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Predictors of Daily Life Functioning in HIV-Infected Individuals

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Abstract

Background: Daily life functioning refers to the skills needed to independently perform day to day routines and deficits of daily life functioning common among people living with HIV. This study aimed to investigate the role of immunologic, virologic, cognitive functioning, and demographic variables to predict daily life function in HIV-infected individuals.

Methods: We recruited 67 HIV-positive individuals who were under the treatment of Anti-Retroviral Therapy (ART) in Imam Khomeini hospital, Tehran, Iran, in 2016. Prospective-retrospective memory questionnaire (PRMQ), Instrumental Activities of Daily Living interview (IADLs), and flow cytometry test to assess CD4 count were used. The data were analyzed with stepwise regression analysis using SPSS-22 software.

Results: The results of stepwise regression analysis showed that the prospective/retrospective memory complaints are predictive of daily functioning in people living with HIV ($p<0.001$, $F(1,42) = 26.86$, R^2 adj=0.381). Our results also indicated that CD4 cell count, viral load, age, gender, and education do not predict instrumental activities of daily living scores among HIV-infected individuals ($p>0.05$).

Conclusion: Future studies should focus on the effects of prospective/retrospective memory rehabilitation to improve the daily function of HIV-infected individuals. Future studies should also focus on the mediating role of muscle mass decreases between the association of daily life functioning with CD4 and viral load.

Keywords: AIDS, CD4 count, Daily living activities, HIV, Prospective memory

Introduction

It has been estimated that in 2016 about 66000 Human Immunodeficiency Virus (HIV)-infected individuals were living in Iran and 5000 new cases of HIV infection have been estimated to add this number, each year (1).

Some of the HIV-infected individuals report problems in their everyday functioning (2). Everyday functioning refers to the skills needed to independently perform day to day routines. It is especially important in chronic illness, where the illness lasts for a long time, and living independently becomes a crucial priority. Lawton and Brody introduce 8 important subscales of everyday functioning including the ability to telephone use, shopping, food preparation, housekeeping, laundry, mode of transportation, responsibility for own medication, and ability to handle finances (3).

HIV-Associated Neurocognitive Disorder (HAND) results in deficits in everyday functioning such as medication adherence (4), driving a car (5), occupation (6) even after controlling for depression. Almost half of the individuals with HAND face problems in independently managing their everyday functioning (7).

Episodic memory is one of the important predictors of everyday functioning in HIV-infected individuals 2,8,9). Almost half of the people living with HIV report complaints of episodic memory (10). Prior researches have reported the association of retrospective and prospective memory complaints as the two principal components of episodic memory and everyday functioning in HIV-infected individuals (11).

CD4 cell count is another factor that contributes to everyday functioning in HIV-infected individuals. If the number of CD4 cell count reduces to less than 200 *cells/µl*, HIV-infected individuals will develop the Acquired Immune Deficiency Syndrome (AIDS) (12). Prior researches have revealed that HIV-infected individuals with lower levels of CD4 cell count are more dependent on everyday functioning than HIV-infected individuals with higher levels of CD4 cell count. Prior studies also reported that those who progressed to AIDS experience more risks of dependence in everyday functioning (13,14).

To our knowledge, no prior studies have investigated virologic and immunologic predictors of everyday functioning in HIV-infected individuals. In this research, we aimed to further elucidate the immunologic, virologic, demographic, and cognitive predictors of HIV.

Materials and Methods

We recruited 67 HIV-infected individuals who were under the treatment of Anti-Retroviral Therapy (ART) from Imam Khomeini hospital of Iran, Tehran in 2016. We orally asked the patients who went to the Imam Khomeini hospital to enter the research and their medical history were screened from their medical records. Table 1 illustrates the demographic and clinical characteristics of the participants. The inclusion criteria were adult patients with ages ≥ 18 years; the participants were excluded if they were under surgical treatment or admission to the hospital. Prospective-Retrospective Memory Questionnaire (PRMQ), Instrumental Activities of Daily Living interview (IADLs), and flow cytometry test to assess CD4 count were used. In regression analysis, 10 observations for each predictor variable are recommended, and we had 6 predictor variables, where the sample size should be more than 60 (15).

Ethical considerations

Participants voluntarily participated in the research and all the information was kept confidential. Participants also signed a voluntary informed consent form before their involvement in the research. They were told, they can leave the study whenever they want, without any explanation.

Data analysis

We used Pearson correlation to assess the correlation between instrumental activities of daily living and the predictor variables, and step-wise regression to investigate the predictive role of immunologic, virologic, cognitive functioning, and demographic variables to explain instrumental activities of daily living. SPSS-22 was used to analyze the data.

Instruments

Prospective-retrospective memory questionnaire (PRMQ)

PRMQ is comprised of two major domains

including retrospective and prospective memory and has been designed by Crawford, Smith (16). Each domain consists of eight items that are rated on a five-point Likert-type scale that ranges from 1 ("never') to 5 ("very often"). Total scores have a range from 18 to 80. In this research, Cronbach's alpha was 0.90 that showed good internal consistency of the scale.

Instrumental activities of daily living (IADLs)

The scale assesses functional status and the amount of dependence in daily activities and have been designed by Lawton and Brody (17). Instrumental activities of daily living scale are comprised of eight domains including the ability to telephone use, shopping, food preparation, housekeeping,

Table 1. Demographic and HIV disease characteristics of the participants (N=67)

Variables	HIV infected
Age (years)	39.85 (8.38)
Sex	
Men	31 (46.26)
Women	36 (53.73)
Education	
Primary school	8 (11.94)
Secondary school	21 (31.34)
High school	31 (46.26)
University	7 (10.44)
Medical history	
Seizure	3 (4.5)
Concussion	5 (7.5)
Schizophrenia	8 (11.9)
Bipolar	2 (3.0)
Learning disorder	4 (6.0)
Attention deficit hyperactivity disorder	1 (1.5)
Stroke	2 (3.0)
Hepatitis	17 (25.4)
Drug use	21 (31.3)
History of physical injury	7 (10.4)
History of using psychiatric medicine	21 (31.3)
HIV disease characteristics	
Duration of using ARV (months)	56.31 (55.51)
Current CD4 count (cells/*µl*)	509.87 (267.51)
Nadir CD4 count (cells/*µl*)	236.44 (177.31)
Baseline CD4 count (cells/*µl*)	202.02 (184.49)
Plasma viral load (copies/*ml*)	2312.36 (3178.48)

Note. CD4=cluster of differentiation 4; ARV= anti-retroviral.

Table 2. Correlation between instrumental activities of daily living scale and predictor variables (N=67)

	1	2	3	4	5	6	7
IADLs							
PRMQ	0.629**						
CD4 count	-0.065	-0.163					
Viral load	0.209	0.310*	-0.308*				
Age	0.015	0.128	0.025	0.034			
Education	-0.263*	-0.389**	0.075	-0.089	-0.131		
Gender	0.088	0.017	-0.057	0.066	0.276*	-0.086	

Note: *Indicate correlation is significant at the 0.05 level (2-tailed)

** Indicate correlation is significant at the 0.01 level (2-tailed)

Table 3. Results of analysis of variance for the suggested model (N=67)

Predictors	Unstandardized variables			t	Sig.
	B	Standard error	B		
Constant	-0.092	0.043		-2.161	0.037
PRMQ	0.005	0.001	0.629	5.183	0.001

laundry, transportation, responsibility for own medications, and ability to handle finance. For men, the areas of food preparation, housekeeping, and laundering are excluded. Summary scores range from 0 (low function, dependent) to 8 (high function, independent) for women and 0 to 5 for men. In the present study, the Cronbach's alpha was 0.93 which showed high reliability of the questionnaire (18).

Medical assessment

HIV serostatus was determined by two ELISA tests and confirmed by a western blot test. Standard flow cytometry methods were used to assess the CD4 cell count in blood samples. Plasma viral load levels were assessed using RT-PCR.

Results

Table 1 shows the demographic and HIV disease characteristics of the participants.

Stepwise regression analysis was used to predict instrumental activities of daily living scale from PRMQ, immunologic, virologic, and demographic variables. Firstly, we screened the data to investigate the assumptions of conducting regression analysis. As we expected, instrumental activities of daily living scale scores had a severe skewness due to the normal function of a high proportion of the HIV-infected individuals who are under the treatment of ARV medication. We transformed the instrumental activities of daily living scores using Log 10 function. Table 2 displays the correlation matrix between instrumental activities of daily living scale and predictor variables.

As shown in table 2, PRMQ scores had a moderate correlation with instrumental activities of daily living scores ($p<0.01$), and education had a weak correlation with instrumental activities of daily living score, but CD4 cell count ($p<0.05$), viral load scores, gender, and age did not correlate

with instrumental activities of daily living scores ($p>0.05$). Table 3 shows the results of analysis of variance for the suggested model. As shown in table 3, PRMQ predicts instrumental activities of daily living among HIV-infected individuals ($p<0.001$, $F(1,41) = 26.86$, R^2 adj $= 0.381$). The results of stepwise regression analysis also showed that CD4 cell count, viral load, age, gender, and education do not predict instrumental activities of daily living among HIV-infected individuals ($p>0.05$).

Discussion

This study aimed to investigate the role of immunologic, virologic, cognitive functioning, and demographic variables to predict daily life function in HIV-infected individuals. We found that retrospective/prospective memory complaints predict the daily life functioning of people living with HIV. Our findings also indicated that the level of CD4 cell count, viral load, age, gender, and education do not predict instrumental activities of daily living score in HIV-infected people.

The study of Hinkin, Castellon (19) was the first to examine the relationship between prospective memory and adherence to prescribed medication, which showed that there is a link between prospective memory impairment and irresponsibility to medication adherence. Another study examined the relationship between HIV-related neuropsychological deficits and daily life functioning, in a sample of 267 HIV-infected individuals. The author used a detailed neuropsychological test battery and found that about half of the HIV-infected individuals have problems in activities such as shopping, cooking, financial management, medication adherence, and vocational abilities (7). Another study investigated the association between prospective memory and daily functioning in a sample of 66 HIV-infected individuals. They used the Memory for Intentions Screening Test (MIST) to measure prospective memory impairment and self-reported instrumental activities of daily living score to measure daily functioning and reported that prospective memory plays a fairly different role than retrospective memory in daily life functions. They found that prospective memory impairment much more than retrospective memory impairment is associated with dysfunction in the daily life functions of HIV-infected individuals (20).

Similarly, in another study, Contardo *et al* found that event-based prospective memory score (as measured by MIST) contributes to adherence to prescribed medication in a sample of 97 HIV-infected individuals. Besides, the results of another study with a sample of 74 HIV-infected individuals showed that poor long-delay time-based prospective memory predicts poor antiretroviral therapy adherence as measured by electronic monitoring in MIST (21). A prior study demonstrated that poor event-based prospective memory is associated with more frequent use of antiretroviral therapy adherence strategies (22). Lack of treatment adherence may also be the consequence of prospective memory problems (23). Therefore, our findings are in line with prior studies that found that PRMQ is a predictor of instrumental activities of daily living score in HIV. One potential explanation for the link between prospective memory deficits and daily functioning is that the neural circuits like prefrontostriatal circuits which contribute to both daily functioning and prospective/retrospective memory are damaged in HIV-infected individuals (7,20,23). Prospective/retrospective memory impairment is a part of HAND which occurs in the initial exposure to the HIV infection when the virus enters the brain during the early hours and days and crosses the Blood-Brain Barriers (BBB) and results in neurophysiological changes in basal ganglia, frontal neocortex, hippocampus, and cerebral white matter (24-26). This deficit results in problems in learning, attention, working memory, and daily life functioning (7).

Future studies should focus on the effects of prospective/retrospective memory rehabilitation to improve the daily function of HIV-infected individuals. We suggest using retrospective memory strategies to improve retrospective memory deficits, prospective memory training to enhance prospective memory, and meta-memory training to educate patients about their memory deficits and their

adverse consequence for their daily life functioning. Using external aids such as an appointment book for important daily tasks or a programmable electronic device that notify the patients of their important daily life tasks such as medication adherence will also be helpful.

One important subscale of instrumental activities of daily living is adherence to the prescribed medication regimen. Adherence to prescribed medication is linked with survival rates in HIV-infected individuals (27,28). Patients with prospective/retrospective memory deficits, face problems in their adherence to prescribed medication regimen during ART. As a result, enhancing medication adherence using prospective/retrospective rehabilitation is an important target for cognitive rehabilitation of HIV-infected individuals.

Our results also demonstrated that age does not predict instrumental activities of daily living score. Our sample did not include older people and people under 18, and it seems that in this age range, the participants' age is not an important factor to predict instrumental activities of daily living score while in older population, the age role becomes more important. Gender did not predict instrumental activities of daily living score and it is likely that gender differences do not exist in the dependence to the everyday activities in HIV-infected people. We also found that although education has a weak correlation with instrumental activities of daily living score, it does not predict instrumental activities of daily living score in HIV-positive individuals.

Numerous studies have investigated the association between instrumental activities of daily living score and CD4 cell count (13,29-34). One study found that mean CD4 cell counts are lower in HIV-infected individuals reporting dependencies in instrumental activities of daily living than those who reported no dependencies (13). Regarding this, a longitudinal study in South Africa found that higher CD4 cell counts and receiving Highly Active Antiretroviral Therapy (HAART) are associated with a decrease in receiving IADL assistance in both cohorts of urban and rural areas (29). Accordingly, medication adherence, physical activity, and a greater sense of functional independence were associated with a higher CD4 cell count (30). Another study reported a significant correlation between nadir CD4 cell count and depression. They reported that lower nadir CD4 cell count was related to higher depression. Furthermore, they showed that nadir CD4 cell count was a significant predictor of medication adherence and dependence in both basic activities of daily living (ADL) and instrumental activities of daily living (31). A prior study demonstrated that the lower CD4 cell count is associated with lower medication adherence and the inability to get groceries, doing laundry, household chores, and mental functioning (32). Similarly, another study reported that low CD4 count is associated with instrumental activities of daily living and activities of daily living dysfunction in a sample of 184 HIV-infected individuals (33). Contrary to these findings, one study showed that CD4 cell count is not associated with activities of daily living scores (34). In line with this study, we found that CD4 cell count does not predict instrumental activities of daily living scores.

We also found that viral load does not predict instrumental activities of daily living scores in HIV- infected individuals. A prior study reported that having a detectable HIV viral load is related to instrumental activities of daily living scores and activities of daily living dysfunction in a sample of 184 HIV-infected individuals (33). Yarasheski *et al* (35) suggested that muscle mass decrease is linked with decreasing in CD4 cell count and viral load. As a result, it may be that muscle mass decrease is a moderator variable that influences daily functions when the CD4 cell count is low and viral load is high. In this study, we found that viral load has no correlation with instrumental activities of daily living scores and do not predict instrumental activities of daily living scores. It may be that muscle mass decrease play a major role in the deficits of instrumental activities of daily living scores and higher viral load does not predict dysfunction in instrumental activities of

daily living scores per se. Future studies should focus on the role of muscle mass decreases between the association of daily functioning with CD4 and viral load.

Instrumental activities of daily living play a prominent role in independence and hospital discharge in chronic illnesses. Instrumental activities of daily living also predict health-related quality of life (HRQoL) in people living with HIV and is important to designing programs for improving HRQoL (36, 37). As a result, knowing the factors related to instrumental activities of daily living plays a prominent role in the independence of HIV-infected individuals (20). Given the association between prospective/retrospective memory and instrumental activities of daily living, intervention programs to improve instrumental activities of daily living should pay more attention to improving retrospective and prospective memory.

A prior limitation of our study was the lack of control over confounding variables (such as muscle mass decrease, medical history, duration of antiviral therapy, and substance use). Another limitation was the cross-sectional nature of the study. Despite these limitations, our study added to the understanding of the factors that predict daily life functioning in HIV-infected individuals. Future studies should focus on the mediator role of muscle mass decrease in the relationship between instrumental activities of daily living with CD4 cell count and viral load. Future studies should also investigate the efficacy of prospective/retrospective memory rehabilitation to improve the daily life functioning of HIV-infected people.

Conclusion

This study showed that complaints of prospective/retrospective memory are a strong predictor of instrumental activities of daily living in HIV-infected individuals. These results indicated that immunologic and virologic markers do not predict instrumental activities of daily living in HIV- infected individuals. Demographic variables such as age, gender, and education level also did not predict instrumental activities of daily living in HIV-infected individuals although a week correlation was observed between the level of education and instrumental activities of daily living. Future research should pay more attention to the longitudinal changes of predictive variables and their association with instrumental activities of daily living.

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Conflict of Interest

This study was not funded by any organization or other individuals and the authors acknowledge that there is no conflict of interest.

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