Bachelor's thesis

NTNU
Norwegian University of Science and Technology
Faculty of Social and Educational Sciences
Department of Psychology

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Prevalence and Predictors of Mild Neurocognitive Impairment Among People Living With HIV in Iran

An Exploratory Cross-Sectional Study

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Supervisor: Maede Sadat Etesami
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Preface

This bachelor’s thesis marks the end of a three-year bachelor’s degree at NTNU Trondheim. The current study is an empirical research project and accounts for the first step in a process of developing neurocognitive treatment programmes for people living with HIV. The project was planned by Maede Sadat Etesami, who also collected the data.

During the project I have had great opportunities to discuss the study with my supervisor Maede and our student assistant. I would like to thank Maede for an introduction to the research field, and for helpful reviews on the thesis assignments. The reviews mostly considered the structure and placement of tables and paragraphs in the result and discussion section, but the thesis was written independently. The analyses used in the thesis were suggested by Maede but were conducted independently. I would like to raise a special thank you to our student assistant for the introduction to the statistical methods used in the project, help related to the interpretation of results, and for reviews on the article structure by APA guidelines. The majority of the literature used in the thesis were collected independently using search engines such as Google Scholar, ScienceDirect and PubMed. Articles regarding the HIV situation in Iran were suggested by Maede.

I would like to thank my fellow student in this bachelor project for valuable discussions during the writing process. In addition, a special thank you is raised to my friends and my boyfriend for all the support and patience during the project.

This bachelor thesis is written in accordance with the Publication Manual of the American Psychological Association, 7th edition (American Psychological Association, 2020).

Abstract

Human immunodeficiency virus (HIV) is a major health problem in many areas, and in the Middle East and North Africa region particularly. Following the introduction of antiretroviral therapy, the severity of the HIV infection has decreased. However, around 30-60% of people living with HIV (PLWH) experience neurocognitive impairments, which affect their quality of life. The current study investigated differences in neurocognitive function between PLWH (*n* = 63), and people living without HIV (PLWoH; *n* = 63) in an Iranian sample. By using computerized neurocognitive tests from the Vienna Test System, the prevalence of neurocognitive impairment in global function and six other domains was determined through implementing receiver operating characteristic (ROC) curve cut off *t*-scores from Iranian PLWoH. Associations between demographic, psychosocial and medical factors and cognitive function were assessed using Spearman Rho and Pearson correlation analyses. Significant covariates were included in an analysis of covariance to investigate neurocognitive differences between groups. We found a prevalence of 59% for neurocognitive impairment in PLWH, and 19% in PLWoH, with gender, educational level, premorbid IQ and CD4+ T-cells/mm^3 identified as significant predictors among PLWH. We found a significant difference between the two groups in global cognitive function and in all domains except from visual memory and selective attention. Our results are important for developing an effective treatment program for neurocognitive impairment in PLWH. We concluded that future research should implement a validated screening program for neurocognitive impairment in PLWH.

Keywords: neurocognitive impairment, HIV infection

Human immunodeficiency virus (HIV) is a major health challenge all around the world. From the first known case in the Democratic Republic of Congo in 1959 (De Cock, 2001), the number of people living with HIV (PLWH) reached 38.4 million in 2021 (UNAIDS, 2022). The virus has developed into a global epidemic, and Joint United Nations Programme on HIV/AIDS (UNAIDS) report estimates of 1.5 million newly infected and 650.000 Acquired Immuno Deficiency Syndrome (AIDS)-related deaths in 2021 (2022). These numbers indicate that HIV is still a major health challenge for the entire world community.

The global trend shows a decreasing prevalence of new HIV infections. However, this is limited to developed countries, while many resource-limited countries still fight the spreading of the virus. This applies in particular to the Middle East and North Africa (MENA) region, where we find Iran amongst others. Iran has been actively engaging in the fight against HIV, with the government implementing national harm reduction programs (Najafi et al., 2020; SeyedAlinaghi et al., 2021) and HIV surveillance systems (SeyedAlinghali et al., 2021).

In 2019, there was an estimated 59.000 PLWH in Iran (SeyedAlingaghi et al., 2021; UNAIDS, 2020), while the Iranian national HIV registry reported a number of 36.000 people diagnosed with HIV in 2017, and almost 39.000 in 2018 (Najafi et al., 2020; SeyedAlinaghi et al., 2021). The main transmission route among the Iranian PLWH has been identified as drug injection by shared needles (Najafi et al., 2020; SeyedAlinaghi et al., 2021; UNAIDS, 2020). UNAIDS country progress report (2020) presented a HIV prevalence of 4.32% among Iranian people who inject drugs (PWID) in 2019. However, the current trend indicates that there is a switch from drug injection to sexual transmission (SeyedAlinaghi et al., 2021).

Establishing national strategic plans and surveillance systems has greatly eased the process of monitoring the prevalence, severity and infection routes among Iranian PLWH

(SeyedAlinaghi et al., 2021). In addition, harm reduction programs have helped creating public awareness about HIV, as well as reducing feelings of shame and taboo. Furthermore, several voluntary HIV counseling and testing (VCT) centres have been established around the country, reporting all newly diagnosed patients to the national HIV program (SeyedAlinaghi, 2021). The VCT centers are run in collaboration with local medical universities (SeyedAlinaghi, 2021) and blood banks (Najafi et al., 2020), from where the data for the current study was collected. Positive Clubs have been established to provide psychological support and information to PLWH in Iran. These clubs are important resources for PLWH, in that they provide services that improve their life quality and ability to manage life (Najafi et al., 2020; SeyedAlinaghi et al., 2021).

Neurocognitive Impairments

HIV is a retrovirus characterized by neurological injury, which manifests itself through neurocognitive disturbances and impairments. It is estimated that around 30-60% of PLWH experience neurocognitive disturbances to some degree (Grant, 2008). Previous research has identified a series of cognitive domains that is found to be impaired in PLWH. Studies investigating specific symptoms in PLWH identified challenges related to working memory and information processing, executive and attentional function and verbal learning (Chan & Valcour, 2021), as well as psychomotor (Grant, 2008) and emotional function (Watkins & Treisman, 2015). Current classification of NCI was developed by the Frascati group, following their establishment of HIV-associated neurocognitive disorder (HAND; Grant, 2008). HAND qualification criteria include test scores of one or two standard deviations below mean scores in minimum two different cognitive domains.

The main biological mechanism of NCI following HIV infection is known to some extent. The virus'(HIV) receptors bind to certain white blood cells (lymphocytes) called CD4+ T-cells in the host. Infected lymphocytes cross the blood-brain barrier and enter the brain, where the virus acts upon microglial cells and reproduce (Alford & Vera, 2018; Watkins & Treisman, 2015). This leads to a chronic inflammation, which has been proposed to be a main characteristic the mechanism resulting in NCI among PLWH. Neurotoxicity caused by inflammation has also been found, in which the proteins gp120 and Tat play a central role (Alford & Vera, 2018; Wallace, 2022).

Following the development and introduction of antiretroviral therapy (ART), the life expectancy for PLWH has increased. Additionally, the number of people with severe NCI has decreased (Alford & Vera, 2018). However, there has been no decrease in the number of PLWH experiencing neurocognitive disturbances (Alford & Vera, 2018; Watkins & Treisman, 2015). As the PLWH population grows older, age and cerebrovascular disease become risk factors, which may also contribute to the neurocognitive impairment that is observed (Alford & Vera, 2018; Watkins & Treisman, 2015). Determining the main effect of age and HIV respectively, and their interaction effect, on cognitive function are therefore important pieces in the puzzle of developing effective neurocognitive treatment methods.

Several previous studies have aimed at identifying risk factors for NCI in PLWH. Demographic factors such as age, gender and educational level have been found to be associated with NCI in several studies from around the world (Haddow et al., 2018). Some studies indicate that educational level is positively correlated with slower progression of symptoms in neurocognitive disorders like Alzheimer's disease, thus functioning as a protective factor (Kim et al., 2022; Rosselli et al., 2020). In addition to demographic factors, psychological and medical factors show associations with NCI. For example, depression has been found to affect cognitive function, and a series of studies have identified depression as a risk factor for NCI (Haddow et al., 2018; Zenebe et al., 2022). HIV duration and CD4+ T-cells/mm^3 has also been found to be related to NCI (Haddow et al., 2018; Zenebe et al., 2022).

The current study accounts for the first phase in a research program that aims to implement neurocognitive treatment programs for PLWH, in order to improve their quality of life and life satisfactory. To develop appropriate treatment programs, the prevalence of NCI and its associated factors in PLWH need to be identified. Our hope is to identify predictors of NCI that previously have been identified in studies from different countries, making it possible to develop universal treatment strategies.

This study aims to identify differences in neurocognitive function between Iranian PLWH and people living without HIV (PLWoH). More specifically, we aim to determine the prevalence of NCI in Iranian PLWH. We also wish to determine the prevalence of impairments in specific cognitive domains. We hypothesize that there is a difference in neurocognitive function between PLWH and PLWoH. Our first prediction is that PLWH will perform poorer in all neurocognitive domains than PLWoH.

Secondly, we aim to determine the effect of demographic, psychosocial and medical factors on neurocognitive function in a sample of PLWH on ART with no history of AIDS, in comparison with a sample of PLWoH. Based on previous studies, we hypothesize that demographic, psychosocial and medical factors affect neurocognitive function among PLWH, thus functioning as predictors.

Method

Ethical Considerations

This study was approved by the Tehran University of Medical Sciences Ethics Committee (Registration code: IR.TUMS.VCR.REC.1396.3323) and the Iran University of Medical Sciences Ethics Committee (Registration code: IR.IUMS.REC1396.30893), and was conducted in accordance with criteria set by the Declaration of Helsinki. All participants provided written informed consent before the start of the study.

Procedures and Design

The study was conducted between August 2017 and January 2019. The data was collected by two trained psychologists. The participants went through a short interview, deciding whether they were eligible for the study. The interview included a demographic questionnaire, the Beck Depression Inventory and the Beck Anxiety Inventory. The next phase involved controlling the potential participants to the exclusion and inclusion criteria discussed later. A future testing appointment were set up for the selected participants to conduct a series of computerized neurocognitive tests. All appointments were in the morning, between 9 am and 12 am. Participants that were not familiar with using a computer completed a 45-minute computer literacy workshop at an appointment prior to the testing.

All participants received breakfast and snacks, in order to keep their blood sugar levels stable. Smoking and coffee consumption was not allowed during the testing, to eliminate the effect of caffeine and nicotine on neurocognitive function (Galindo et al., 2020). The tests were conducted in a closed, dark room with suitable acoustics. Only one participant was in the room at any given time. A licensed cognitive psychologist was present to supervise the participants. An anti-reflexive screen was used to minimize distractions by self-reflection. The neurocognitive tests were administered in the same order for all participants. Each participant was allowed to take a ten-minute break during the tests, without any opportunity to talk to other participants.

Participants

The sample was extracted from the VCT center in Imam Khomeini Hospital Complex, which is the national reference center for HIV and AIDS in Iran. Information was obtained from 200 PLWH and 124 PLWoH, of which a total of N = 126 participants were eligible for the study in accordance with the exclusion criteria that follows. The participants were assigned to two groups – PLWH and PLWoH (control group), each with a sample size of n = 63. In order to have comparable groups, PLWH and PLWoH were matched in relation to sociodemographic factors, and all participants were from an impoverished district in Iran. PLWoH participants were selected from individuals who received negative test results, confirmed using an enzyme-linked immunosorbent assay (ELISA)-test, at the VCT centre and from a blood donation drive run by the Iranian Blood Transfusion Organization.

With regard to the sex and gender equity in research (SAGER) guidelines, the participants' gender was registered to the categories "male" and "female" based on their self-reported gender, and not of their sex as listed in ID papers. In this study there was one transgender participant, assigned to the "female" category. The number of male and female participants in the PLWH group were matched to create as equal group sizes as possible, in order to produce generalizable data. However, there was a larger proportion of men in the group of PLWoH. This is due to less frequent blood donations from women, because of differences in medical factors such as iron levels and blood pressure, among others (Kasraian et al., 2017).

Participants were eligible for the study if they were between the age of 18 and 50 (Cheval et al., 2021). Further inclusion criteria involved being diagnosed with HIV, confirmed using an ELISA test, for at least two years preceding the study (Etesami et al., 2022). Participants were required to be on ART for a minimum of six months prior to the study, as PLWH on ART medication "Efavirenz" may experience disturbances in neurocognitive function during the first six months of treatment (Giancola et al., 2018). Further on, the participants were eligible for the study if they had no history of CD4+ T-cell count below 200/mm^3 (AIDS), based on their medical records (Uldrick et al., 2017). In addition, participants were required to be fluent in Farsi, in order to be able to carry out the initial interview and test procedure.

Participants with a history of traumatic brain injury, according to the DSM-5-criteria, were excluded from the study (Pavlovic et al., 2019) Previous opportunistic CNS infection, previous or active hepatitis C infection, comorbid diseases like cardiovascular disease, cerebrospinal disease or diabetes, led to the exclusion of potential participants (Bar et al., 2021; Chan & Valcour, 2021; Johansen et al., 2020). In addition, participants with a history of alcohol or drug dependence, following the DSM-5-criteria, in the past two years were also excluded (Lappin & Sara, 2019; Spies et al., 2022). Participants currently on psychiatric pharmacotherapy, e.g., benzodiazepines, selective serotonin reuptake inhibitors (SSRIs) etc., were excluded (McNamara et al., 2016). To minimize the possibility that test performance was affected by physical limitations, participants with uncorrected auditory and visual deficits were excluded. In addition, potential participants who regularly performed heavy exercise were excluded, as this is found to enhance cognitive functioning (Mandolesi et al., 2018).

Measurement Instruments

Demographic and Medical Measures

Demographic and medical measures were assessed through a questionnaire, using self-report. The demographic questionnaire included questions about age (continuous variable), marriage status (married, single widowed, divorced-separated), ethnicity (Fars, Kurdish, Turkish, Lor, other), education (under 12 years at school, high school diploma, two years university education, bachelor's degree, master's degree, PhD, other), drug use (yes, no) and smoking (yes, no). Medical measures included transaction route (drug injection, sexual, blood transmission, other, don't know). Years since HIV diagnosis (continuous variable), years on ART (continuous variable), CD4+ T-cells/mm^3 (continuous variable), and history of hepatitis C (yes, no) were confirmed through their medical records.

Psychosocial Measures

Psychosocial measures included depression and anxiety, which was assessed using Beck inventories. In addition, a measure of premorbid IQ was included as a psychosocial measure. Premorbid IQ was assessed using standard progressive matrices from Vienna Test System (VTS).

Beck Depression Inventory Short Form. Depression was assessed using the Beck Depression Inventory Short Form (BDI-SF/BDI-13), which contains 13 items. Depressive symptoms are assessed by grading statements from 0 to 3. Scores above 10 indicate moderate to severe depressive symptoms (Furlanetto et al., 2005). The BDI-SF was performed using pen and paper. The Farsi (Persian) version of the BDI-SF was used for this study, for which Cronbach's alpha values ranging from .89 to .94 have been identified (Dadfar & Kalibatseva, 2016; Rajabi, 2005). This makes the BDI-13 a suitable instrument for psychological testing in Iranian populations.

Beck Anxiety Inventory. Anxiety was assessed using the Beck Anxiety Inventory (BAI), which contains 21 items. Symptoms are assessed by participants grading statements from 0 to 3. Scores from 16 to 25 indicate moderate anxiety, while scores from 26 to 63 indicate severe anxiety (Lashkari et al., 2021). The BAI was performed using pen and paper. A study implementing the BAI on an Iranian population demonstrated a Cronbach's alpha value around .90 (Lashkari et al., 2021). This makes BAI a suitable instrument for assessing anxiety symptoms in Iranian populations.

Raven Standardized Progressive Matrices Short Form. Premorbid IQ was assessed using the Raven Standardized Progressive Matrices Short Form (SPM-S4). The test was computerized and comprised 32 items. SPM-S4 is a non-verbal test that assesses the participants' ability to find a certain pattern in geometric designs, in which a piece is missing. Each task (item) has six to eight alternative solutions (Schuhfried GmbH, 2023). The short form has a time limit of 15 minutes. Reliability measures show values between .77 and .96 for SPM-S4 (Schuhfried GmbH, 2023).

Neurocognitive Measures

The participants' neurocognitive function was mapped using six different tests from the VTS. The neurocognitive tests measure ability in several domains that are related to NCI in PLWH, including, non-verbal learning, planning, visual memory, divided attention, selective attention and spatial attention (Watkins & Treisman, 2015). Cut-off scores were based on receiver operating characteristic (ROC) curve, using scores from Iranian PLWoH (Etesami et al., 2022).

The tests used in this study require about 85-110 minutes to finish, with a mean time of 90 minutes in our sample. Scores from the neurocognitive tests were reported as *t*-scores. A measure of global cognitive function (GCF) was calculated by averaging the participants' *t*-scores in all six domains. Using Iranian norms, the cut-off point for GCF was set to 39.4 (Etesami et al., 2022).

Non-verbal Learning Test. Non-verbal learning was assessed using the Non-verbal Learning Test (NVLT) short form, which consists of 120 items. The test involves a presentation of a meaningless, irregular or regular geometric figure for three seconds, to which the respondents should decide whether or not they have seen the figure before. In the short test, eight of the figures are presented five times. Higher scores indicate better function. Reliability values for NVLT short form lies between .80 and .90 (Schuhfried GmbH, 2023). The cut-off point for NVLT was set to 47 (Etesami et al., 2022).

Tower of London. Planning was assessed using the Tower of London – Freiburg Version (TOL-F) test. The TOL-F includes a planning task that covers a series of different problems. The aim is to assess the participants' ability to plan an action and reflect on its' consequences before it is carried out. Higher scores indicate better function. A cut-off point at 34 was set to identify participants with impairments in the planning domain (Etesami et al., 2022). There is one standard and one short form of the TOL-F test, who both show Cronbach's alpha values above .70 (Schuhfried GmbH, 2023).

Visual Memory Test. Memory was assessed using the Visual Memory Test (VISGED). The test assesses the ability to memorize the position of specific symbols. The participants are presented with a city map, where different symbols are marked. After a short period of time, the map appears without the symbols, and the participants are asked to identify the symbols' previous location. The number of items used varies in relation to the degree of desired precision, and a 14-item version was used for this study. Higher scores indicate better function. The cut-off point for VISGED was set to 61 (Etesami et al., 2022). Reliability measures vary with the number of items included, ranging from .64 to .84 (Schuhfried GmbH, 2023).

Attention tests. Three tests were used to measure different subfunctions of attention – Divided Attention Test, Selective Attention Test, and Spatial Attention and Visual Field Test. In these tests, cognitive function is operationalized as reaction time, meaning that there is a negative relationship between time used and cognitive function scores. The participants' reaction time scores indicate the logarithmic mean of the individual's reaction time (Sturm, 2011).

Divided Attention Test. In the Divided Attention Test, the participants are presented with stimuli in two different sensory channels – either two visual channels or one auditory and one visual, with the latter version applied in the current study. The aim of the test is to determine whether a target stimulus appears two successive times (Schuhfried GmbH, 2023). The cut-off point was set to 31 (Etesami et al., 2022). The Divided Attention Test includes two subtests, and Cronbach's alpha has been calculated to values between .96 and .97 (Schuhfried GmbH, 2023).

Selective Attention Test. The Selective Attention Test involves presentation of stimuli in one or two sensory modalities. The participant is required to discriminate between changes in relevant information and irrelevant information, with the latter being ignored (Schuhfried GmbH, 2023). A cut-off point at 36 was set to distinguish participants with and without spatial attention deficits (Etesami et al., 2022). The Selective Attention Test includes three subtests, and the Cronbach's alpha value lies between .94 and .97 (Schuhfried GmbH, 2023).

Spatial Attention and Visual Field Test. In the Spatial Attention and Visual Field Test, spatial cues are presented in different locations of the participants' visual fields. Both peripheral end central spatial cues are used to measure spatial orienting of attention, by presenting them in four to eight positions in the left or right visual field. A cut-off point at 35.33 was set to determine impairment in this domain (Etesami et al., 2022). The test has fours subtests, and an additional test for visual field/neglect under extinction conditions (Schuhfried GmbH, 2023). The reliability coefficient for the Spatial Attention Test has been calculated to values between .88 and .97 (Schuhfried GmbH, 2023).

Data Analysis

Frequency analyses showed that various items of the education and marriage variables were poorly represented in the sample, with some items being represented by only one or two participants. The education variable was therefore transformed and recoded into new items. PhD, bachelor's degree, master's degree and two years university education were transformed into "higher education" (=3), while high school diploma (=2) and under 12 years at school (=1) remained as independent items. The item "other" remained a separate item but was recoded into a new value (=4). The same procedure was applied to the marriage variable.

Divorced-separated, widowed and single were transformed into “single” (=2), while married remained a separate item (=1).

T-tests were performed on continuous variables and chi-square tests were performed on categorical variables to compare PLWH and PLWoH. The assumption of normality was assessed using Q-Q plots, which showed a somewhat good fit overall for all data points. *t*-values were reported from Welch t-test, thereby controlling for unequal variances. Group comparisons, descriptive and frequency statistics for demographic, psychosocial and medical measures are reported in Table 1.

Neurocognitive test scores for every domain were transformed into new variables differing between scores above cut off point (=0) and scores below cut off point (=1). Frequencies are presented in a prevalence diagram (see Figure 1). The prevalence was reported as percentages.

Figure 1

*Prevalence Diagram for Neurocognitive Impairments in Six Domains and GCF in PLWH and PLWoH (*N = *63).*

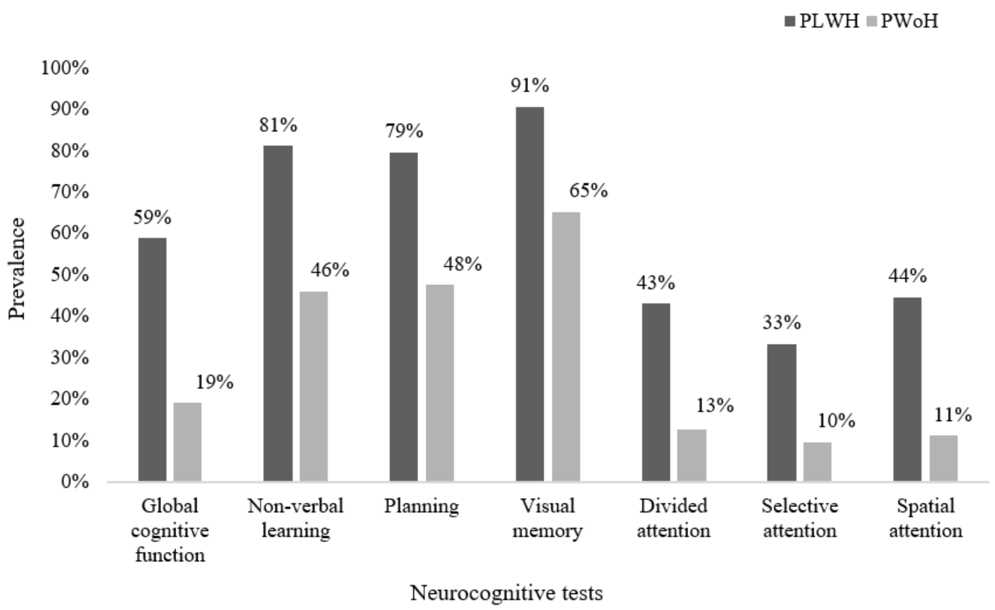

Table 1

Comparison of Demographic, Medical and Psychosocial Characteristics Between PLWH and PLWoH in an Iranian Sample.

	PLWH (*n* = 63)	**PLWoH (*n* = 63)**	**Comparison analysis**
Gender[a] [male], *n* (%)	34 (54)	46 (73)	$x^2(1) = 4.87$, $p = .027$
Marital status[b] [married], *n* (%)	29 (46)	37 (59)	$x^2(1) = 2.12$, $p = .146$
Educational level[c] [under 12 years at school], *n* (%)	32 (51)	21 (33)	$x^2(1) = 4.13$, $p = .042$
Ethnicity[d] [Fars], *n* (%)	31 (49)	30 (48)	$x^2(1) = 0.01$, p = .913
Drug use[e] [no], *n* (%)	45 (71)	57 (91)	$x^2(1) = 8.12$, $p = .004$
Smoking[f] [no], *n* (%)	47 (75)	45 (71)	$x^2(1) = 0.25$, $p = .615$
Transmission route[g] [sexual], *n* (%)	30 (48)	N/A	N/A
	***M (SD)* (*n* = 63)**	***M (SD)* (*n* = 63)**	**Comparison analysis**
Age in years [min, max]	36.76 (8.01) [22, 50]	33.86 (7.56) [19, 50]	$t(123.65) = -2.09$, $p = .039$
Years since diagnosis [min, max]	7.33 (3.74) [2, 18]	N/A	N/A
Years on ART [min, max]	5.54 (3.63) [0, 18]	N/A	N/A
CD4+ T-cells/mm^3 [min, max]	550.73 (186.15) [280, 943]	N/A	N/A
Anxiety score [min, max]	10.66 (9.75) [0, 36]	6.05 (6.35) [0, 27]	$t(105.28) = -3.11$, $p = .002$
Depression score [min, max]	7.36 (5.91) [0, 26]	4.37 (4.93) [0, 18]	$t(115.57) = -3.01$, $p = .003$
Premorbid IQ [mi, max]	91.08 (12.24) [69, 111]	93.94 (16.90) [69, 132]	$t(113.02) = 1.09$, $p = .140$

[a]Gender: 1 = male, 2 = female (transgender registered under self-reported gender).

[b]Marital status – HIV+ group: single = 34 (54%); HIV- group: single = 26 (41%).

[c]Educational level – HIV+ group: high school diploma = 20 (32%), higher education = 11 (18%); HIV- group: high school diploma = 25 (40%), higher education = 16 (25%).

[d]Ethnicity – HIV+ group: Kurdish = 6 (10%), Turkish = 17 (27%), Lor = 3 (5%), other = 4 (6%); HIV- group: Kurdish = 8 (13%), Turkish = 14 (22%), Lor = 6 (10%), other = 2 (4%).

[e]Drugs – HIV+ group: yes = 18 (29%); HIV- group: yes = 6 (10%).

[f]Smoking – HIV+ group: yes = 16 (25%); HIV- group: yes = 18 (29%).

[g]Transmission route - HIV+ group: drug injection = 13 (21%), blood transmission = 3 (5%), other = 6 (10%), don't know = 11 (18%); HIV- group: N/A.

Demographic, psychosocial and medical correlates of GCF were calculated using Spearman and Pearson correlation coefficients in order to establish relationships between variables. Spearman correlation coefficients were reported for ordinal, categorical variables, e.g., gender and educational level. Pearson correlation coefficients were reported for continuous variables, e.g., age and years since diagnosis. The assumption of normality was assessed visually using Q-Q plots, which indicated an acceptable overall fit to the line for all data points. Tests of linearity also showed a linear relationship between variables. Q-Q plots were also used to assess outliers, which was at an acceptable level.

Hierarchical regression analyses were conducted to identify predictors of neurocognitive impairments, using GCF as a dependent variable. The regression analysis was conducted using two blocks, including age, gender, marital status, education and premorbid IQ as predictors for PLWoH. The same variables were included in the analysis of PLWH, in addition to CD4+ T-cells/mm^3 and was analysed using three blocks. Normally distributed residuals were assessed using P-P plots, which showed that the assumption was met for both PLWH and the PLWoH. The assumption of homoscedasticity was assessed using scatter plots, and multicollinearity was controlled for using Variance Inflation Factor values. Both assumptions were met for both groups.

A series of analysis of covariances (ANCOVAs) using group as fixed factor was conducted to compare differences in neurocognitive function between PLWH and the PLWoH, controlling for age, gender, marital status, educational level and premorbid IQ. Pairwise comparisons were performed using Bonferroni post hoc test. Assumptions were investigated and found acceptable.

The significance level was set to $p < .05$ in the current study. Different significance levels were marked with * in tables.

All statistical analyses were performed using IBM SPSS 28.0, except from comparing proportions (chi-square tests) which was performed using MedCalc, and prevalence diagrams which was made using Microsoft Excel.

Results

Participant Characteristics

Descriptive and frequency statistics for demographic, psychosocial and medical measures are summarized in Table 1. Chi-square tests and t-tests were conducted to compare PLWH and PLWoH, and results were reported under "comparison analysis". The groups differed in both demographic and psychosocial measures.

For demographics, there was a significant difference between groups in terms of gender, age, educational level and drug use. There was a higher proportion of male participants in both groups, with 34 participants (54%) among PLWH, and 46 participants (73%) among PLWoH. For PLWoH, there was an almost threefold number of male participants, in contrast to female participants (n = 17, 27%). PLWH (M = 36.76, SD = 8.01) were on average three years older than PLWoH (M = 33.86, SD = 7.56). Among PLWH, the most frequent educational level was "under 12 years at school" (n = 32, 51%). Among PLWoH, "high school diploma" (n = 25, 40%) was the most frequent educational level. The majority of the participants from both groups had never used drugs (71% in PLWH; 90% in PLWoH). The proportion of participants that had used drugs, however, was larger among PLWH (18, 29%) than PLWoH (6, 10%).

The main transmission route of HIV in this sample was sexual. This is consistent with the national trend in Iran, in which there is a shift from transmission through unsafe needle injections to sexual transmission.

For psychosocial measures, there was a significant difference in anxiety and depression scores between the groups. PLWH scored higher than PLWoH for anxiety, with an average score of 10.66 (*SD* = 9.75) for anxiety, in contrast to 6.05 (*SD* = 6.35). For depression, PLWH had an average score of 7.36 (*SD* = 5.91), which was higher than among PLWoH (*M* = 4.37, *SD* = 4.93).

Prevalence of neurocognitive impairment in all six domains and GCF for both groups were identified by transforming test score variables, and results are presented in Figure 1. The diagram shows a higher prevalence of neurocognitive impairments in all domains for PLWH than for PLWoH. For PLWH, the most affected domain was visual memory (VISGED), in which 91% were impaired, followed by non-verbal learning (81%) and planning (79%). For PLWoH, visual memory was the most affected domain, in which 65% were impaired, followed by planning (45%) and non-verbal learning (46%). The largest difference between groups was found for GCF, in which the prevalence of impairment among PLWH (59%) was about threefold the prevalence among PLWoH (19%).

Demographic, Medical and Psychosocial Measures Associated With NCI

Demographic correlates of GCF were calculated using correlation analyses and results for both groups are reported in Table 2. For PLWH, gender was negatively associated with GCF, $r(124) = -.40$, $p = .001$. For PLWoH, there was a negative correlation between age and GCF, $r(124) = -.32$, $p = .010$. This finding is consistent with our second hypothesis.

Table 2

Demographic, Psychosocial and Medical Correlates of GCF in PLWH and PLWoH.

PLWoH		***n***	***M***	***SD***	**GCF**
	GCF	63	44.14	5.39	-
	Gender	63	1.27	0.45	.09
	Age	63	33.86	7.59	-.32**
	Education	62	1.92	0.77	.47***
	Marital status	63	1.41	0.50	.37**
	Ethnicity	60	2.03	1.21	-.06
	Drug	63	1.90	0.30	.08
	Smoking	63	1.71	0.46	-.02
	Anxiety	60	6.05	6.35	.04
	Depression	59	4.37	4.93	.12
	Premorbid IQ	63	93.94	16.90	.69***
PLWH					
	GCF	63	39.17	5.35	-
	Gender	63	1.46	0.50	.40***
	Age	63	36.76	8.01	-.09
	Education	63	1.67	0.76	.51***
	Marital status	63	1.54	0.50	-.12
	Ethnicity	61	2.07	1.26	-.09
	Drug	63	1.71	0.46	-.19
	Smoking	63	1.75	0.44	-.10
	Anxiety	62	10.66	9.75	-.11
	Depression	61	7.36	5.91	.01
	Premorbid IQ	63	91.08	12.24	.38***
	Transmission route	63	2.56	1.39	.14
	Years since diagnosis	63	7.33	3.74	-.05
	Years on ART	63	5.54	3.63	-.05
	CD4+ T-cells/mm^3	63	550.73	186.15	.38**

Note. Spearman correlation coefficients were reported for gender, education, marital status, ethnicity drug use, smoking. Pearson correlation coefficients were reported for remaining variables.

**p* < .05, ***p* < .01, ****p* < .001.

Running a correlation analysis including GCF, educational level, ethnicity, marital status, drug use and smoking showed that educational level was positively associated with GCF in both PLWH, $r(61) = .51$, $p < .001$, and PLWoH, $r(60) = .46$, $p < .001$. Marital status was also positively associated with GCF in PLWoH, $r(61) = .37$, $p = .003$.

Correlation analyses run using GCF, anxiety, depression and premorbid IQ showed that premorbid IQ was positively correlated with GCF in PLWH, $r(61) = .38$, $p = .002$, and at $r(61) = .69$, $p < .001$ in PLWoH. Of medical factors, CD4+ T-cells/mm^3 was positively related to GCF, $r(61) = .38$, $p = .002$.

Predictors of NCI

In order to identify predictors of NCI in both groups, hierarchical regression analyses were conducted based on significant correlates of GCF. For PLWoH, the regression analysis was performed using two blocks. Results are reported in Table 3. The regression analysis indicated that age and marital status predicted 16% of GCF, $R^2_{adj} = .16$, $F(2,59) = 6.76$, $p = .002$, in PLWoH. When adding the predictors education and premorbid IQ, R^2 increased by 32%, $R^2_{adj} = .47$, $F(4,57) = 14.58$, $p < .001$, $\Delta R^2 = .32$, $p < .001$. The final model including age, marital status, educational level and premorbid IQ showed that higher premorbid IQ was the strongest predictor of higher GCF, $B = .18$, $p < .001$, 95% confidence interval [0.11, 0.25]. Higher education, $B = 1.21$, $p > .05$, 95% confidence interval [-0.27, 2.69], being single, $B = .81$, $p > .05$, 95% confidence interval [-1.49, 3.10] and higher age, $B = -.01$, $p > .05$, 95% confidence interval [-0.16, 0.13] were not significant predictors of higher GCF in PLWoH.

Table 3

*Hierarchical Regression Analysis Summary for Predicting GCF in PLWoH (*N *= 63).*

Predictor	*B*	*B* 95% CI	*SE B*	*p*	*F(df)*	R^2_{adj}
Model 1	45.39	[37.35, 53.42]		.002	6.78 (2, 59)	.16**
Age	-0.17	[-0.34, 0.01]	0.09	.058		
Marital status	2.98*	[0.32, 5.63]	1.33	.029		
Model 2	24.43	[14.74, 34.12]		< .001	14.58 (4, 57)	.47***
Age	-0.01	[-..16, 0.13]	0.07	.859		
Marital status	0.81	[-1.49, 3.10]	1.15	.485		
Education	1.21	[-0.27, 2.69]	0.74	.108		
Premorbid IQ	0.18***	[0.11, 0.25]	0.04	< .001		

* $p < .05$, *$p < .01$, *** $p < .001$

For PLWH, the regression analysis was performed using three blocks. Results are reported in Table 4. The regression analysis indicated that gender predicted 20% of GCF, $R^2_{adj} = .20$, $F(1,61) = 16.08$, $p < .001$, in PLWH. When adding the predictors education and premorbid IQ, R^2 increased by 18%, $R^2_{adj} = .36$, $F(3,59) = 12.51$, $p < .001$, $\Delta R^2 = .18$, $p < .001$. A third predictor, CD4+ T-cells/mm^3, was added, leading to a 5% increase in R^2, $R^2_{adj} = .39$, $F(4,58) = 11.10$, $p < .001$. The final model showed that female gender predicted lower GCF scores, $B = -3.77$, $p < .01$, 95% confidence interval [-5.99, -1.55], higher education predicted higher GCF scores, $B = 1.78$, $p < .05$, 95% confidence interval [0.01, 3.56] and higher CD4+ T-cells/mm^3 predicted higher GCF, $B = .01$, $p < .05$, 95% confidence interval [0.00, 0.01]. Higher premorbid IQ, $B = .07$, $p > .05$, 95% confidence interval [-0.04, 0.18] was not a significant predictor of higher GCF in PLWH.

Table 4

*Hierarchical Regression Analysis for Predicting GCF in PLWH (*N *= 63).*

Predictor	***B***	**95% CI**	***SE B***	***p***	***F(df)***	R^2_{adj}
Model 1	46.28	[42.54, 50.03]		< .001	16.08 (1, 61)	.20***
Gender	-4.87***	[-7.29, -2.44]	1.21	< .001		
Model 2	33.60	[24.53, 42.66]		< .001	12.51 (3, 59)	.36***
Gender	-3.97***	[-6.24, -1.70]	1.14	< .001		
Education	2.01*	[0.19, 3.82]	0.91	.031		
Premorbid IQ	0.09	[-0.02, 0.29]	0.05	.111		
Model 3	31.72	[22.74, 40.69]		< .001	11.10	.39*
Gender	-3.77**	[-5.99, -1.55]	1.11	.001		
Education	1.78*	[0.01, 3.56]	0.89	.049		
Premorbid IQ	0.07	[-0.04, 0.18]	0.05	.189		
CD4+ T-cells/mm3	0.01*	[.00, .01]	0.00	.037		

* p < .05, **p < .01, *** p < .001

Controlling for Covariates

A series of one-way ANCOVAs were conducted to compare the effect of HIV on global neurocognitive function and on six different cognitive domains, while controlling for age, gender, marital status, educational level and premorbid IQ. There was a significant difference in the non-verbal learning domain, $F(1, 118) = 14.68$, $p < .001$, between the groups. Cohens *d* indicated a moderate to large effect, $d = .78$. There was also a significant difference in the planning domain, $F(1, 118) = 6.28$, $p = .014$, between the groups. Cohens *d* indicated a moderate effect, $d = .60$. In the divided attention domain, there was a significant difference between the two groups, $F(1, 115) = 5.75$, $p = .018$. Cohens *d* indicated a moderate effect, $d = .60$. There was a significant difference in the spatial attention domain between the two groups, $F(1, 116) = 7.02$, $p = .009$. Cohens *d* indicated a moderate to large effect, $d = .77$. For GCF, there was a significant difference between the groups, $F(1, 118) = 15.83$, $p < .001$. Cohens *d* indicated a large effect, $d = .92$. There was not a significant difference in the visual memory domain, $F(1, 116) = 0.45$, $p = .504$, or in the selective attention domain, $F(1, 117) = 1.26$, $p = .263$, between the two groups. Results from one-way ANCOVAs are presented in Table 5.

Table 5

ANCOVA Results for Global Neurocognitive Performance and Six Cognitive Domains in PLWH and PLWoH.

	PLWH			PLWoH		
NC test[a]	***n***	***M (SD)***	***M*** $(SD)_{adj}$	***n***	***M (SD)***	***M*** $(SD)_{adj}$
Global function	63	39.17 (5.35)	39.97 (4.29)	62	43.95 (5.23)	43.14 (4.33)
Learning	63	39.97 (9.55)	40.50 (8.41)	62	47.02 (8.87)	46.48 (8.43)
Planning	63	31.78 (6.53)	32.19 (7.22)	62	35.81 (7.60)	35.46 (7.17)
Visual memory	63	51.13 (9.13)	52.04 (8.25)	60	54.03 (9.96)	53.08 (8.29)
Divided attention	60	34.07 (7.64)	34.71 (6.89)	62	38.40 (6.81)	37.78 (6.85)
Selective attention	62	40.39 (8.36)	41.28 (7.56)	62	43.75 (7.33)	42.86 (7.56)
Spatial attention	61	38.59 (9.77)	39.38 (8.90)	62	45.09 (8.75)	43.77 (8.90)
		F	***p***	η^{2b}	***d***[c]	**1- β**[d]
Global function		15.83	< .001	.12	.92	.98
Learning		14.68	< .001	.11	.78	.97
Planning		6.28	.014	.05	.60	.70
Visual memory		0.45	.504	.00	.36	.10
Divided attention		5.75	.018	.05	.62	.66
Selective attention		1.26	.236	.01	.43	.20
Spatial attention		1.02	.009	.06	.77	.75

Note. Adjusted means reported for including covariates age, gender, marital status, education and premorbid IQ.

[a]NC test = neurocognitive test. [b]η^2 = partial eta squared, [c]*d* = Cohen's *d*. [d]1-β = observed power.

Discussion

NCI Prevalence

In this study, we sought to determine the prevalence of NCI in Iranian PLWH, in general as well as in specific cognitive domains. Our analyses showed that NCI is significantly more common in PLWH than in PLWoH, with prevalence rates of 59% and 19% respectively. This finding is similar to earlier studies of Iranian samples, where a prevalence of 50% for HAND was found (Mazaheri-Tehrani et al., 2020). However, HAND require stricter diagnosis criteria than measures of NCI, meaning that prevalence of NCI in Mazaheri-Tehrani et al.'s study might have been higher than 50% if it was based on ROC curve cut off scores. In the current study, we cannot make any inferences about the prevalence of HAND or HIV-associated dementia (HAD), as the participants' performance was not assessed up against the Frascati criteria.

A European study by Haddow et al. (2018) found a lower prevalence of NCI, standing at 35% in a sample of participants from four European cities. Compared to a systematic review and meta-analysis that compared worldwide studies of neurocognitive decline in PLWH, our findings are in line with previous studies, identifying a prevalence of NCI around 50% in PLWH in Europe, Asia, Africa, and the United States of America (Zenebe et al., 2022).

The Effect of HIV on Neurocognitive Functioning

Furthermore, we aimed at identifying differences in cognitive function between PLWH and PLWoH. The ANCOVA results presented in Table 5 showed that PLWH and PLWoH differed in all neurocognitive domains, except for visual memory ($p > .05$) and selective attention ($p > .05$) PLWH performed poorer than PLWoH in all domains, which is consistent with our first prediction. The largest difference between groups was in the global domain, where PLWH performed worse than PLWoH ($F = 15.83$, $\Delta M = -3.17$, $p < .001$), with measures of effect sizes indicating a large effect. In terms of specific domains, the largest difference between groups was in the non-verbal learning domain ($F = 14.69$, $\Delta M = -5.98$, $p < .001$), followed by spatial attention ($F = 7.02$, $\Delta M = -4.38$, $p = .009$), with PLWH performing worse than PLWoH, when controlling for covariates age, gender, marital status, educational level and premorbid IQ.

For visual memory, PLWH had lower scores than PLWoH, but there was no significant difference between the two groups. In contrast to our finding, previous research that has included visual memory in assessment of NCI found that this domain is usually significantly impaired in PLWH, when compared to PLWoH (Egbert et al., 2020; Kato et al., 2020). However, there are few previous studies on NCI in PLWH that have taken visual memory into account (Egbert et al., 2020; Kato et al., 2020), and we can therefore not say if this finding is unique for the current sample, or if visual memory in fact is not specifically affected by the mechanisms of HIV. Memory has been found to be impaired in PLWH in previous studies. However, this effect may not be present here because the domain measured in our study is too narrow, in that it only focuses on *visual* memory. This is an interesting finding, nevertheless, as visual memory has the highest prevalence rate of NCI in both groups. However, it is important to point out that this measure lacks statistical power, meaning that there may be an undetectable significant difference between groups.

PLWH had lower scores than PLWoH in the selective attention domain, but no significant difference was found between the two groups in this domain. This finding stands in contrast to earlier studies, in which PLWH show impairments in the selective attention domain (Lew et al., 2018; Wang et al., 2017). As for visual memory, there may be a significant difference between the two groups that our study failed to identify, due to lack of power. The lack of power found in both selective attention and visual memory indicate that the neurocognitive tests used to measure these domains are not suitable in our sample, which may be due to the sample size. This calls for the need of a validated screening programme for NCI in PLWH.

Correlates and Predictors of NCI

Another goal of this study was to determine the effect of demographic, psychosocial and medical factors on neurocognitive function in a sample of PLWH on ART in comparison with a sample of PLWoH. For PLWoH, we found that age, educational level, marital status and premorbid IQ were significant correlates of GCF. For PLWH, gender, educational level, premorbid IQ and CD4+ T-cells/mm^3 were significant correlates of GCF. Regression analyses further showed that premorbid IQ was the only significant predictor of NCI in PLWoH, while gender, educational level and CD4+ T-cells/mm^3 were significant predictors of NCI in PLWH.

Premorbid IQ was a significant correlate and predictor of GCF in both groups, meaning that higher premorbid correlated with and predicted higher GCF scores. The positive correlation seen in Table 2 may be due to the design of the SPM S4 used to assess participants' IQ. Intelligence measures involves factors such as perception, pattern recognition and problem solving, among others. These are abilities that are usually considered as "executive functions", and they are central in solving the neurocognitive tests administered in this study. Thus, executive functions and neurocognitive functions seem to be related to intelligence definitions. Based on this, premorbid IQ being a significant predictor may be due to the possibility that measures of IQ measure the same aspects as neurocognitive tests. From the regression results, one can imply that higher IQ may function as a protective factor of NCI, while lower IQ may be a risk factor. However, a low premorbid IQ would also indicate that the individual's cognitive abilities are weaker than an individual with a higher premorbid

IQ. This means that the individual would attain a lower score on neurocognitive tests, independent of an HIV diagnosis.

Educational level was a significant correlate of GCF in both groups, which is in line with previous studies. These results indicate that higher educational levels correlated with higher GCF scores. The two groups differed in that PLWH on average were less educated than PLWoH. However, it was only a significant predictor in PLWH ($B = 1.78$, $p = .049$). This result translates to lower educational levels being a predictor of NCI. Low educational level has been identified as a risk factor of NCI in several previous studies, including studies from African countries as well as European studies (Haddow et al., 2018; Zenebe et al., 2022). A lot of research supports the claim that education improves cognitive function, which could be the reason to why it functions as a protective factor (Chen et al., 2019; Ritchie & Tucker-Drob, 2018).

Age was another significant correlate of GCF in PLWoH, but not in PLWH. The negative association means that higher age is associated with lower GCF scores, which is supported by previous research (Mudrák & Slepička, 2015). Decline in cognitive function is often found with increasing age (Mudrák & Slepička, 2015), and this was therefore an expected finding. However, in the following regression analysis, age was not found to be a significant predictor of NCI. As our study only identified an association between these two variables, we cannot make any inferences about causality. The significant correlation between age and GCF was only found in PLWoH, and not in PLWH. This may be due to the participants' age, as age related cognitive decline normally starts around the age of 50 years old (Cheval et al., 2021). In our sample, participants' age range makes it likely that age has only a limited effect on their cognitive function, which can explain why there was no significant correlation between age and GCF in PLWH.

For PLWoH, marital status was a significant correlate of GCF. The positive correlation translates to being single is associated with higher GCF scores. This finding is interesting, as it stands in contrast to earlier research. A study by Jennings et al. (2022) found that being divorced and widowed had a negative effect on cognitive function. Married individuals are more likely to engage in more cognitively stimulating activities than single individuals, thus maintaining their cognitive functions, leading to higher GCF scores. This is contrary to our findings. However, as we have only identified an association between these factors, we cannot make any causal claims about marital status and GCF. In addition, marital status was not a significant predictor of NCI in either group.

Gender (B = -3.77, p = .001) was identified as a significant correlate and predictor of GCF in PLWH, meaning that female gender is the strongest predictor. This is an interesting result, as the HIV population of Iran consists of an almost threefold number of males (42.952) compared to women (15.501) (UNAIDS, 2020). However, several studies have identified female gender as a risk factor for NCI in PLWH. Psychosocial factors such as low literacy and educational levels are expected to contribute to the gender differences seen in GCF among PLWH by reducing women's cognitive reserve (Rubin et al., 2020). Table 1 shows that the majority of PLWH participants have under 12 years at school, implying that these factors may have an effect in our sample. It is important to point out that Iran is a country strongly driven by an Islamic rule (Aghaei et al., 2020), and as the main transmission route of HIV in Iran is shifting to sexual, strong feelings of shame are associated with an HIV diagnosis (Aghaei et al., 2020). Thus, many women do not visit testing stations or treatment facilities, thereby increasing the severity of HIV and also the chance of it affecting their cognitive function. Due to the lack of female participants in the PLWoH group, these results should be interpreted with caution.

In this sample, participants were assigned to the categories "male" or "female" based on their self-reported gender. Earlier studies have identified transgender people as a high-risk group of HIV infection in Iran (SeyedAlinaghi et al., 2021). Including transgender as a separate category in studies of NCI in PLWH could therefore be appropriate. However, the current study includes only one transgender participant, and adding a separate category in this case would not be useful or yield specifically varying results.

Our study identified CD4+ T-cells/mm^3 as a significant predictor of GCF in PLWH. This finding is in line with earlier studies (Haddow et al., 2018; Zenebe et al., 2022). Zenebe et al. (2022) found that levels of CD4+ T-cells below 500/mm^3 was a risk factor for HAND, and thus also for NCI. Based on this, one can imply that the risk of NCI in PLWH increases with the severity of HIV infection. In our study, CD4+ T-cells/mm^3 in PLWH was on average 550.73, with values ranging from 280 to 943. As normal levels of CD4+ T-cells lies between 500-1500/mm^3 in healthy people (Duro et al., 2018), this indicates that the group in general is at the lower end of this scale.

Psychosocial measures of depression and anxiety showed no association with GCF. This stands in contrast to previous studies that have identified depression as a risk factor for NCI (Zenebe et al., 2022). Descriptive statistics (Table 1) shows that PLWH have higher scores on depression than PLWoH, but neither group means are above 10, which is the cut off for moderate to severe symptoms. Our finding can therefore be due to the severity of depression, in that low to moderate levels of depression may not affect neurocognitive function to a noticeable degree.

Limitations and Future Directions

In relation to the sample size, the two groups have a small number of participants. This is due to the strict inclusion and exclusion criteria, which could also be considered a strength.

Future studies should strive for a larger sample size to achieve more generalizable findings. PLWH and PLWoH were matched for sociodemographic factors to have comparable groups. All participants were collected from a low socioeconomic region, but people with a higher socioeconomic status should be considered in future research.

The gender distribution was equal in the PLWH group, but the control group (PLWoH) lacked female participants, as there was a threefold number of male participants compared to women in this group. As mentioned earlier, this limitation is due to less frequent blood donations made by women in Iran. Future studies should include more female participants in order to balance the gender distribution in both groups. The unequal distribution in the current study may cause problems with generalizability, and findings including gender effects should be interpreted with caution.

In addition, participants were registered as “male” or “female” based on self-reports. Previous studies have identified transgender people as a high-risk group for HIV (Najafi et al., 2020), which was not included as a separate category in our study. Future studies should include transgender participants as a separate category, as this may yield interesting results. However, there was only one transgender participant in our sample, which would not affect our results to a noticeable degree.

Previous research has found physical activity to be associated with higher cognitive functioning, while lack of physical activity and obesity have been found to be associated with poorer cognitive performance (Burkhalter & Hillman, 2011). The current study did not consider these factors, which should be included in future studies. In relation to this, malnutrition has also shown a positive association with cognitive impairment (Suryawan et al., 2022). Our sample consisted of participants from a lower socioeconomic region, meaning that some of the participants may have suffered from malnutrition. This factor should be considered in future studies to determine any confounding effects of malnutrition on neurocognitive function in PLWH.

Participants with a history of CD4+ T-cells/mm^3 below 200 (AIDS) were not eligible for the study, following the strict inclusion and exclusion criteria. Neurocognitive function in PLWH with current or previous AIDS diagnosis was therefore not assessed. The current and previous studies have identified low levels of CD4+ T-cells/mm^3 as a risk factor of NCI in PLWH, and future studies should therefore include participants with current or previous AIDS diagnosis, to determine its effect on neurocognitive function.

In terms of variables included, alcohol consumption was not measured as there was no reliable source of information in the current study, due to Iranian laws forbidding alcohol. Alcohol consumption has been included in several previous studies regarding risk factors of NCI in PLWH and has shown a significant effect in several of them (Haddow et al., 2018; Zenebe et al., 2022). As alcohol is known to effect cognitive function (Rehm et al., 2019), it should be considered in future studies.

When investigating differences between groups while adjusting for covariates (ANCOVA), measures of differences between PLWH and PLWoH in visual memory and selective attention domains lacked statistical power. This means that the tests were not appropriate for the current study, and that there might be differences that our study was unable to identify. A validated test battery for assessing neurocognitive impairment in Iranian PLWH and PLWoH should be applied in future studies.

Conclusion

In this exploratory cross-sectional study, we sought to determine the prevalence of NCI and differences in neurocognitive function between PLWH compared to PLWoH in an Iranian sample. Our findings showed that the prevalence of NCI in PLWH was 59%, and 19%

in PLWoH. We found that PLWH performed poorer than PLWoH in all domains, except from visual memory and selective attention. Lower premorbid IQ, female gender, lower educational level and lower CD4+ T-cells/mm^3 were identified as predictors of NCI in PLWH. Our results were supported by previous research, except from the finding that the two groups did not differ significantly in the visual memory and selective attention domain. These findings are of important for the development of effective treatment methods for neurocognitive impairment. Due to some measures lacking statistical power, a validated screening programme for NCI in PLWH should be developed and implemented. Future research should strive for equal gender distributions in both groups and include additional factors that may affect cognitive functioning in PLWH such as current or previous AIDS diagnosis, as well as investigate alcohol consumption, lack of physical activity, obesity, and malnutrition.

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