RESEARCH ARTICLE

Blood Lead Concentration Correlates with All Cause, All Cancer and Lung Cancer Mortality in Adults: A Population Based Study

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Abstract

Background: This study used National Health and Nutrition Examination Survey III to study the relationship between blood lead concentration and all cause, all cancer and lung cancer mortality in adults. Patients and Methods: Public use National Health and Nutrition Examination Survey (NHANES III) data were used. NHANES III uses stratified, multistage probabilistic methods to sample nationally representative samples. Household adult, laboratory and mortality data were merged. Sample persons who were available to be examined in aMobile Examination Center (MEC) were included in this study. Specialized survey analysis software was used. Results: A total of 3,482 sample participants with complete information for all variables were included in this analysis. For all cause death, the odds ratios (S.E.) for statistically significant variables were body mass index, 1.03 (1.01-1.06); age 1.01 (1.01-1.01); blood lead concentration, 1.05 (1.01-1.08); poverty income ratio, 0.823 (0.76-0 .89); and drinking hard liquor, 1.01 (1.00-1.02). For all cancer mortality, the odds ratios (S.E.) of the statistically significant variables were: age, 1.01 (1.01-1.01); blood lead concentration, 1.07 (1.04-1.12), black race, using non-Hispanic white as reference, 1.69 (1.12-2.56); and smoking, 1.02 (1.01-1.04). For lung cancer mortality, the odds ratios (S.E.) of the statistically significant variables were: age, 1.01 (1.01-1.01); blood lead concentration, 1.09 (1.05-1.13); Mexican Americans, using non-Hispanic white as reference, 0.33 (0.129-0.850); other races, 1.80 (0.53-6.18); and smoking, 1.03 (1.02-1.05). Conclusion : Blood lead concentration correlated with all cause, all cancer, and lung cancer mortality in adults.

Keywords: Blood lead concentration - mortality - all causes - lung cancer - NHANES III

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Introduction

Lead is a known weak carcinogen of human (Steenland and Boffetta, 2000). A study used lead concentration data available in National Health and Nutrition Examination Survey (NHANES) II (1976-1980) study found a correlation between high concentrations available in NHANES II study with higher all cancer mortality, but there was no significant correlation between overall blood lead level and cancer mortality (Jemal et al., 2002). In a later study using NHANES III (1988-1994) data, contemporary blood lead level in NHANES III was found to be associated with higher all cause and all cancer mortality at low concentrations (Menke et al., 2006; Schober et al., 2006). Further studies found increased mortality related to cancer and hypertension related cardiac diseases. Since there was no dose response, blood lead level was often thought to be surrogate for other factors (Wong and Harris, 2000). Other studies found blood lead level correlated with kidney disease and hypertension (Cooper, 1988), lung stomach and liver, hypertension, chronic nephritis and heart disease and other conditions (Cooper et al., 1985). However, many of these earlier studies did not have enough socio-demographic data to adjust for potential covariates. This study investigated if contemporary blood lead concentration was related to all cause, all cancer and lung cancer. This was a part of a more extensive study to screen the potential predictors of adult cancer mortality using that NHANES III data that were representative of U.S. population. The vital status of NHANES III participant was followed passively up to December 31, 2006. The data were contained in NHANES III linked mortality (Menke et al., 2010). This study used the extensive socio-demographic factors available in NHANES III data to adjust for the effects of blood lead level and all cause, all cancer and lung cancer mortality.

Materials and Methods

NHANES and NHANES III

NHANES is a major program of National Center of Health Statistics (a part of Center of Disease Control (CDC) of United States of America) started in 1971. NHANES III was a national study based on a complex,

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multi-stage probability sampling design. For details of NHANES III and NHANES III linked mortality data and statistical guidance as well as their analysis examples see NHANES website (http://www.cdc.gov/nchs/nhanes.htm). In brief, NHANES studies were approved by CDC internal institutional review boards. The public use data were made available to the public and researchers. The NHANES sample weights were calculated to represent non-institutionalized general U.S. population to account for non-coverage and non-response. Only participants who were interviewed at home and examined in mobile examination centers (MEC) were included in this study. This eliminated the cofounding effects of sample persons being too frail, too young or old to go to the MEC for examinations. In this study, NHANES III (conducted between1988-1994) household adult data file was merged with NHANES III laboratory data and the NHANES III linked cancer mortality data.

NHNAES III linked mortality data

Detailed information about the data and analysis guidelines are available at their website (http://www.cdc.gov/nchs/data_access/data_linkage/mortality/nhanes3_linkage.htm). In brief, probability matching was used to link NHANES III with National Death Index for vital status and mortality. NHANES used multiple sources including the use of death certificates and with the National Death Index to ascertain vital status and cause of death. NHANES III codes of death (ucod_113) were used in this study.

Statistical analysis

NHANES III employed a complex sampling strategy and analysis (Ezzati-Rice and Murphy, 1995; Graubard and Korn, 1999; Lemeshow and Cook, 1999; Chang et al., 2010). Matlab programs (posted on Matlab File Exchange) were developed to convert SAS files provided by NAHNES to STATA programs to download NHANES III data files for further analysis. Specialized survey software is needed for NHANES complex data analysis (Cohen, 1997). STATA 12 (College Station, TX) was among those recommended by CDC to analyze the complex NHANES data and was used in this study. The sampling weight used was WTPFEX6 because only the sample persons had examinations in the MEC were included in this study, SDPPSU6 was used for the probability sampling unit (PSU) and SDPSTRA6 was used to designate the strata for the STATA survey commands. STATA scripts were written for this analysis, and will be submitted for publication separately. Univariate and multivariate logistic regressions (Jewell, 2004) were used to study the relationship between predictors and mortality (using ucod_113 codes) in adults. The symbols used were as follows: lungCancer (death from lung cancer (ucod_113 = 027, malignant neoplasms of trachea, bronchus and lung)): 0=alive, 1=dead, BMI (body mass index), IndicatorDeath (death from all causes) and cancerDeath (death form all cancer causes). MXPAXTMR (age at the MEC final examination), HSSEX (sex, _IHSSEX2=female, using male as the reference group), PBP (blood lead level, ug/dL), DMPMETRO (urban rural residence status, _IDMPMETRO_2=rural residence, urban residence used as the reference group), DMARETHN (race and ethnicity, _IDMARETHN_2=non-Hispanic black, _IDMARETHN_3=Mexican-American, _IDMARETHN_4=others, non-Hispanic white was used as the reference group), HAN6JS (alcohol consumption), and HAR4S (smoking), DMPPIR (poverty index ratio status). N=3482 samples with complete data were analyzed. Linearized Taylor Standard Error estimation was used.

For STATA analyses, only the patients without missing values for all of WTPFEX6, SDPPSU6, SDPSTRA6, BMI, MXPAXTMR, HSSEX, DMPMETRO, HAM5S, HAM6S, DMARETHN, DMPPIR, HAR4S, and HAN6JS, MORTSTAT, PBP were included in this study. Further, these additional NHANES III codes considered not eligible: HAM6S (888), HAM6S (999), DMPPIR (888888), the numerator of DMPPIR was the midpoint of the observed family income category in the Family Questionnaire variable:HFF19R, and the denominator was the poverty threshold, the age of the family reference person, and the calender year in which the family was interviewed, HAR4S (666), HAR4S (777), HAR4S (888), HAR4S (999), HAN6JS (888), HAN6JS (999), not in BMI>15 and BMI<50, PBP(8888), HAM5S (888), HAM5S(999), HAM6S(888), HAM6S(999), DMPPIR(888888), youth sample persons and incomplete mortality data. A total of 3482 sample persons were eligible for this study.

Results

3482 sample participants with complete information for all variables were included in this analysis.

The mean risk (95% CI) of death in this study population for all cause death was 0.1583263 (0.142-0.175) (Table 1), the means (95% CI) of the other demographic variables were: body mass index (BMI), 25.22 (24.94-25.50); age at the mobile examination center (MXPAXTMR), 473.39 months (465.50-483.28); blood lead concentration (PBP), 4.44 ug/dL (4.15 -4.72); and follow up in months from the medical examination

Table 1. Socio-demographic Factors of Sample Population

	Mean	Linearized Std. Err.	[95% Conf. Interval]	
IndicatorDeath	0.1583263	0.0080966	0.1420555	0.1745971
BMI	25.2196300	0.1393679	24.9395600	25.4997000
MXPAXTMR	474.3924000	4.4231220	465.5038000	483.2810000
HSSEX	1.4561690	0.0079412	1.4402110	1.4721280
PBP	4.4378600	0.1423587	4.1517800	4.7239410
DMPMETRO	1.5695540	0.0526919	1.4636660	1.6754420
DMARETHN	1.3545530	0.0330656	1.2881050	1.4210010
DMPPIR	2.6829130	0.0675556	2.5471550	2.8186710
HAN6JS	2.8127020	0.2798529	2.2503160	3.3750880
HAR4S	19.8460400	0.4370535	18.9677500	20.7243400
permth_exm	169.9669000	2.8635330	164.2124000	175.7214000

*The symbols are as follows: IndicatorDeath: 0=alive, 1=dead, BMI (body mass index), MXPAXTMR (age at the MEC final examination), HSSEX (sex, 1=male, 2=female), PBP (blood lead concentration), DMPMETRO (urban rural residence status, 1=urban, 2=rural), DMARETHN (race and ethnicity, 1=non Hispanic white, 2=non-Hispanic black, 3=Mexican-American, and 4=others), DMPPIR (poverty income ratio), HAN6JS (alcohol consumption, hard liquor drinks per month), and HAR4S (smoking, cigarettes smoked per day), N=3482 samples

Table 2. Univariate Analysis of Covariates of All Cause Survival

IndicatorDeath	Odds Ratio	Linearized Std. Err.	t	P>|t|	[95% Conf. Int]	
BMI	1.029	0.013	2.20	0.033	1.002	1.055
MXPAXTMR	1.009	0.001	16.35	0.000	1.008	1.010
HSSEX	0.866	0.105	-1.19	0.239	0.678	1.104
PBP	1.110	0.028	4.19	0.000	1.056	1.167
DMPMETRO	1.111	0.124	0.94	0.352	0.887	1.390
DMARETHN	1.018	0.072	0.26	0.799	0.883	1.174
DMPPIR	0.918	0.031	-2.52	0.015	0.857	0.983
HAN6JS	1.016	0.008	2.11	0.040	1.001	1.032
HAR4S	1.012	0.005	2.13	0.038	1.001	1.023

*The symbols are as follows: IndicatorDeath: 0=alive, 1=dead, BMI (body mass index), MXPAXTMR (age at the MEC final examination), HSSEX (sex, 1=male, 2=female), PBP (blood lead concentration), DMPMETRO (urban rural residence status, 1=urban, 2=rural), DMARETHN (race and ethnicity, 1=non Hispanic white, 2=non-Hispanic black, 3=Mexican-American, and 4=others), DMPPIR (poverty income ratio), HAN6JS (alcohol consumption, hard liquor drinks per month), and HAR4S (smoking, cigarettes smoked per day), N=3482 samples

Table 3. Multivariate Analysis of Effects of Lead on All Cause Mortality

IndicatorDeath	Odds Ratio	Linearized Std. Err.	t	P>|t|	[95% Conf. Int]	
BMI	1.034	0.015	2.33	0.024	1.005	1.064
MXPAXTMR	1.009	0.001	16.12	0.000	1.008	1.010
_IHSSEX_2	0.813	0.141	-1.19	0.239	0.573	1.153
PBP	1.045	0.016	2.83	0.007	1.013	1.079
_IDMPMETRO_2	1.054	0.124	0.44	0.659	0.832	1.335
_IDMARETHN_2	1.355	0.239	1.72	0.091	0.951	1.930
_IDMARETHN_3	0.668	0.168	-1.61	0.114	0.403	1.106
_IDMARETHN_4	0.690	0.223	-1.15	0.257	0.360	1.322
DMPPIR	0.823	0.033	-4.79	0.000	0.758	0.893
HAN6JS	1.013	0.005	2.76	0.008	1.003	1.022
HAR4S	1.002	0.008	0.20	0.839	0.986	1.018
_cons	0.001	0.000	-14.52	0.000	0.000	0.002

*The symbols are as follows: IndicatorDeath: 0=alive, 1=dead, BMI (body mass index), MXPAXTMR (age at the MEC final examination), HSSEX (sex, 1=male, 2=female), PBP (blood lead concentration), DMPMETRO (urban rural residence status, 1=urban, 2=rural), DMARETHN (race and ethnicity, 1=non Hispanic white, 2=non-Hispanic black, 3=Mexican-American, and 4=others), DMPPIR (poverty income ratio), HAN6JS (alcohol consumption, hard liquor drinks per month), and HAR4S (smoking, cigarettes smoked per day), N=3482 samples

Table 4. Multivariate Analysis of Effects of Blood Lead Concentration on All Cancer Mortality

CancerDeath	Odds Ratio	Linearized Std. Err.	t	P>|t|	[95% Conf. Int]	
BMI	1.014	0.021	0.65	0.516	0.972	1.058
MXPAXTMR	1.007	0.001	10.98	0.000	1.006	1.008
_IHSSEX_2	0.998	0.183	-0.01	0.990	0.690	1.442
PBP	1.071	0.017	4.22	0.000	1.036	1.106
_IDMPMETRO_2	0.995	0.239	-0.02	0.982	0.614	1.612
_IDMARETHN_2	1.692	0.350	2.54	0.014	1.117	2.562
_IDMARETHN_3	0.534	0.187	-1.79	0.079	0.264	1.079
_IDMARETHN_4	1.355	0.615	0.67	0.506	0.544	3.374
DMPPIR	0.971	0.057	-0.51	0.613	0.863	1.091
HAN6JS	0.100	0.004	-0.10	0.920	0.992	1.008
HAR4S	1.021	0.008	2.61	0.012	1.005	1.037
_cons	0.000	0.000	-11.61	0.000	0.000	0.001

*The symbols are as follows: cancerDeath: 0=alive, 1=dead, BMI (body mass index), MXPAXTMR (age at the MEC final examination), HSSEX (sex, 1=male, 2=female), PBP (blood lead concentration), DMPMETRO (urban rural residence status, 1=urban, 2=rural), DMARETHN (race and ethnicity, 1=non Hispanic white, 2=non-Hispanic black, 3=Mexican-American, and 4=others), DMPPIR (poverty income ratio), HAN6JS (alcohol consumption, hard liquor drinks per month), and HAR4S (smoking, cigarettes smoked per day), N=3482 samples

Table 5. Multivariate Analysis of Effect of Blood Lead Concentration on Lung Cancer Mortality

LungCancer	Odds Ratio	Linearized Std. Err.	t	P>|t|	[95% Conf. Int]	
BMI	1.009	0.030	0.30	0.767	0.950	1.070
MXPAXTMR	1.007	0.001	7.84	0.000	1.005	1.008
_IHSSEX_2	0.839	0.201	-0.73	0.467	0.518	1.359
PBP	1.090	0.018	5.18	0.000	1.054	1.127
_IDMPMETRO_2	0.817	0.241	-0.68	0.497	0.452	1.479
_IDMARETHN_2	1.153	0.386	0.42	0.673	0.588	2.260
_IDMARETHN_3	0.331	0.155	-2.36	0.022	0.129	0.850
_IDMARETHN_4	1.804	1.105	0.96	0.340	0.527	6.179
DMPPIR	0.913	0.090	-0.93	0.359	0.750	1.112
HAN6JS	0.993	0.009	-0.72	0.474	0.975	1.012
HAR4S	1.032	0.008	4.28	0.000	1.017	1.047
_cons	0.000	0.000	-9.51	0.000	0.000	0.0013

*The symbols are as follows: lungCancer: 0=alive, 1=dead, BMI (body mass index), MXPAXTMR (age at the MEC final examination), HSSEX (sex, 1=male, 2=female), PBP (blood lead concentration), DMPMETRO (urban rural residence status, 1=urban, 2=rural), DMARETHN (race and ethnicity, 1=non Hispanic white, 2=non-Hispanic black, 3=Mexican-American, and 4=others), DMPPIR (poverty income ratio), HAN6JS (alcohol consumption, hard liquor drinks per month), and HAR4S (smoking, cigarettes smoked per day), N=3482 samples

(permth_exm) was 169.97 (164.21-175.72).

Table 2 shows the univariate analysis of the covariates of all cause death. The odds ratios (S.E.) of the statistically significant variables were: body mass index, 1.03 (1.00-1.06); age, 1.01 (1.01-1.01); blood lead concentration, 1.11 (1.06-1.17); poverty income ratio, 0.92 (0.86-0.98); drinking hard liquor, 1.02 (1.00-1.03); and cigarette smoking, 1.01 (1.00-1.02). Table 3 shows the multivariate analysis of the covariates of all cause death. The odds ratios (S.E.) of the statistically significant variables were body mass index, 1.03 (1.01-1.06); age 1.01 (1.01-1.01); blood lead concentration, 1.05 (1.01-1.08); poverty income ratio, 0.823 (0.76-0 .89); and drinking hard liquor, 1.01 (1.00-1.02).

Table 4 shows the multivariate analysis of the covariates of all cancer mortality. The odds ratios (S.E.) of the statistically significant variables were: age, 1.01 (1.01-1.01); blood lead concentration, 1.07 (1.04-1.12), black race, using non-Hispanic white as reference, 1.69 (1.12-2.56); and smoking, 1.02 (1.01- 1.04). Table 5 shows the multivariate analysis of the covariates of lung cancer mortality. The odds ratios (S.E.) of the statistically significant variables were: age, 1.01 (1.01-1.01); blood lead concentration, 1.09 (1.05-1.13); Mexican Americans, using non-Hispanic white as reference, 0.33 (0.129-0.850); other races, 1.80 (0.53-6.18); and smoking, 1.03 (1.02-1.05).

Discussion

The relationship between blood lead and increased mortality due to heart, kidney and cancer cause is known but appears to be complex (Steenland and Boffetta, 2000). A major limitation of prior studies was a lack of data to adjust for the covariates of the effects of blood lead level on human illnesses. It has been observed that blood lead level correlated with increase mortality due to cancer, and hypertension related cardiac diseases (Wong and Harris, 2000). For cancer, studies have found an association between blood lead level and lung, stomach and liver cancer mortality (Cooper et al., 1985). Earlier studies suggested that lead level at 1975-1976 after control the lead content of gasoline might be enough to normalize the mortality (Malcolm and Barnett, 1982), but later studies found an increase in mortality at low concentrations (Menke et al., 2006; Schober et al., 2006). Lung cancer mortality was associated with blood lead level, but it was thought that lead concentration could be a surrogate for smoking (Wong and Harris, 2000). This study made use of the extensive socio-demographic NHANES III data to adjust for the covariates of the effects of blood lead level on all cause, all cancer, and lung cancer mortality.

All of the results were obtained by using specialized survey software taking into account the primary sampling unit and stratification variables and the weights assigned to the sample persons examined in the MEC. Thus these results are representative of the US population. 3482 sample participants with complete information for all variables were included in this analysis. All of the univariables were included in the final multivariate analysis of all cause, all cancer and lung cancer mortality so as not to omit potentially important covariates. For all cause death, the statistically significant variables were body mass index, age, blood lead concentration, poverty income ratio and drinking hard liquor. For all cancer mortality, the statistically significant variables were: age, blood lead concentration, black race, using non-Hispanic white as reference, and smoking. For lung cancer mortality (Table 5), the statistically significant variables were age, blood lead concentration, Mexican Americans, using non-Hispanic white as reference, other races, and smoking.

Alcohol consumption, poverty, minority race and smoking have been associated with increased all cause and cancer mortality (Rothman et al., 2008). This study confirmed these earlier results. This study found an association of black race and increased all cancer mortality. The finding that Mexican-American and other races were correlated with lower lung cancer mortality needs to be further examined to see they are confounders of other hidden socio-economic covariates. This study found a correlation of blood lead level, as in the contemporary NHANES III data and blood lead concentrations, and increase in all cause, all cancer and lung cancer mortality after adjusting for other socio-economic covariates. However, the mechanism of how an increase in blood lead level increased all lung cancer mortality will need further studies.

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