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Body burden of heavy metals among HIV high risk population in USA☆

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ABSTRACT

Objective: HIV high risk population may face not only the threat of HIV infection but also a higher chance of exposure to environmental contaminants. However, no previous studies have examined the body burden of environmental pollutants including heavy metals among HIV high risk populations. The aim of this study was to investigate whether adults aged 20–59 years old at high risk of HIV infection have higher blood levels of heavy metals compared to those with low risk of HIV infection in United States.
Material and methods: We used the National Health and Nutrition Examination Survey (NHANES) 1999–2010 to compare exposures to heavy metals including cadmium, lead, and total mercury by HIV risk status.
Results: The results showed that people at high risk of HIV had higher blood concentrations of all heavy metals compared to their counterparts with lower HIV risks. In multivariate linear regression models, HIV risk status was significantly associated with increased blood cadmium, lead, and total mercury after adjusting for age, sex, race, education, and poverty income ratio.
Conclusions: Our study suggests that people at high risk of HIV have significantly higher body burden of heavy metals including cadmium, lead, and mercury compared to those with low risk of HIV. Further longitudinal study collecting more pollutants are warranted to determine the potential health effects of these elevated pollutants on both HIV-infected and HIV high-risk populations.

1. Introduction

Human Immunodeficiency Virus (HIV) high risk groups usually include injection drug users and the individuals who engage in unsafe sex (Broz et al., 2009). These groups often have a low socioeconomic status and poor quality of food and living condition (Galea and Vlahov, 2002). It has been well reported that population with low socioeconomic status are more likely exposed to environmental pollutions due to poor neighborhood and contaminated food, air and water (Adler and Newman, 2002; Evans and Kantrowitz, 2002). Thus, HIV high risk population may have differential exposure to environmental risks, which may lead to a long term health consequences in later life, especially after they are infected with HIV.

Thanks to the advancement of prevention and treatment, the incidence of new HIV infections has levelled off, but the number of people living with HIV has been increasing steadily (Losina and Freedberg, 2011; CDC, 2014). Globally, more than 35 million people are currently living with HIV (UNAIDS, 2014); and in US, more than 1.1 million have also been infected (CDC, 2014). Compared to the general population, HIV infected population has higher prevalence of noninfectious comorbidities such as impaired neurocognitive function, cardiovascular disease, hypertension, bone fractures, renal failure, and diabetes mellitus (Deeks and Phillips, 2009; Heaton et al., 1995). Although previous studies have only linked HIV infection and the use of antiretroviral therapy (ART) medications to these noninfectious comorbidities (Avdoshina et al., 2013; Garg et al., 2013; Gandhi et al., 2012), environmental pollutants interacting with HIV infection may have implicated with the

List of abbreviations: Antiretroviral Therapy, ART; The National Health and Nutrition Examination Survey, NHANES; Sexual Transmitted Infection, STI; Mobile Examination Center, MEC; Confidence intervals, CIs; Centers for Disease Control and Prevention, CDC.

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elevated risks of noninfectious comorbidities in this population as HIV infection may increase individual susceptibility to environmental pollutant through chronic inflammation, impaired blood brain barrier, renal and/or hepatic functions (Sacktor et al., 2002; Gongvatana et al., 2013; Xu et al., 2013). Nevertheless, limited data are available regarding environmental risks in people infected with HIV or at risk of HIV.

The effects of heavy metals including lead (Bihaqi et al., 2014; Baranowska-Bosiacka et al., 2012), cadmium (Ciesielski et al., 2013; Rigon et al., 2008), and mercury (Woods et al., 2013; Murata et al., 2007) on noninfectious comorbidities have been well studied in general population. These heavy metals are widespread environmental exposures, ranking in the top 10 on the current Agency for Toxic Substances and Disease Registry Priority List of Hazardous Substances (Registry AfTSaD, 2005). Individual exposure to heavy metals can come from both occupational sites and background environment. Given the ubiquitous nature of these heavy metals and the fact that HIV high risk populations generally have a lower socio-economic status and live in poorer communities (Piot et al., 2001), HIV high risk population may be more likely to be exposed to these toxins compared to the general population.

In this analysis, we used the data from the 1999–2010 NHANES to examine HIV high risk subjects' body burden of heavy metals such as cadmium, lead, and mercury in the population aged 20–59 years old.

2. Materials and methods

2.1. Study population

The NHANES is conducted by the Centers for Disease Control and Prevention (CDC) to assess the health and nutritional status of the non-institutional civilian U.S. population using the complex, multistage, probability sampling design (CDC, 2013). Since 1999, the survey examines about 5000 nationally representative samples each year. In this study, the 1999–2010 NHANES survey data were used and analyzed with a total of 77,154 participants. Among them, 62,160 (80.6%) of those were interviewed and 59,367 (76.9%) had the information on physical examination (NCHS, 2011). In this study, blood cadmium, lead, and mercury were the primary measures of environmental toxins and were selected for analysis. The information of blood cadmium and lead were available among 50,753 participants while blood mercury was tested among 39,053 participants in the 1999–2010 NHANES data. Furthermore, information on risks related to HIV infection such as risky sexual behaviors, self-reported sexual transmitted infections, and injection drug uses were collected by interviews among participants aged 20–59 years. Therefore, this study was limited to adults aged 20–59 years who have not been diagnosed with HIV ($N = 16{,}565$), which is a representative for the US population with this age range.

2.2. Data of blood cadmium, lead, and mercury measurements

The NHANES data provided all measures of blood heavy metals including cadmium, lead, and mercury. The description of laboratory methodology and quality control of blood heavy metals tests were described somewhere else (CDC, 2013). Briefly, individual whole blood samples were collected, processed, stored and shipped to the Division of Environmental Health Laboratory Sciences at the CDC for testing. The atomic absorption spectrometer was used to analyze blood heavy metals in 1999–2002 while the inductively coupled plasma mass spectrometry using quadrupole ICP-MS technology was applied for testing in 2003–2010 (CDC, 2004). The detection limit of heavy metals in blood specimens was determined by three times the standard deviation of blood blank run for a minimum of 20 runs (CDC, 2004). Thus, they were varied by data cycles and metals (Blood cadmium: 0.30 μg/L in 1999–2002 data cycles and 0.20 μg/L in 2003–2010 data cycles; blood lead: 0.30 μg/dL in 1999–2004 data cycles and 0.25 μg/dL in 2005–2010 data cycles; and blood total mercury: 0.14 μg/L in 1999–2002 data cycles, 0.20 μg/L in 2003–2006 data cycles, 0.28 μg/L in 2007–2008 data cycles, and 0.33 μg/L in 2009–2010 data cycle). As recommended by the NHANES, the detection limit divided by the square root of two was assigned for individuals with the testing result below the limit of detection.

2.3. HIV high risk population

The NHANES collected information on HIV risk related behaviors. The predefined behaviors included risky sexual behaviors, sexual transmitted infections, and injection drug use by interviews. Participants were determined as high-risk individuals for HIV if they had any one of the following high-risk behaviors (Broz et al., 2009): multiple sex partners in the past year (Galea and Vlahov, 2002), self-reported diagnosis of any sexual transmitted infections including genital herpes, genital warts, gonorrhea, and chlamydia, and (Adler and Newman, 2002) life-time injection drug use. This definition is similar to previous studies (Bacon et al., 2005; Kelly et al., 1994). The rest of individuals were defined as low-risk group for HIV.

2.4. Covariates

The NHANES demographic questionnaire was used to collect individual demographic information. For this analysis, these information including age (categorized as 20–29, 30–39, 40–49, or 50–59), gender, and race/ethnicity (Non-Hispanic white, Non-Hispanic black, or Hispanic and others), and socioeconomic status such as poverty income ratio (PIR; <1.0, 1.0–2.0, ≥2.0, or missing) and education (<high school, high school or equivalent, or > high school) were selected.

2.5. Statistical analysis

In descriptively statistical analyses, two-sided Student t-tests were used for continuous variables while Wald chi-square analysis was performed for categorical variables to make a comparison between groups. In addition, the distributions of laboratory tests such as blood heavy metal concentrations were most likely to be skewed and log-transformation would be applied to make the data conform more closely to the normal distribution if necessary. Multivariate linear regression models were used to examine the associations between HIV risk status and each heavy metal after adjusting for demographic information including age, sex, and race/ethnicity, education and poverty income ratio. If the concentrations of heavy metals were log-transformed, the coefficients from the regression modelling represented as log of the ratios of heavy metals between two comparison groups (i.e. $\text{Log}(Y_2/Y_1)$). Thus, the coefficients were interpreted as a ratio after their transformation of exponential function in the results. Further, the appropriate subsample weight was calculated for the combined 1999–2010 NHANES data. The SAS survey procedures were applied to analyze the data after considering the survey stratification and clustering design variables and sample weights to ensure the correct estimation of sampling error. Finally, we also examined the interactions between HIV risk status and age, gender, or race/ethnicity. All statistical analyses were performed using SAS 9.4 survey procedures software (SAS Institute Inc., Cary, NC).

To examine the potential bias introduced by the way how the values below limit of detection were handled, we further