AIDS Care

Psychological and Socio-medical Aspects of AIDS/HIV

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/caic20

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To cite this article: Ranveig Langseth, Rigmor C. Berg, Ole Rysstad, Tore Sørlie, Birgit Lie & Vegard Skogen (2021): Prevalence and predictors of fatigue among people living with HIV in Norway, AIDS Care, DOI: 10.1080/09540121.2021.1934379

To link to this article: https://doi.org/10.1080/09540121.2021.1934379

Published online: 01 Jun 2021.

AIDS CARE
https://doi.org/10.1080/09540121.2021.1934379

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Prevalence and predictors of fatigue among people living with HIV in Norway

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ABSTRACT

Fatigue is the most commonly noted symptom among people living with human immunodeficiency virus (PLHIV). The aim of this study was to investigate the prevalence and predictors of fatigue among PLHIV in Norway. Two hundred and forty-four people were recruited from two hospitals to participate in a survey, which contained seven instruments used to investigate mental health, addiction, quality of life, and fatigue. More than a third of the participants (38.5%) suffered from fatigue. Predictors of fatigue were the presence of mental distress (adjusted odds ratio [AOR] 8.98, 95%CI 3.81, 21.15), multimorbidity (AOR 5.13, 95%CI 1.40, 18.73), living alone (AOR 2.99, 95%CI 1.36, 6.56), trouble sleeping (AOR 2.67, 95%CI 1.06, 6.71), and increased body pain (AOR 1.44, 95%CI 1.25, 1.67). To improve the quality of life for many PLHIV, the continuum of HIV care must address fatigue and its predictors.

ARTICLE HISTORY
Received 9 September 2020
Accepted 19 May 2021

KEYWORDS
HIV; fatigue; Norway; mental – and somatic health

Introduction

The introduction of highly active antiretroviral therapy (HAART) in 1996 and the further development of combined ART (cART) have greatly impacted the health of people living with human immunodeficiency virus (PLHIV). Consequently, the life expectancy gap between PLHIV and the general population has narrowed (Antiretroviral_Therapy_Cohort_Collaboration, 2008, 2017). However, many PLHIV experience a multitude of comorbidities and associated diseases (Battegay & Elzi, 2009), with fatigue as one of the most prevalent and disabling conditions experienced (Barroso et al., 2014; Perazzo et al., 2017; Wilson et al., 2016).

Fatigue is described as an overwhelming sense of tiredness, lack of energy, inertia, or fragility that increases with activity and reduces the person's normal capacities. It is a heterogeneous condition of complex and multifactorial etiology, which is often unknown (Afari & Buchwald, 2003; Barroso & Voss, 2013; Davis & Walsh, 2010). The prevalence of fatigue reported in international studies range from 33% to 88% in PLHIV (Henderson et al., 2005; Jong et al., 2010), and from 7% to 42% in the general population (Finsterer & Mahjoub, 2014; Lewis & Wessely, 1992).

To the best of our knowledge, this is the first study to examine the prevalence of fatigue and its predictors among PLHIV in a Scandinavian country.

Materials and methods

All adult HIV-positive patients at the HIV outpatient clinics at the Hospital of Southern Norway (SSHF) and University Hospital of North Norway (UNN) were eligible to participate in this cross-sectional study. We excluded ten participants with a pre-existing diagnosis of a severe mental disorder or cognitive impairment (Figure 1).

The survey comprised seven validated instruments: the Chalder Fatigue Questionnaire (CFQ), 36-Item Short Form Health Survey (SF-36), Hopkins symptom checklist-25 (HSCL-25), Beck's Depression Inventory, version 2 (BDI-II), 16-Item Post Traumatic Stress Scale (PTSS-16), Alcohol Use Disorder Identification Test (AUDIT), and Drug Use Disorder Identification Test (DUDIT).

Fatigue was measured with the CFQ, a validated scale for assessing mental and physical fatigue (Chalder et al., 1993; Jackson, 2015). We used this definition of fatigue

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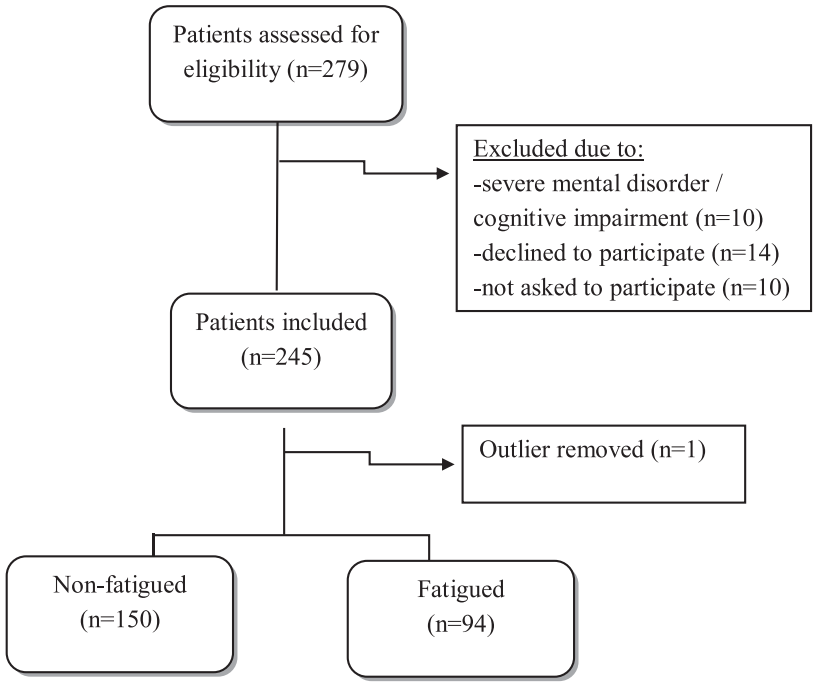

Figure 1. Flowchart of included participants.

as our dependent variable in this analysis, and fatigue was deemed chronic if the symptoms had been present for 6 months or longer. A cut-off above 1.75 based on the HSCL-25 indicated mental distress (Nettelbladt et al., 1993; Winokur et al., 1984).

The study was approved by the Regional Committee for Medical Research Ethics in Norway (ref: 2011/1925 REK Nord).

Using SPSS version 24, we applied descriptive statistics to summarize the demographic and clinical characteristics of the patients (shown as the mean ± the standard deviation, SD) and logistic regression to calculate odd ratios (ORs). To identify the regression model with the best model fit, we entered all the potential explanatory variables (age, sex, education level, origin as an immigrant, men who have sex men (MSM), employment status, cohabitation status, time since diagnosis, anti-viral treatment, virus-suppression treatment, CD4+ count, viral hepatitis, anemia, comorbidities, body pain, mental distress, trouble sleeping, and risk of alcohol or drug abuse) as covariates and ran a backward model with a 0.10% probability of stepwise removal. Five covariates (living alone, high education level, body pain, multimorbidity, mental distress) were significant at a 5% level and were kept in the analysis. The other variables were then re-entered into the analysis and removed several times to check for changes in the model. We eventually identified ten variables representing the socio-demographic, mental health, HIV, and other health-related characteristics of this cohort.

Results

The prevalence of fatigue among the 244 participants (Figure 1) was 38.5%, and 18% (n=44) suffered from chronic fatigue. The fatigue intensity (mean CFQ) increased with the duration of fatigue (data not shown). Table 1 shows the sociodemographic characteristics of the participants and Table 2 presents the HIV and health-related characteristics.

Ten predictors independently contributed to the regression model: age, sex, cohabitation status, high education level, MSM, CD4+ count, multimorbidity, body pain, mental distress, and trouble sleeping (Table 3). Five predictor variables were significantly associated with fatigue: mental distress (AOR 8.98, 95%CI 3.81, 21.15), multimorbidity (AOR 5.13, 95%CI 1.25, 21.15), living alone (AOR 2.99, 95%CI 1.36, 6.56), trouble sleeping (AOR 2.67, 95%CI 1.06, 6.71), and body pain (AOR 1.44, 95%CI 1.25, 1.67). The crude MSM variable was significantly associated with fatigue (OR 2.51, 95%CI 1.17, 5.41), but became non-significant after adjustment (AOR 1.43, 95%CI 0.38, 5.23).

Discussion

We found that the prevalence of fatigue among PLHIV in Norway was 38.5% and 18% suffered from chronic fatigue. This is in the lower range of previously reported findings (Baye et al., 2020; Gebreyesus et al., 2020;

Table 1. Sociodemographic characteristics of the study sample (*N*=244).

		Chalder Fatigue Scale		Gender	
Characteristics	Total	Non-fatigued	Fatigued	Female	Male
Participants, *N* (%)	244	150 (61.5)	94 (38.5)	114 (46.7)	130 (53.3)
Age (y), mean (SD)	43.7 (11.7)	42.8 (11.6)	45.2 (11.9)	41.7 (10.7)	45.5 (12.3)
Hospital *N* (%)					
UNN	135 (55.3)	89 (59.3)	46 (48.9)	63 (55.3)	72 (55.3)
SSHF	109 (44.7)	61 (40.7)	48 (51.1)	51 (44.7)	58 (44.7)
Gender, *N* %					
Female	114 (46.7)	76 (50.7)	38 (40.4)		
Male	130 (53.3)	74 (49.3)	56 (59.6)		
Cohabitation, *N* (%)					
Living together	117 (48)	88 (58.7)	29 (30.9)	64 (65.1)	53 (40.8)
Living alone	127 (52.0)	62 (41.3)	65 (69.1)	50 (43.9)	77 (59.2)
Education, *N* (%)					
Low education	142 (58.2)	94 (62.7)	48 (51.1)	80 (70.2)	62 (47.7)
High education	102 (41.8)	56 (37.5)	46 (48.9)	34 (29.8)	68 (52.3)
Work status, *N** (%)					
Working full time	85 (35.1)	61 (40.7)	24 (26.1)	36 (32.1)	49 (37.7)
Unemployed	28 (11.6)	17 (11.3)	11 (12.0)	16 (14.3)	12 (9.2)
Disable pensioner	28 (11.6)	10 (6.7)	18 (19.6)	11 (9.8)	17 (13.1)
Student	27 (11.2)	21 (14)	6 (6.5)	15 (13.4)	12 (9.2)
Other	74 (30.6)	41 (27.3)	33 (35.9)	34 (30.4)	40 (30.8)
Native country, *N* (%)					
Norway	80 (32.8)	40 (26.7)	40 (42.6)	16 (14.0)	64 (49.2)
Europe	16 (6.6)	11 (7.3)	5 (5.3)	6 (5.3)	10 (7.7)
South-America	10 (4.1)	5 (3.3)	5 (5.3)	1 (0.9)	9 (6.9)
Asia	38 (15.6)	25 (16.7)	13 (13.8)	29 (25.4)	9 (6.9)
Africa	100 (41.0)	69 (46.0)	31 (33.0)	62 (54.4)	38 (29.2)

Note: Mental health and quality of life among people living with HIV in Northern and Southern Norway, 2014–2015.
SD: standard deviation; UNN: University hospital of North Norway; SSHF: Hospital of Southern Norway.
**N*=242, 2 missing fatigued female cases from SSHF.

Henderson et al., 2005; Jong et al., 2010). Possible explanations for the lower prevalence we identified are the improved treatments available today and that all residents in Norway have access to free, high-quality healthcare services and other social support systems. Crucially, the fatigue prevalence among PLHIV was considerably higher than that found in the general Norwegian population. Using the CFQ, Loge et al. found that 22% scored four or more points and 11% had chronic fatigue (Loge et al., 1998).

Mental distress, trouble sleeping, body pain, multimorbidity, and living alone were significant predictors of fatigue. Nearly a third of the participants reported symptoms of anxiety and depression, which mirrors previous findings (Barroso et al., 2010; Barroso & Voss, 2013; Baye et al., 2020; Gebreyesus et al., 2020; Jong et al., 2010; Noh et al., 2012; Rodkjaer et al., 2010). Thus, it seems that identifying and treating depression are important when assessing fatigue treatment strategies. Related, PLHIV have often experienced traumatic events (Corless et al., 2013; Whetten et al., 2008). In our study, all the participants who had PTSD also had severe depression and fatigue, which indicates a link between these three conditions. Similar to findings in Jong et al.'s review (2010), we also found that trouble sleeping was associated with fatigue. In a one-year follow-up study, Barroso et al. (2016) demonstrated that changes in depression correlated with fatigue among PLHIV and that providing coping strategies for depression, encouraging better sleep hygiene, and increased physical activity led to a decrease in the intensity of the participants' fatigue.

Along with fatigue, Wilson et al. (2016) identified muscle aches/joint pain and sleep difficulty as the most prevalent and bothersome symptoms among PLHIV. We identified a strong association between fatigue and the pain experienced by the patients, although we did not assess the underlying cause of this pain. We agree with Loades and Kagee (2017) that further research is required to investigate the role of pain concerning HIV-related fatigue.

We also found that participants diagnosed with one chronic disease were less fatigued compared to those with two or more diseases. This agrees with the findings in Jong et al. (2010), Corless et al (2013) and Gebreyesus et al. (2020), who documented a relationship between the number of comorbidities and the severity of fatigue. Lastly, there was a strong relationship between living alone and fatigue. This relationship was also found in a recent study among adult PLHIV in Ethiopia (Baye et al., 2020), and in the general case, marriage is found to have a protective effect on health and survival (Zhu & Gu, 2010), which supports our finding.

Concerning implications, to improve quality of life of PLHIV, healthcare providers should consider implementing routines that identify and address symptoms

Table 2. HIV and health-related characteristics of the study sample ($N = 244$).

Characteristics	Total $N = 244$	Chalder Fatigue Scale: Non-fatigued $N = 150$	Chalder Fatigue Scale: Fatigued $N = 94$
Time since diagnose (y), mean (*SD*)	9.36 (7.39)	9.15 (6.85)	9.7 (8.22)
Transmission route, *N* (%)			
Heterosexual	97 (39.8)	62 (41.3)	35 (37.2)
MSM	31 (12.7)	13 (8.7)	18 (19.1)
Other	9 (3.7)	5 (3.3)	4 (4.3)
Unknown	107 (43.8)	70 (46.7)	37 (39.4)
Antiretroviral therapy, *N* (%)	227 (93.0)	138 (92.0)	89 (94.7)
HIV RNA viral load < 50 copies/mL, *N* (%)	211 (86.5)	130 (86.7)	81 (86.2)
CD4+ ($\times 10^9$/L), mean (*SD*)	0.53 (0.26)	0.54 (0.29)	0.52 (0.22)
Hopkins Symptoms Checklist-25, mean (*SD*)	1.64 (.58)	1.35 (.32)	2.09 (.60)
Mental distress, *N* (%)	77 (31.5)	16 (10.6)	61 (64.9)
Beck's Depression Inventory, N^a (%)			
Minimal depression	16 (6.6)	5 (3.3)	11 (12.0)
Mild depression	25 (10.3)	7 (4.7)	18 (19.5)
Moderate depression	15 (6.2)	4 (2.7)	11 (12.0)
Severe depression	19 (7.9)	0 (0)	19 (20.6)
Post-Traumatic Stress Disorder, N^b (%)	15 (6.1)	0 (0)	15 (16.1)
Trouble sleeping, *N* (%)	63 (25.8)	16 (10.7)	47 (50.0)
Body pain, mean (*SD*)	2.93 (2.96)	1.69 (2.21)	4.90 (5.50)
Drug abuse risk, *N* (%)	18 (7.4)	5 (3.3)	13 (13.8)
Alcohol abuse risk, *N* (%)	35 (14.3)	18 (12.0)	17 (18.1)
Hepatitis C antibody, *N*	28 (11.5)	15 (10.0)	13 (13.8)
Anemia, *N* (%)	23 (9.4)	13 (8.7)	10 (10.6)
Comorbidity, *N* (%)			
No comorbidity	191 (78.3)	121 (80.7)	70 (74.5)
Comorbidity	32 (13.1)	21 (14.0)	11 (11.7)
Multimorbidity	21 (8.6)	8 (5.3)	13 (13.8)

Note: Mental health and quality of life among people living with HIV in Northern and Southern Norway, 2014–2015.
SD: standard deviation; MSM: Men who have sex with men, CD4+: T–lymphocyte cell bearing CD4+ receptor; Mental distress: Hopkins Symptoms Checklist-25 > 1.75, Anemia (< 11.5 g/dl for women and < 13.0 g/dl for men).
$N^a = 75$ participants with HSCL-25 score > 1.75.
$N^b = 243$, one missing fatigued case.

Table 3. Logistic regression of factors associated with fatigue ($N = 244$).

	Crude Odds Ratio			Adjusted Odds Ratio		
	OR	95% CI	*p*	AOR	95% CI	*P*
Age	1.02	(0.99, 1.04)	.120	1.01	(0.98, 1.05)	.515
Male gender	1.49	(0.89, 2.51)	.131	0.82	(0.35, 1.94)	.654
Living alone	3.18	(1.84, 5.49)	.000*	2.99	(1.36, 6.56)	.006*
High education	1.58	(0.94, 2.66)	.085	2.15	(0.95, 4.87)	.068
MSM	2.51	(1.17, 5.41)	.018*	1.43	(0.39, 5.23)	.586
CD4+ ($\times 10^9$/L)	0.97	(0.88, 1.07)	.514	0.90	(0.78, 1.04)	.179
Multimorbidity	2.85	(1.13, 7.16)	.026*	5.13	(1.40, 18.73)	.013*
Body pain	1.54	(1.37, 1.73)	.000*	1.44	(1.25, 1.67)	.000*
Mental distress	15.48	(7.93, 30.24)	.000*	8.98	(3.81, 21.15)	.000*
Trouble sleeping	8.38	(4.34, 16.16)	.000*	2.67	(1.06, 6.71)	.037*

Note: Mental health and quality of life among people living with HIV in Northern and Southern Norway, 2014–2015.
OR: crude odds ratio; AOR: adjusted odds ratio; CI: confidence interval; High education level: ≥13 years of school; MSM: men who have sex with men; CD4+: T–lymphocyte cell bearing CD4+ receptor; Mental distress: Hopkins Symptoms Checklist-25 > 1.75.
AOR: all the scores in the logistic regression with 10 covariates (age, sex, living alone, high education level, MSM, CD4+ ($\times 10^9$/L), multimorbidity, body pain, mental distress, and trouble sleeping) are shown in this table.
Age: OR per year increase (scale 18–77); CD4+ ($\times 10^9$/L): OR per 0.10 increase (scale 0.01–1.83); Body pain: OR per 1-unit increase (scale 0–10).
*Significant at 5% level.

of fatigue, depression, pain, and sleep disturbance. Barroso et al. (2016) found that providing depression, sleep, and physical activity support led to a decrease in the intensity of the participants' fatigue. Importantly, depression, sleep disturbances, and fatigue have been found to be associated with treatment failure (Huynh et al., 2013). While we found no independent association between fatigue and CD4 count, viral load, time since diagnosis, we concur with Gay et al. (2011) who list the treatment of fatigue as a strategy to improve ART adherence. We note that there are conflicting results regarding the relationship between fatigue and advanced HIV disease, marked by measures such as clinical stage, CD4 count, and ART regiment (Baye et al., 2020; Gebreyesus et al., 2020), and encourage further research into these associations. Similar to our study, these are cross-sectional investigations that do not allow for causal inferences. On the other hand, we had high response rate, few exclusions, and multivariate analyses, which increase the validity in our results.

Conclusions

More than a third (38.5%) of our sample of PLHIV suffered from fatigue. This is almost two times higher than the estimated prevalence in the general Norwegian population. The strongest predictors of fatigue were mental distress and multimorbidity, along with living alone, trouble sleeping, and body pain. More research on prevention and treatment strategies for PLHIV suffering from fatigue is needed so that these recommendations can be implemented in everyday clinical routines.

Acknowledgements

We would like to acknowledge the participants of this study for taking the time to complete the interviews, and the nurses at the outpatient clinics at SSHF and UNN for supporting the research processes and its implementation.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

The Norwegian Directorate of Health funded part of this work. This report is independent research. The views expressed in this publication are those of the authors and not those of the funder of the project.

Declaration of interest statement

The Project group comprised Vegard Skogen, M.D., Ph.D., a specialist in clinical microbiology, internal medicine, and infectious diseases at UNN and University of Tromsø, The Arctic University (UiT); Tore Sørlie, M.D., Ph.D., a specialist in psychiatry at UNN and UiT; Ole Rysstad, M.D., a specialist in internal medicine and pulmonary diseases at the SSHF; and Birgit Lie, M.D., Ph.D., a specialist in community medicine at the SSHF.

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