected at 37 years due to the HIV/AIDS infections.

AIDS related illnesses were contributing to over 50% of bed occupancy in most hospitals [1]. Health facility assessments suggest that the pandemic is crowding out patients suffering from conditions that are seemingly less severe than HIV/AIDS thus denying them their right to care. As a result from the HIV/AIDS related mortality, the number of orphans increased to about 800,000 [1, 4;,7]. In 2004, President Mwanawasa declared HIV/AIDS a national emergency and promised to provide antiretroviral medications to 10,000 people by the end of the year. Having exceeded this target, he set another to provide free treatment for 100,000 by the end of 2005. By the end of 2007, 46% of the 330,000 people in Zambia needing ARV treatment were receiving it which is above the African average [8]. Although Zambia currently, has a national strategy to respond to the epidemic, the HIV/AIDS picture is changing but has not made drastic positive changes.

In Zambia HIV/AIDS studies have focused on knowledge, counseling, behavior change, mother-to-child transmission and clinical presentation [9, 10, 11, 12, 13, 14, 15, 16, 17, 18] but there are no published studies which examine the effects of living with HIV/AIDS on a person's quality of life and on adherence to antiretroviral drugs. The long term goal of the paper is to provoke and to encourage development of culturally sensitive interventions to improve quality of life and adherence to antiretroviral drugs at every stage of the HIV/AIDS disease. Empirical evidence has shown that adherence to antiretroviral drugs of less than 95% may lead to treatment failure, development of HIV resistance to drugs and subsequent disease progression [19, 20].

PURPOSE

The purpose of this literature review was to analyze quality of life and adherence to antiretroviral drugs.

METHODS

This compendium of literature was obtained from electronic searches on CINAHL, PUBMED, AIDSLINE, PSYCINFO and also search conducted on individual journals on Ohio link, and manual retrieval of articles that were not retrieved from electronic search but were cited in articles reviewed. The search words were 'quality of life and HIV/AIDS; HIV/AIDS functional status and general health perceptions; and adherence to antiretroviral drugs'. Each manuscript was analyzed individually according to all the following characteristics: purpose, conceptual framework, research questions/hypothesis, variables, sample, measures/instruments, method/statistical procedures, results, interpretation, recommendations and implications for health care.

Quality of Life

Quality of life is an existential multi-dimensional concept that is a semantic representation which typically symbolizes ideas and meaning and expresses an abstraction [21; 22; 23; 24]. Quality of life has received special attention in the last decade because it has been recognized as an outcome of health care and a determinant of disease progression. There are several definitions of quality of life.

In a qualitative study [25] quality of life is defined as a culturally dynamic and uniquely subjective perception that reflects values, preferences and

reactions related to what is important, satisfying or the focus of attention in lives of individuals. The World Health Organization Quality of Life group [26] defines quality of life as "individual's perception of their position in life in the context of the culture and value system in which they live and in relation to their goals, expectations, standards and concerns'. Quality of life, therefore, is not an empirical but rather an entity whose definition is based on consensus. Shumaker, Ellis & Navghton [27] suggest that there is a need for a definition of quality of life that can be used for evaluating the current and potential future measures of quality of life in HIV clinical research and should be sufficiently broad to capture aspects of the concept that have persisted in literature and have been empirically supported.

Although quality of life has been described differently in literature, there are two widely agreed upon areas. Firstly, quality of life is a broad raging multidimensional concept incorporating in a complex way individual's physical health, psychological state, level of independence, social relationships, personal beliefs and their relationships to salient features of the environment [26; 28; 29; 30; 31; 32; 23; 6]. In their analysis Sousa, Holzemer, Henry & Slaughter [33] suggest that symptom status, functional status and general health perceptions are key dimensions of health related quality of life.

Secondly, quality of life is defined in subjective terms of individual's subjective experiences; hence it is not necessarily directly observable. Quality of life is a conceptualization that can be measured and used as a quality indicator. Measures should therefore focus on self rating including both positive and negative dimensions as opposed to clinical assessment [33]. Henry & Slaugher, [33] further urge researchers to conduct research based on conceptual models for further clarification and development of the concept. Studying quality of life assessment is a way of restating its commitment to the promotion of a holistic approach to health and health care. Health care is essentially a humanistic transaction between a health care professional and a patient, where the patient's well-being is the primary aim. The above concerns suggest that quality of life cannot be generalized from the western countries (where most studies have been conducted) to sub-Saharan Africa where the culture and economic situation is very different. There is a need to come up with a definition of quality of life suitable for Zambia to guide research and intervention. The definition by the WHO is more appropriate because it is culturally sensitive.

Autonomy was also found to be an important dimension related to health related quality of life which is valued in some cultures but has pejorative connotations of selfishness and rejection in others [26]. The diverse understanding of this concept and the diverse culture has led to the development of several quality of life measures. The World Health Organization Quality of Life (WHOQOL) questionnaire has been developed and translated in several languages to assess individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns [26]. This measure has been developed on the premise that having an international quality of life assessment makes it possible to carry out research collaboratively in different cultural settings to compare directly results obtained in these different settings. Studies can be undertaken to improve the understanding of quality of life concept itself and the extent to which it is individually, socially and culturally determined.

Understanding the dimensions and linkages among the dimensions of quality of life will facilitate the design of optimally effective interventions and organizational structures for quality patient care and also provide information to reveal trends, suggest linkages between practice variations and patient outcomes and identify potentially problematic patterns of care. Improving the length and quality of life is the ultimate objective in treating people living with HIV/AIDS [35]. Literature indicates that quality of life is related to adherence to antiretroviral drugs. The emphasis on management of symptoms in HIV/AIDS at whatever stage of the disease often with a goal of maintaining adherence to antiretroviral drugs enhances quality of life and is clearly in keeping with the philosophy of palliative care [19].

Empirical evidence has shown that symptom status affects quality of life regardless of disease status and needs to be addresses through out the disease trajectory. Patients who were less bothered by symptoms exhibited better general health

perceptions, role functioning, social functioning, mental health, vitality and quality of life, they have shown less pain and less health distress [19]. Some studies have shown that viral load, gender and education are correlated with adherence to antiretroviral drugs [24; 36; 37; 38; 39; 40] while others have shown no significant relationship between adherence to antiretroviral drugs and gender, education or viral load [41; 42]. These findings indicate a need for further research in pursuit for clarification in these diverse findings. In Zambia, there is need to determine quality of life and adherence to antiretroviral medications in order to guide interventions that seek to improve adherence and quality of life. Quality of life has generally shown a positive relationship with adherence to antiretroviral drugs. It has been argued that adherence to antiretroviral drugs leads to better quality of life.

ADHERENCE TO ANTIRETROVIRAL DRUGS

Adherence to medication has been defined as the degree of concurrence between the client's behavior (taking medicine, sticking to diet, taking the right dose and at the right time) and following medical advice on medication regimens [35; 41]. Efficacy of antiretroviral drugs in HIV/AIDS is showing inhibition of viral replication and reduction of viral load to a point where viral particles are undetectable in the blood of infected individuals [35; 38; 43]. Precise dosing schedules must be followed rigorously and other treatment requirements followed religiously to attain the mentioned benefits. Empirical evidence has further shown persons with HIV/AIDS that adhere to medication for at least one year are less likely to experience AIDS related mortality [39, 40, 44]. Therefore, the critical goal for persons with HIV/AIDS is to understand and to enhance medication adherence.

However, adherence to antiretroviral drugs has been frequently sub-therapeutic [45, 46]. Poor adherence to antiretroviral drugs could lead to rapid replication of the HIV leading to generation of resistant mutant strains no longer responsive to available antiretroviral drugs [47; 48; 49]. While adherence to antiretroviral drugs is vital, health care professionals are not accurately able to predict which individuals are likely to adhere to their regimen [39; 40; 46]. Studies are needed to better understand the antecedents and correlates of medication adherence and these factors are not expected to be similar across disease stages [39; 42; 44]. Determining medication adherence will lead to development of innovative, effective interventions needed to facilitate behavior change, improve quality of life and prevent resistance to antiretroviral drugs among HIV positive persons.

Antiretroviral regimens are demanding and difficult, with numerous possible side effects and patients need to take the pills for indefinite periods of time. If patients do not take antiretroviral drugs essentially as prescribed, if doses are missed or taken improperly, resistance is expected, leading to clinical failure. Resistant HIV may be transmitted leading to an untreatable form of disease. Hence adherence to antiretroviral regimens is imperative not only for the health of individual patients but also for the health of the public as a whole [50].

Better understanding of the pathogenesis of HIV and viral activity has suggested that for the highly active antiretroviral therapy (HAART) regimen to be effective, nearly perfect (95%) adherence is necessary to minimize viral load and prevent drug resistance. Non-adherence has public health implications as well. High viral load increases the likelihood of transmission during risky behavior and non-adherent individuals may be more likely to transmit drug resistant strains of virus [36; 41; 43]. The degree of patient adherence to antiretroviral drugs is increasingly recognized to be a key factor.

Non-adherence with prescribed drugs is common in all branches of medicine with quoted varied levels of around 50% or more on a 0-100% range. However, the prevalence and patterns of non-adherence to antiretroviral drugs remain unclear, largely because of the lack of any gold standard for its measurement. A number of studies have found that 90-95% of doses must be taken for optimum viral load suppression. In addition suboptimal adherence to highly active antiretroviral therapy has been associated with more rapid disease progression. It is less certain what the minimum thresholds necessary to maintain long-term suppression of HIV plasma viral load are [19; 45; 51].

Even short periods of sub-optimal adherence to antiretroviral drugs may lead to viral rebound and risk treatment failure and progression of HIV disease. Unfortunately these regimens are among the complex ever prescribed and low adherence to antiretroviral drugs could be directly related to treatment complexity. Adherence to antiretroviral drugs must be considered before attributing treatment failure to emergence of viral resistance alone. Although the emergence of viral resistance to antiretroviral drugs is driven by a variety of factors, low adherence is the most amenable to intervention [40; 41; 52].

Generally, adherence declines with the number of tablets/pills, the frequency of the dosages and the increasing complexity and duration of treatments. It has been argued that the complexity of the regimens, the large number of capsules that must be taken, the numerous side effects, the variety of dosages, the various interactions among the medications as well as between food and the medications may easily lead to confusion and thus poor adherence. Despite the complexity and multiplicity of the factors that influence adherence to antiretroviral drugs, it is only through a thorough understanding of them that we will be able to propose new strategies for promoting diligence in Zambia and the world over. Adherence to antiretroviral drugs has led to a substantial reduction in HIV-associated morbidity and mortality and HIV infection has entered the stage of chronic disease management.[53]. Hence, greater efforts to design and evaluate interventions are likely to lead to increase in adherence to antiretroviral drugs and will thus improve treatment effectiveness.

Non adherence may mean not taking medication at all, taking reduced amounts, taking more medication than prescribed, not taking doses at prescribed frequencies or intervals or not matching medication to food requirements and self initiated holidays. Factors associated with non adherence include lower income, lower education, alcohol use, higher dose frequency and fewer adherence aids such as pillboxes and timers [19; 41]. The frequency and severity of side effects conflicts with daily routine, dietary recommendations, frequency of medication dosages, number of medication dosages, psychological factors such as stress, anger, or denial and physical consideration such as fatigue and sleep [35].

However, there have been no published studies to determine factors associated with adherence to antiretroviral drugs or to identify interventions that can improve adherence behavior in Zambia. Four dimensions of adherence merit consideration when focusing on the behavioral dimension of adherence to antiretroviral drugs include: taking adherence (the extent to which a patient is taking a prescribed drug regimen) timing adherence (the extent to which a patient is adhering to the prescribed schedule for the drug intake) drug holidays (the extent to which a patient is missing several doses in a row), food restrictions (the extent the patient is adhering to drug intake in relation to food restriction) [53].

There are different ways of determining adherence to antiretroviral drugs. The Medication Event Monitoring System (MEMS) is the most reliable and sensitive method of assessing adherence, but it is not feasible in a large HIV-infected population or highly impoverished settings such as Zambia, largely due to cost. Patient self reports has the advantage of low cost, simplicity, and feasibility and correlates reasonably well with viral load and suppression but it can overestimate adherence rates due to recall bias and social desirability [53]. There is no agreed upon standard for adherence and hence it is measured as it is defined either as self reports of pills missed, counts of pills or record keeping from devices of times and dates of bottle openings [41].

Schonnesson, Ross & Bergbrant [30] conducted a study among individuals living with HIV/AIDS. Nearly all women noted that the antiretroviral regimens were exceptionally difficult to follow. A 35-year-old participant wrote '*I take about 16 pills a day and I hate it because you have to eat at a certain time before and after … this is such a hassle for me*'. Another participant stated that '*taking these medications is like being imprisoned; one no longer has freedom regarding one's schedule and daily activities, and this affects one's emotions as well as one's body*'. Taking several pills and sticking to prescribed regimen often constituted barriers to adherence to antiretroviral drugs for the women.

In another HIV/AIDS study findings showed that age, HIV transmission risk factor, primary payer for health care, stage of the disease, employment status, prior participation in HIV research, living alone, use of reminders to take medication, hospitalization within preceding 12 months and complexity of

antiretroviral therapy regimen were unassociated with adherence. Male sex, non-black race, endorsement of perfect adherence to prior HIV therapies, fewer urgent appointments, being antiretroviral therapy naïve at study entry were associated with better adherence to antiretroviral drugs [45].

Another study showed that 90.3% did not miss any doses the day before the interview, a drug holiday exceeding one day was reported by 14.2% during the preceding month and the median duration was 5 days; 52% reported taking all doses exactly on time [40]. While some authors [39] found that the predictors of missing appointments and antiretroviral treatment included being younger, or a member of an ethnic minority, having less severe form of the illness, or having low social support. However other authors have found that demographic factors such as age, sex and ethnicity are not reliable factors in predicting adherence[33; 41; 54]. The studies indicate that the more non-adherent individuals were, the worse the HIV infection profile became. Again the findings of these studies amplify the need to determine the Zambian picture that will serve as basis for intervention.

There is need for further research to identify targets for intervention to facilitate adherence to antiretroviral drugs and serve to caution health care workers against a simplistic view of adherence. Proposed interventions should be as sophisticated as the problems they seek to overcome [40]. Health care providers need to provide the foundation and support for the behavioral dimension of long term disease management [53].

CONCLUSION AND IMPLICATIONS

In Zambia, it is not clear how quality of life is described and what its dimensions are. The lack of delineation of the construct has probably led to inadequate research in this area. However, since Zambia tends to adopt several WHO recommendations and also because the definition of quality of life by WHO is comprehensive and more appropriate, it will be beneficial to adapt and adopt this definition.

Meanwhile studies on medication adherence have shown that there are three main ways of measuring medication adherence; pill count, self reports and the MEMS cap. There is need to identify measurement suitable for different economic and cultural groups such as Zambia to enhance the development of interventions that would be appropriate.

Medication adherence leads to improved quality of life which is the key determinant of the patient's response to treatment and measuring it will help guide strategies. Empirical evidence on quality of life and adherence to antiretroviral drugs can be used to develop implementable interventions that are focused on enhancing quality of life with an ultimate goal of influencing adherence to antiretroviral drugs. Patients could be closely followed up and monitored to enhance adherence to antiretroviral drugs. The other benefits of such a move include enhancing clinician-patient communication and promotion of quality of life.

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