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Original Article

Sleep disturbances at the time of a new diagnosis: a comparative study of human immunodeficiency virus patients, cancer patients, and general population controls☆

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ABSTRACT

Objectives: Sleep disturbances are a prevalent and troubling symptom of patients with highly stressful illnesses, such as human immunodeficiency virus (HIV) and cancer. The aim of this study was to compare the prevalence and incidence of sleep disturbances among persons with HIV, those with cancer, and the general population of Taiwan.
Methods: A matched cohort study design was used to compare the risk of sleep disturbances among three groups using reimbursement claims recorded in Taiwan's National Health Insurance Research Database (NHIRD). A total of 14,531 HIV-infected persons were compared with 1493 cancer patients and 1373 general population controls matched by gender and age. Cox proportional hazard regression models were used to test the hazard risk of sleep disturbances among the groups.
Results: The mean durations between the date of the initial HIV/cancer diagnosis and onset of sleep disturbances of HIV-infected persons, cancer patients, and controls were 1.7, 2.3, and 1.8 years, respectively. The risk of developing sleep disturbances was significantly higher in HIV-infected persons (adjusted hazard ratio [AHR] = 3.74, $p < 0.001$) and cancer patients (AHR = 2.72, $p < 0.001$) than in controls. HIV-infected persons had a 20% higher risk of sleep disturbances than cancer patients (AHR = 1.20, $p < 0.001$).
Conclusions: HIV-infected persons exhibited a higher risk of developing sleep disturbances than cancer patients and general population controls. With efficacious treatments for sleep disturbances, we should focus on training and research programs for health care providers to intervene and treat earlier for the present and future health of cancer patients and HIV-infected persons.

1. Introduction

Sleep disturbance is one of the major complaints of patients with human immunodeficiency virus (HIV) infection and those with cancer [1–4]. The estimated prevalence of sleep disturbances range from 47% to 58% in patients with HIV [1,2] and from 31% to 59% [3,4] in patients newly diagnosed with cancer. New diagnoses of HIV and cancer are stressful life events, as they both have the potential to cause debilitation and/or death and are associated with negative images, a loss of personal control [5,6] and an increasing frequency of symptoms [7]. Furthermore, attribution of HIV infection or cancer can be externally or internally caused and associated with stigma. The nature of attribution will affect the

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level of stigma attached to the illness [8]. Although the diagnosis of HIV and cancer may be associated with fear and stigma, studies have reported that cancer stigma does not invoke the attribution of blame that HIV often carries [7,9]. Stigma not only increases negative evaluation linked to the illness but also contributes to secondary psychological and social morbidity, which affects physical well-being [8] and sleep [10]. Sleep disturbance associated with HIV or cancer is often due to the anticipation of increasing debilitation, death, and stigma-related psychological stress. However, there is a lack of comparative data on sleep disturbances experienced by cancer and HIV patients at the time of diagnosis. Considering that sleep patterns change over time, current sleep quality measures do not allow a comprehensive analysis of the differences in sleep disturbance between patients with HIV and those with cancer, because there are limited numbers of participants, many studies use a cross-sectional design, and there is a lack of control regarding other associated comorbidities, such as depression, anxiety, and prior sleep problems. To perform such an analysis, we require data from a large representative population that also has a long follow-up time.

The severity of sleep problems has been significantly associated with dysregulated immune function; specifically, it is associated with lower T-cytotoxic/suppressor (CD3+CD8+) cell counts in HIV-infected patients [11] and with higher inflammatory markers (interleukin-6/interleukin-1 receptor antagonist) in cancer patients [12]. In patients with HIV or cancer, sleep disturbances are significantly associated with a decrease in quality of life [13,14] and in medication adherence [15–17]. However, sleep problems among 73% of HIV-infected persons [18] and 35.5% of cancer patients [19] are poorly recognized by health care providers. One study found that 65% of 120 cancer patients in ambulatory care discussed their sleep problems with providers, and only 5% of patients received specific recommendations by clinicians to monitor insomnia [20]. It is critical to identify the occurrence of sleep disturbances at the time of first diagnosis with HIV and cancer for early prevention and intervention.

Patients with HIV were found to have a higher risk of sleep disturbances than the general population [21]. A limited number of studies have evaluated the clinical severity of sleep disturbances in HIV patients. There has been some debate regarding the possible benefits of highly active anti-retroviral therapy (HAART) on sleep quality. Previous studies found that HAART might possibly induce sleep disturbances, particularly specific antiretroviral agents (eg, efavirenz) [22,23]. However, a recent study showed that, in the post-HAART era, patients with an early-treated HIV infection might have rates of sleep disturbances similar to those of non-HIV-infected persons [24]. Previous studies have shown that HIV and cancer have the same factors that lead to sleep problems, including treatment side effects [25,26], fatigue [27], and psychiatric disorders (eg, depression and anxiety) [28,29]. However, several aspects, such as age, gender, psychological response to receiving a diagnosis (eg, discrimination, shame, guilt) [7,8], and lifestyle-related sleep disturbance risk factors (eg, alcohol abuse and substance use) [30] are probably substantially different between patients with HIV and patients with cancer.

A sleep disturbance is recognized as a reversible and manageable symptom or condition [31,32]. Among cancer survivors [31] and patients with comorbid psychiatric illnesses such as depression, posttraumatic stress disorder (PTSD), or chronic pain [32], cognitive-behavioral therapy (CBT) has been shown to be effective in improving sleep problems. However, sleep disturbances among HIV and cancer populations have been overlooked, underdiagnosed, and undertreated. The purpose of this study was to compare the incidence of sleep disturbances among patients with HIV, patients with cancer, and general population controls.

2. Methods

2.1. Study design and data source

A matched cohort study was conducted using the National Health Insurance Research Database (NHIRD), which is composed of several population-based, longitudinal databases that cover more than 99% of the 23 million persons who live in Taiwan. The NHIRD has contracts with 99% of the hospitals and clinics under a mandatory, single-payer health insurance system [33]. Three databases from the NHIRD were used in the current study. First, we included the HIV cohort database, which contains the outpatient and inpatient medical claims of all newly diagnosed HIV-infected persons from 2000 to 2010. Duplicate cases were removed from analysis. Second, we also used the serious illness dataset, which includes 30 types of serious illnesses, such as HIV and cancer. Patients with a serious illness certificate were exempt from co-payments for medical visits from 2000 to 2010. Third, we included the Longitudinal Health Insurance Database 2005 (LHID-2005), which comprises medical claims (1997–2010) of a randomly selected sample of 1,000,000 beneficiaries who were registered in the National Health Insurance (NHI) program in 2005. Each database consists of de-identified clinical and administrative data from the NHIRD. This study obtained ethical approval from the institutional review board of the National Cheng Kung University Hospital.

2.2. Study participants

2.2.1. Matched cohort study procedure

The HIV group was the group of interest, and both the cancer and general population controls were used for comparison. The frequency matching method was used to select two study groups: cancer patients and general population controls. The subjects were matched according to their gender, age group (15–19, 20–29, 30–39, 40–49, 50–59, and ≥60 years) and index year (only for general population controls). The majority of HIV patients were male, were 20–39 years of age, and were diagnosed with HIV after 2006. In total, a maximum of 1493 cancer patients, who were young and mostly male, and 1473 general population controls, who were free of HIV and cancer, were matched to 14,351 HIV patients.

2.2.2. HIV-infected persons

We identified all persons (n = 15,178) who visited ambulatory care facilities with a principal diagnosis of HIV International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes (042 or V08) after confirmation by identifying the 91 code for reimbursement from the Taiwan Center for Disease Control between 2001 and 2009. HIV-infected persons who had a history of cancer (n = 338, 2.23%), who had missing information on gender (n = 1, 0.01%), or who were younger than 15 years of age (n = 25, 0.16%) were excluded. Participants were 15 years of age and older based on the definition of adult HIV prevalence (age 15–49 years) from Joint United Nations Programme on HIV/acquired immune deficiency syndrome (AIDS) (UNAIDS) [34]. In Taiwan, youth aged 15–24 years are at increased risk for HIV infection and accounted for 29.0% of new HIV infections in 2016 [35]. Any HIV-infected persons with a history of a sleep apnea/hypopnea syndrome (n = 283, 1.86%) (ICD-9 code: 78051, 78053, 78057) [36] were also excluded. Sleep apnea/hypopnea syndrome is associated with upper airway collapse due to physical abnormalities. For the purpose of this study, only sleep disturbances associated with psychosocial factors were studied. The HIV-infected cohort included 14,531 individuals (92.0% male).