Blood lead levels in relation to smoking and chronic obstructive pulmonary disease (COPD): a study from Korean National Health and Nutrition Examination Survey (KNHANES)

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Background: Lead exposure is a resurgent environmental issue globally. Smoking can be a source of lead exposure, although the majority of lead poisonings originate from workplace exposures. However, no study has been undertaken concerning the blood lead levels based on the chronic obstructive pulmonary disease (COPD), smoking status, and other risk factors of COPD. This cross-sectional study was conducted to investigate the blood lead levels according to COPD and clinical variables associated with COPD.

Methods: Data (total number =53,829) were collected from the Korean National Health and Nutrition Examination Survey (IV in 2008 and 2009, V in 2010–2012, and VI in 2013). Multivariable linear regression analyses were performed to determine variables associated with elevated blood lead levels.

Results: Univariate regression analysis showed that male sex, older age, smoking, occupation level, income level, education level, and presence of COPD were related to higher blood lead levels, whereas the other co-morbidities including diabetes, hypertension, cerebral stroke, osteoporosis, asthma, and depression were not related (P<0.05). Multivariable regression analysis demonstrated that older age, male sex, smoking, occupation, and education level were independently associated with higher blood lead levels (P<0.05).

Conclusions: Smoking status, occupation, and education level along with old age and male sex were independently associated with higher blood lead levels; however, COPD was not after adjustment of all confounding factors.

Introduction

Although lead concentrations in the general population have declined over the past two decades, lead exposure is a resurgent environmental issue globally (1-3).

Chronic lead exposure has a wide spectrum of multi-systemic adverse effects through various biochemical mechanisms (4). Adult lead toxicity is defined as blood lead level ≥10 μg/dL; however low-level environmental lead exposure (blood lead level lower than 10 μg/dL) may accelerate progressive renal insufficiency and can be an important risk factor for cardiovascular mortality in US adults (5,6), It is recommended that pregnant women should avoid occupational lead exposure that would result in blood lead concentrations >5 μg/dL due to the possible consequences of spontaneous abortion and postnatal developmental delay (4).

The association between blood lead levels and increased all-cause and organ-specific mortality was reported on a worldwide level (3,7). One report showed that blood lead levels were linked to increased all-cause and cardiovascular mortality at substantially lower levels (below 10 μg/dL) than previously reported (7).

Lead as a pollutant originating from traffic-related and industrial emissions contributes to air pollution (8). Although a majority of elevated blood lead levels in adults originate from workplace exposures, smoking can be a source of lead exposure (9,10). Smoking is a major causative risk factor for chronic obstructive pulmonary disease (COPD); nevertheless, outdoor air pollution is considered a significant factor for the development of COPD (11,12). However, no study has been conducted so far concerning the blood lead levels based on risk factors of COPD and the smoking status in patients with COPD.

Therefore, this study investigated the association between elevated blood levels and clinical variables and attempted to examine the blood lead levels based on COPD and clinical variables associated with COPD, such as smoking status and socioeconomic factors.

Methods

Study design

Our data (total number =53,829) were collected from participants in the Korean National Health and Nutrition Examination Survey (KNHANES). Six cycles of KNHANES data, IV (n=9,744 in 2008, n=10,533 in 2009), V (n=8,958 in 2010, n=8,518 in 2011, n=8,058 in 2012), and VI (n=8,018 in 2013) were selected to represent South Korea population. KNHANES is a nationally representative cross-sectional complex survey including approximately 10,000 individuals each year, collecting information on socioeconomic status, health-related behaviors, quality of life, healthcare utilization, anthropometric measures, biochemical and clinical profiles for non-communicable diseases, and dietary intakes with three component surveys: health interview, health examination and nutrition survey (13). The health interview and health examination were conducted by trained staff members comprising physicians, medical technicians, and health interviewers (13). This data includes additional information to account for complex survey design such as sample weight, description of computing and adjusting weights, primary sampling units, sampling size, and stratification levels. The data were adjusted and weighted for non-response and unequal selection probability to provide national estimates.

Definition of each comorbidity

COPD was determined using the spirometric airflow limitation (forced expiratory volume in one second/forced vital capacity <0.70) (14). Former smokers were defined as those who answered that they used to smoke daily but now does no longer smoke every day and have smoked more than 100 cigarettes in their lifetime. Never smokers were defined as those who answered either they have never smoked at all or have smoked less than 100 cigarettes in their lifetime. Current smokers were defined as those

who answered that they smoke daily or sometimes and have smoked more than 100 cigarettes in their lifetime. Comorbidities, including cerebral stroke, osteoporosis, asthma, diabetes, and depression, were defined based on the physician's diagnosis or patient's affirmative answer in the survey questionnaire. Hypertension was defined as systole ≥140 mmHg and diastole ≥90 mmHg or being on antihypertensive medication after a physician's diagnosis.

Measurements

According to the guidelines of the American Thoracic Society and European Respiratory Society, spirometry (Elite-DX or CPFS; Medgraphics, St Paul, MN, USA) was performed, and the acceptability and repeatability criteria of the spirometry were established (15). Normal predictive values of spirometry in the Korean population were obtained based on the second KNHANES (16). Economic status was divided based on quartile value of income level, as follows: 1Q, lowest 0–25 percentile; 2Q, lower-middle 25–50 percentile; 3Q, upper-middle 50–75 percentile; and 4Q, highest 75–100 percentile.

Blood samples for lead measurements were drawn into trace-metal-free ethylenediaminetetraacetic acid (EDTA) tubes, and specimens were immediately transferred at 2–8 ℃ to a central laboratory for analysis (NeoDin Medical Institute, Seoul, Korea). Lead concentrations in venous whole blood were measured using graphite furnace atomic absorption spectrometry (model AAnalyst 600; PerkinElmer, Finland) (17). The limits of detection (LODs) were 0.12 μg/dL for blood lead, and none of the adult samples exhibited values below the LOD. For internal quality assurance and control, commercial standard reference materials were obtained from Bio-Rad (Lyphochek® Whole Blood Metals Control; Bio-Rad, Hercules, CA, USA). The NeoDin Medical Institute has a certified license from the Korean Ministry of Labor for external quality control of heavy metals laboratory analyses and has passed the German External Quality Assessment Scheme, the US CDC program, and the Korea Occupational Safety and Health Administration (Korea OSHA) program.

Statistical analysis

Given that KHANES data were obtained from a complex sampling survey, for all analyses, appropriate sample weights to account for the unequal probability of sampling and non-response were used for computing reliable estimates, and primary sampling unit was also specified in the analysis to account for design effects of clustering and stratification. Standard errors were estimated using Taylor series linearization. The characteristics of all survey participants are presented with a weighted percentage and standard error, which were compared based on the Rao-Scott modified chi-square test. Univariate regression analyses were performed to select meaningful risk factors associated with blood lead levels. Then, multivariable regression analysis using significant factors obtained from univariate analyses was conducted to find meaningful variables independently associated with blood lead levels among covariates, including demographics and comorbidities. Another multivariable analysis adjusting for significant risk factors proven by univariate analysis was done to find the association among smoking, COPD, and blood lead levels. As a subgroup analysis, it was stratified with sex, age group (≥50 vs. <50 years), education level (higher education vs. lower education), occupation level (farmer or fisherman, technician, labor worker vs. manager or professional, office worker, service, unemployed) to assess the association solely between COPD and smoking on blood lead level. The results of regression analysis were provided and the estimation of blood lead levels was presented with a 95% confidence interval. Statistical analyses were performed with SAS software version 9.4 (SAS Institute, Cary, NC, USA). A P value of less than 0.05 was deemed statistically significant.

Ethics statement

The current study was approved by the institutional review board of Ajou Medical Center (approval number: AJIRB-MED-EXP-9-161). The requirement for informed consent is waived by the ethics review board due to the retrospective nature of the study.

Results

Baseline characteristics

Table 1 presents the demographic profile: an almost equal sex ratio (men 49.2%), a high proportion of older subjects (≥50 years 40.6%, 40–49 years 21.3%, 30–39 years 20.5%, 20–29 years 17.6%), smoking status (current 31.5%, former 11.6%, never 56.9%), and education levels (below middle school 20.3%, middle school 10.3%, high school 38.1%,

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Table 1 Demographic distribution of the weighted adjusted proportion (%) for Korean population

Demographics	Weighted percentage	Standard error of weighted percentage	P value
Sex			<0.001
Male	49.2	0.27	
Female	50.8	0.27	
Age group (years)			<0.001
≥50	40.6	0.49	
40–49	21.3	0.37	
30–39	20.5	0.41	
20–29	17.6	0.38	
Smoking status			0.001
Current	31.5	0.31	
Cigarette/day	15.3	0.12	
Former	11.6	0.21	
Cigarette/day	16.6	0.21	
Never	56.9	0.33	
Occupation			<0.001
Manager or professional	13.7	0.29	
Office worker	9.1	0.21	
Service	13.9	0.28	
Farmer worker or fisherman	5.9	0.40	
Technician	11.8	0.27	
Labor worker	8.5	0.20	
Unemployed	37.2	0.38	
Income level			0.002
Lowest quartile (1Q)	25.7	0.46	
Lower middle (2Q)	25.3	0.39	
Upper middle (3Q)	24.8	0.37	
Highest quartile (4Q)	24.2	0.51	
Education level			<0.001
Below middle school	20.3	0.39	
Middle school	10.3	0.21	
High school	38.1	0.42	
Above high school	31.4	0.48	

Table 2 The associations between demographics and blood lead levels by univariate regression analysis

Demographics	Estimated blood lead level (µg/dL)	Standard error	95% confidence interval	P value
Sex				<0.001
Male	2.91	0.025	2.87–2.96	
Female	2.13	0.020	2.09–2.17	
Age group (years)				<0.001
20–29	1.94	0.057	1.83–2.06	
30–39	2.34	0.057	2.23–2.46	
40–49	2.41	0.030	2.35–2.47	
≥50	2.67	0.024	2.62–2.72	
Smoking status				<0.001
Never smoker	2.21	0.021	2.17–2.25	
Former smoker	2.80	0.055	2.69–2.90	
Current smoker	2.94	0.034	2.87–3.00	
Occupation				<0.001
Manager or professional	2.40	0.044	2.31–2.48	
Office worker	2.51	0.061	2.39–2.63	
Service	2.44	0.044	2.36–2.53	
Farmer or fisherman	2.79	0.059	2.67–2.91	
Technician	3.02	0.053	2.91–3.12	
Labor worker	2.58	0.056	2.47–2.69	
Unemployed	2.33	0.028	2.28–2.39	
Income level				0.002
Lowest quartile (1Q)	2.58	0.036	2.51–2.65	
Lower middle (2Q)	2.57	0.035	2.50–2.64	
Upper middle (3Q)	2.45	0.034	2.38–2.52	
Highest quartile (4Q)	2.44	0.033	2.38–2.50	
Education level				<0.001
Below middle school	2.64	0.037	2.56–2.71	
Middle school	2.77	0.052	2.66–2.87	
High school	2.46	0.028	2.41–2.52	
Above high school	2.32	0.028	2.27–2.38	

above high school 31.4%).

Univariate analyses of clinical variables including comorbidities

Demographic data showed that blood lead levels were higher among men, older subjects, smokers, lower education group, and lower income group (P value <0.05) (*Table 2*). Comparison based on occupation revealed that blood lead levels were higher among farmers, fishermen, and technicians than among managers or professionals, office workers, employees in the service sector, and

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Table 3 The association between co-morbidities and blood lead levels by univariate regression analysis

Co-morbidities	Estimated blood lead level (µg/dL)	Standard error	95% confidence interval	P value
COPD				<0.001
Yes	2.93	0.062	2.80–3.05	
No	2.46	0.018	2.42–2.49	
Hypertension				0.926
Yes	2.67	0.040	2.59–2.75	
No	2.66	0.098	2.47–2.85	
Cerebral stroke				0.955
Yes	2.62	0.161	2.31–2.94	
No	2.61	0.153	2.31–2.91	
Osteoporosis				0.317
Yes	2.31	0.122	2.07–2.55	
No	2.57	0.236	2.11–3.04	
Asthma				0.070
Yes	2.74	0.137	2.47–3.01	
No	2.41	0.122	2.17–2.65	
Diabetes				0.931
Yes	2.56	0.068	2.43–2.70	
No	2.54	0.230	2.09–2.99	
Depression				0.312
Yes	2.25	0.104	2.05–2.45	
No	2.37	0.050	2.27–2.47	

COPD, chronic obstructive pulmonary disease.

the unemployed (P value <0.05) (*Table 2*). COPD was associated with higher blood lead (P value <0.001), but other comorbidities such as hypertension, cerebral stroke, osteoporosis, asthma, diabetes, and depression were not related (*Table 3*).

Multivariable regression analysis

Multivariable linear regression analysis using significant factors obtained from univariate analyses demonstrated that male sex (P value <0.001), older age (P value <0.001), smoking (P value <0.001), occupation (P value =0.002), and education levels (P value <0.001) were significantly associated with higher blood lead levels, whereas income level (P value =0.384) and COPD (P value =0.386) were not (*Table 4*). Another multivariable linear regression analysis

according to the smoking status and the presence of COPD with adjusting for other covariates demonstrated that current smoking was independently associated with high blood lead levels, and COPD was not related (*Figure 1*).

Subgroup analysis

Multivariable linear regression analyses of estimated blood lead levels were performed by stratification according to age, sex, education level, and occupation with a reference group as never-smokers. Subgroup analyses showed that never-smokers with COPD had higher blood lead levels in male, female, higher education subgroup (high school or more), and the subgroup of office workers and managerial workers, compared to never-smokers without COPD (P value <0.05) (*Figures 2,3*).

Table 4 The association between blood lead levels and each variable by multivariable linear regression analysis

Demographics	Estimated blood lead level (μg/dL)	Standard error	95% confidence interval	P value
Sex				<0.001
Male	2.85	0.032	2.79–2.92	
Female	2.19	0.029	2.13–2.24	
Age group (years)				<0.001
20–29	1.97	0.058	1.86–2.08	
30–39	2.38	0.055	2.27–2.49	
40–49	2.44	0.031	2.38–2.50	
≥50	2.65	0.024	2.60–2.69	
Smoking status				<0.001
Never smoker	2.42	0.027	2.37–2.47	
Former smoker	2.40	0.060	2.28–2.52	
Current smoker	2.71	0.038	2.63–2.78	
Occupation				0.002
Manager or professional	2.46	0.045	2.37–2.54	
Office worker	2.52	0.064	2.39–2.64	
Service	2.56	0.042	2.48–2.64	
Farmer or fisherman	2.52	0.061	2.40–2.64	
Technician	2.69	0.053	2.59–2.80	
Labor worker	2.52	0.054	2.41–2.62	
Unemployed	2.44	0.027	2.39–2.50	
Income level				0.384
Lowest quartile (1Q)	2.55	0.032	2.49–2.61	
Lower middle (2Q)	2.52	0.032	2.46–2.58	
Upper middle (3Q)	2.47	0.032	2.41–2.54	
Highest quartile (4Q)	2.49	0.034	2.43–2.56	
Education level				<0.001
Below middle school	2.66	0.042	2.57–2.74	
Middle school	2.64	0.049	2.54–2.74	
High school	2.49	0.027	2.43–2.54	
Above high school	2.33	0.034	2.26–2.40	
COPD				0.386
Yes	2.56	0.060	2.44–2.68	
No	2.50	0.018	2.47–2.54	

COPD, chronic obstructive pulmonary disease.
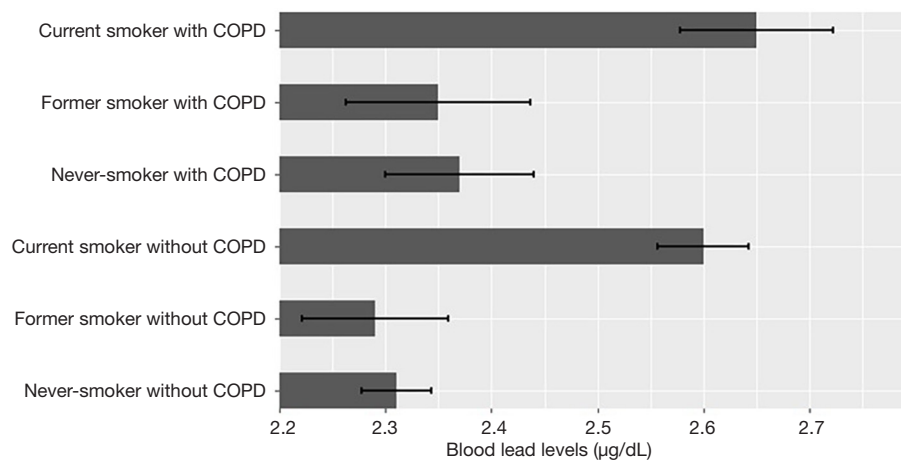
Figure 1 Multivariable linear regression analysis of estimated blood lead levels according to COPD and smoking status, adjusted with sex, age, smoking, occupation, income level, education, and COPD (data shown as mean ± standard error). Current smoker with COPD = 2.65±0.072 µg/dL (95% CI: 2.51–2.80, P value =0.009); Former smoker with COPD =2.35±0.087 µg/dL (95% CI: 2.18–2.52, P value =0.441); never-smoker with COPD =2.37±0.070 µg/dL (95% CI: 2.23–2.51, P value =0.386); current smoker without COPD =2.60±0.043 µg/dL (95% CI: 2.51–2.68, P value <0.001); former smoker without COPD =2.29±0.069 µg/dL (95% CI: 2.16–2.43, P value =0.758); never-smoker without COPD =2.31±0.033 µg/dL (95% CI: 2.25–2.39, reference group). COPD, chronic obstructive pulmonary disease.

Discussion

Our multivariable regression analyses demonstrated that older age, male sex, smoking, occupation, and lower education levels were independently associated with higher blood lead levels; however, COPD was not related after adjustment of all possible confounding variables. These findings suggest that the higher blood lead levels in COPD should be attributable to the smoking status and socioeconomic factors, such as lower education level and occupation, rather than COPD per se. A careful history inquiring about a broad spectrum of potential lead sources is required and many confounding variables should be considered in analyzing the high blood level of COPD, because COPD has many phenotypes and heterogeneous origins (14). Although smoking is the dominant etiologic source, COPD is often associated with lower socioeconomic status (18). Nevertheless, further studies are necessary concerning the effect of higher blood lead levels on the clinical course of COPD, considering our subgroup analyses showing that some COPD subgroups had higher blood lead levels regardless of smoking behavior.

The average blood lead level of each subgroup in our study was lower than 5 µg/dL. However, blood lead levels lower than 10 µg/dL can have detrimental health consequences including renal injury, cardiovascular mortality, cognitive dysfunction, and adverse reproductive outcomes

in women in a dose-dependent manner (4-7). Inorganic lead adversely affects multiple physiologic functions and organ systems throughout various biochemical events (4).

This study revealed that lower education levels and certain occupations were independently associated with higher blood lead levels. These findings highlight the association between socioeconomic factors and blood lead levels reported by other environmental studies (1,19). Most lead exposure is occupational because individuals in lower educational levels usually work in environments with more lead exposure (1,10,19). Our data showed higher blood lead levels in farmers, fishermen, and technicians than among those in managerial jobs and unemployed groups. Hence, occupational sources of lead exposure should be further investigated for reducing environmental lead pollution and improving public health.

The current study revealed that older age and smoking were independently associated with higher lead levels. Our study could not explain the causal linkage which requires further studies, but previous evidence indicated that clinical variables, such as lead absorption through the gastrointestinal tract and nutritional deficiencies including iron deficiency and calcium deficiency rendered older subjects more susceptible to lead poisoning (20,21). Recent evidence also suggested that despite declining smoking rates and secondhand smoke exposure, tobacco smoke continues
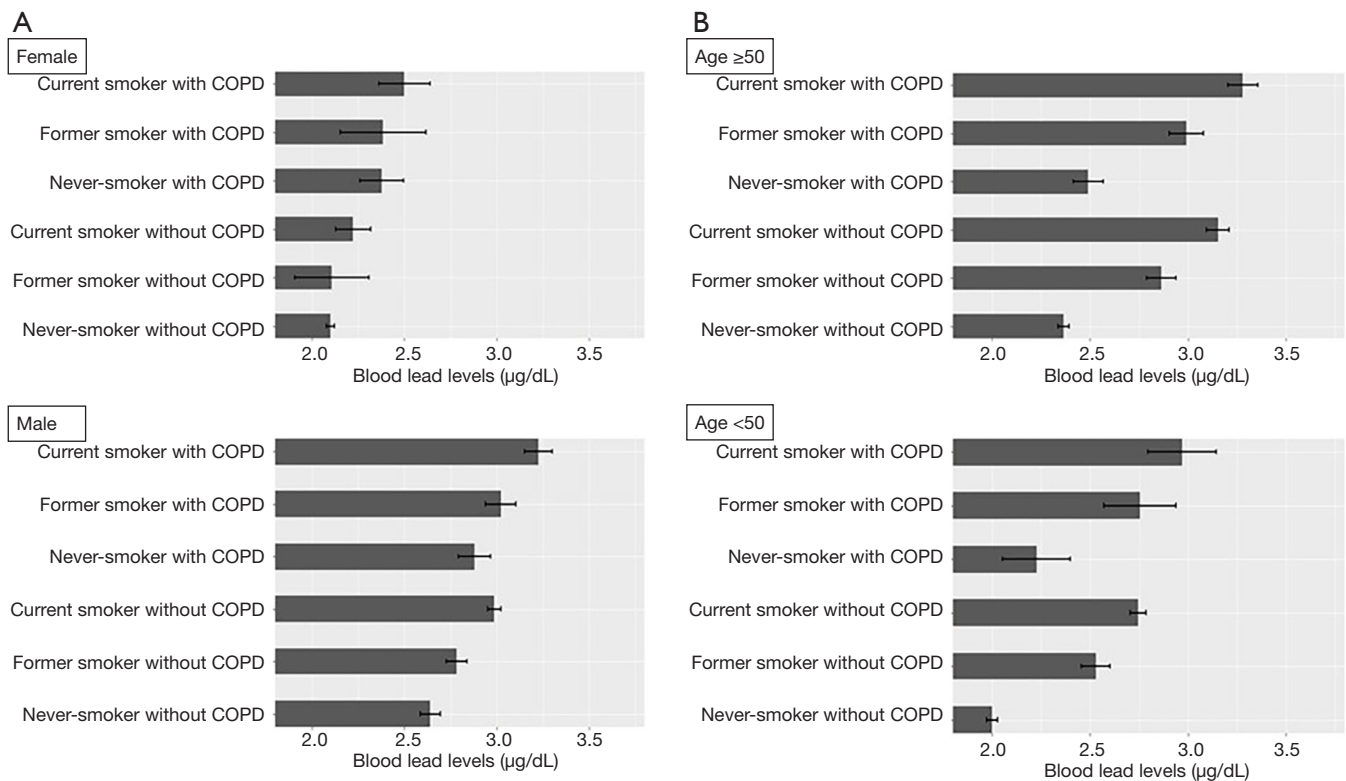

Figure 2 Multivariable linear regression analyses of estimated blood lead levels according to COPD and smoking status, by stratification with sex and age, adjusted for COPD and smoking (data shown as mean ± standard error). Male: current smoker with COPD =3.23±0.075 µg/dL (95% CI: 3.078–3.373, P value =0.293); former smoker with COPD =3.02±0.082 µg/dL (95% CI: 2.860–3.183, P value =0.401); never-smoker with COPD =2.88±0.088 µg/dL (95% CI: 2.706–3.052, P value =0.001); current smoker without COPD =2.99±0.035 µg/dL (95% CI: 2.917–3.055, P value <0.001); former smoker without COPD =2.78±0.057 µg/dL (95% CI: 2.670–2.894, P value =0.073); never-smoker without COPD =2.64±0.055 µg/dL (95% CI: 2.532–2.747, reference group). Female: Current smoker with COPD =2.50±0.140 µg/dL (95% CI: 2.226–2.773, P value =0.346); former smoker with COPD =2.38±0.233 µg/dL (95% CI: 1.927–2.840, P value =0.2554); never-smoker with COPD =2.38±0.119 µg/dL (95% CI: 2.143–2.610, P value =0.0206); current smoker without COPD =2.22±0.094 µg/dL (95% CI: 2.038–2.407, P value =0.202); former smoker without COPD =2.11±0.202 µg/dL (95% CI: 1.7101–2.5033, P value =0.971); never-smoker without COPD =2.10±0.0208 µg/dL (95% CI: 2.059–2.140, reference group). Age ≥50: current smoker with COPD =3.28±0.076 µg/dL (95% CI: 3.131–3.429, P value <0.001); former smoker with COPD =2.99±0.088 µg/dL (95% CI: 2.820–3.163, P value =0.002); never-smoker with COPD =2.49±0.076 µg/dL (95% CI: 2.342–2.639, P value =0.091); current smoker without COPD =3.15±0.057 µg/dL (95% CI: 3.041–3.263, P value <0.001); former smoker without COPD =2.86±0.075 µg/dL (95% CI: 2.718–3.010, P value <0.001); never-smoker without COPD =2.36±0.028 µg/dL (95% CI: 2.308–2.419, reference group). Age <50: current smoker with COPD =2.97±0.175 µg/dL (95% CI: 2.626–3.315, P value =0.004); former smoker with COPD =2.75±0.184 µg/dL (95% CI: 2.394–3.115, P value =0.111); never-smoker with COPD =2.23±0.172 µg/dL (95% CI: 1.889–2.563, P value =0.192); current smoker without COPD =2.75±0.042 µg/dL (95% CI: 2.664–2.827, P value <0.001); former smoker without COPD =2.53±0.073 µg/dL (95% CI: 2.386–2.672, P value <0.001); never-smoker without COPD =2.00±0.028 µg/dL (95% CI: 1.946–2.056, reference group). COPD, chronic obstructive pulmonary disease.

to be a substantial source of lead exposure in vulnerable and general populations (9,10). Therefore, smoking status should be considered in identifying sources of lead exposure and developing preventative strategies for the management of lead poisoning.

Our study did not prove the relationship between blood lead levels and some comorbidities including diabetes, hypertension, cerebral stroke, etc. except COPD. COPD was associated with higher blood lead levels in the univariate analysis, not in the multivariable analysis adjusted for all
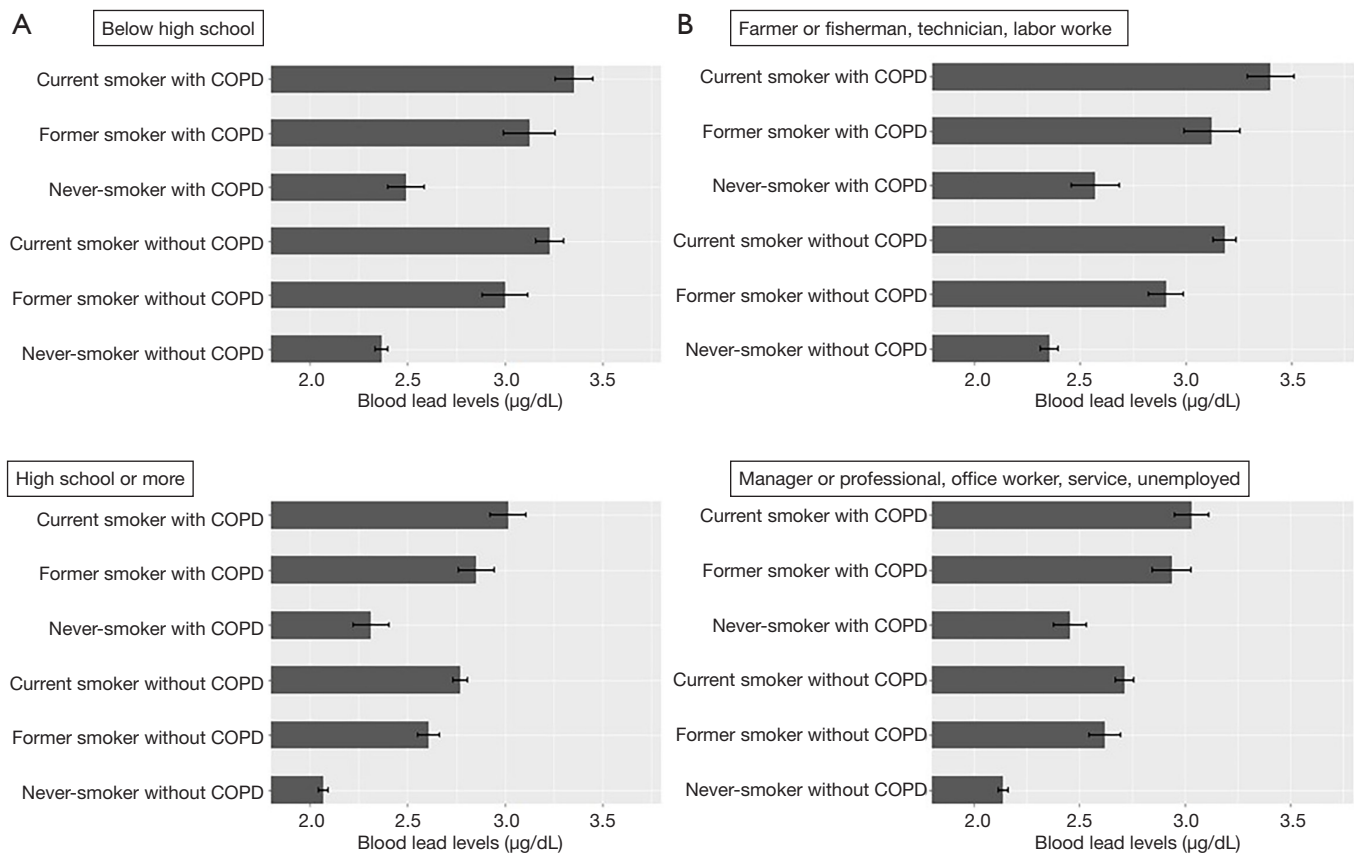
Figure 3 Multivariable linear regression analyses of estimated blood lead levels according to COPD and smoking status, by stratification with education level, and occupation, adjusted for COPD and smoking (data shown as mean ± standard error). Education: below high school: current smoker with COPD =3.35±0.097 μg/dL (95% CI: 3.163–3.544, P value <0.001); former smoker with COPD =3.12±0.133 μg/dL (95% CI: 2.863–3.385, P value =0.002); never-smoker with COPD =2.49±0.094 μg/dL (95% CI: 2.308–2.675, P value =0.198); current smoker without COPD =3.23±0.073 μg/dL (95% CI: 3.085–3.372, P value <0.001); former smoker without COPD =3.00±0.117 μg/dL (95% CI: 2.770–3.229, P value <0.001); never-smoker without COPD =2.37±0.033 μg/dL (95% CI: 2.302–2.432, reference group). Education: high school or more: current smoker with COPD =3.02±0.092 μg/dL (95% CI: 2.835–3.196, P value <0.001); former smoker with COPD =2.85±0.093 μg/dL (95% CI: 2.670–3.033, P value =0.013); never-smoker with COPD =2.31±0.092 μg/dL (95% CI: 2.132–2.492, P value =0.0069); current smoker without COPD =2.77±0.037 μg/dL (95% CI: 2.698–2.845, P value <0.001); former smoker without COPD =2.61±0.056 μg/dL (95% CI: 2.499–2.717, P value <0.001); never-smoker without COPD =2.07±0.025 μg/dL (95% CI: 2.020–2.117, reference group). Occupation: farmers or fishermen, technicians, labor workers: current smoker with COPD =3.40±0.112 μg/dL (95% CI: 3.183–3.620, P value < 0.001); former smoker with COPD =3.12±0.132 μg/dL (95% CI: 2.8654–3.3819, P value =0.0233); never-smoker with COPD =2.57±0.114 μg/dL (95% CI: 2.348–2.795, P value =0.050); current smoker without COPD =3.18±0.054 μg/dL (95% CI: 3.077–3.290, P value <0.001); former smoker without COPD =2.91±0.083 μg/dL (95% CI: 2.742–3.070, P value <0.001); never-smoker without COPD =2.35±0.042 μg/dL (95% CI: 2.273–2.435, reference group). Occupation: manager or professional, office workers, service, unemployed: current smoker with COPD =3.03±0.080 μg/dL (95% CI: 2.874–3.190, P value =0.009); former smoker with COPD =2.94±0.092 μg/dL (95% CI: 2.756–3.119, P value =0.175); never-smoker with COPD =2.46±0.079 μg/dL (95% CI: 2.300–2.610, P value <0.001); current smoker without COPD =2.71±0.043 μg/dL (95% CI: 2.631–2.798, P value <0.001); former smoker without COPD =2.62±0.074 μg/dL (95% CI: 2.475–2.766, P value <0.001); never-smoker without COPD =2.14±0.023 μg/dL (95% CI: 2.093–2.183, reference group). COPD, chronic obstructive pulmonary disease.

confounding factors. However, when stratified and adjusted only with smoking in the subgroup analysis, COPD was statistically associated with higher blood lead levels among males, females, higher education subgroup, and office workers.

A previous study performed in Copenhagen County, Denmark, suggested a significant univariate association of blood lead levels with total mortality, coronary heart disease, and cardiovascular disease (22). Current evidence suggests that increased bone lead levels are associated with hypertension (23,24). Some studies have attempted to further examine the linkage between blood lead levels and environmental factors, such as stress and diet, though further validations are required (25,26). One study reported that the effect of lead on hypertension is most pronounced among highly stressed individuals (25). Western dietary patterns are also reported to be associated with increased lead concentrations (26,27).

Some genes including delta-aminolevulinic acid dehydratase gene, vitamin D receptor gene, and hemochromatosis gene can make certain individuals more vulnerable to environmental lead exposure, influencing the lead absorption and thereby affecting the blood and bone lead levels in human populations (28,29). Genetic polymorphisms are also reported to have a relationship with the impact of lead exposure on neurodegenerative diseases such as Alzheimer's disease and neurodevelopmental disorder (30,31).

This study had some limitations. First, the etiologic causes of lead exposure were not analyzed in our study, as it was not a longitudinal cohort study. Second, environmental factors, including water supply source, residence, alcohol consumption, and diet, were not accounted for in this study. Third, significant outcomes such as the mortality and cancer risk based on blood lead levels in each comorbidity were not investigated. Fourth, comorbidities, including osteoporosis, asthma, and diabetes were diagnosed using survey questionnaire and physician diagnosis rather than by actual measurements. Fifth, air pollution was not investigated as a variable in our analysis. Sixth, post-bronchodilator values were not obtained due to the lack of information in KNHANES data, and the definition of COPD by less than 70% of FEV_1/FVC can harbor the potential risk of overdiagnosis in older patients.

In conclusion, our findings demonstrated that smoking, occupation, and lower education levels along with old age and male sex were independently associated with higher blood lead levels, whereas COPD was not related after adjustment of all possible confounding variables.

Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jtd-20-739). The authors have no conflicts of interest to declare.

Ethics Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The current study was approved by the institutional review board of Ajou Medical Center (approval number: AJIRB-MED-EXP-9-161). The requirement for informed consent is waived by the ethics review board due to the retrospective nature of the study.

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